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Iron-Catalyzed Direct Synthesis of Imines from Amines or Alcohols and Amines via Aerobic Oxidative Reactions under Air

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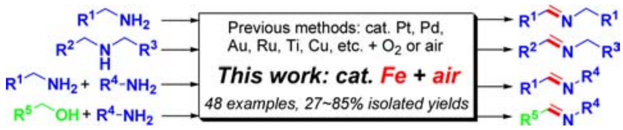
ABSTRACT



Abundant and cheap iron readily catalyzed the aerobic oxidative reactions of primary amines, secondary amines, benzylamines with anilines, and alcohols with amines by directly using air as the economic and safe oxidant, providing several direct, practical, and greener approaches for the preparation of useful imines.

Since they bear the reactive C=N bond and are capable of undergoing various types of transformations, imines are versatile nitrogen sources and reactive intermediates in the synthesis of a wide range of biologically and pharmaceutically active compounds, heterocycles, and natural products.[1] Since the traditional condensation method[2] suffers from the drawbacks of using the odorous and unstable aldehydes that also require in situ purification prior to use, developing efficient and greener methods is still an important task in current imine chemistry.[3−11] Although the methods for imine preparation have now been greatly improved,[3−11] especially by employing the one-pot tandem reactions of amines with the greener, cheaper, and more available alcohols[4,6,8,10] and direct oxidation of the amines,[5,7,9,11] drawbacks still remain and many issues have yet to be satisfactorily addressed. For example, early methods require large excess amounts of oxidants, which will also produce large amounts of undesired waste.[4,5] The dehydrogenation methods are highly atom economic, but they suffer from the use of active, sensitive, expensive, and capricious ligands; not easily accessed noble metal complexes; and harsh reaction conditions such as high reaction temperatures and inert atmosphere protection.[6,7] In contrast, the aerobic oxidative reactions are comparatively greener, more preferable, and more practical methods because of the use of pure oxygen or air as the pollution-free oxidant, much more easily disposable catalysts, and milder reaction conditions, along with generating water as the byproduct.[8−11] However, with only a few exceptions,[8,9] most reactions still require high reaction temperatures, expensive and rare noble metal catalysts, special conditions,

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(1) (a) Patai, S. *The Chemistry of the Carbon−Nitrogen Double Bond (Chemistry of Functional Goups)*; Wiley−Interscience: New York, 1970. (b) Ma, J.-A. *Chem. Soc. Rev.* **2006**, *35*, 630. (c) Dömling, A. *Chem. Rev.* **2006**, *106*, 17. (d) Erkkilä, A.; Majander, I.; Pihko, P. M. *Chem. Rev.* **2007**, *107*, 5416. (e) Gawronski, J.; Wascinska, N.; Gajewy, J. *Chem. Rev.* **2008**, *108*, 5227. (f) Ordóñez, M.; Rojas-Cabrera, H.; Cativiela, C. *Tetrahedron* **2009**, *65*, 17. (g) Martin, S. F. *Pure Appl. Chem.* **2009**, *81*, 195. (h) Kobayashi, S.; Mori, Y.; Fossey, J. S.; Salter, M. M. *Chem. Rev.* **2011**, *111*, 2626. (i) Xie, J.-H.; Zhu, S.-F.; Zhou, Q.-L. *Chem. Rev.* **2011**, *111*, 1713. (j) Adrio, J.; Carretero, J. C. *Chem. Commun.* **2011**, *47*, 6784. (k) Marques, C. S.; Burke, A. J. *ChemCatChem* **2011**, *3*, 635. (l) Ramadhar, T. R.; Batey, R. A. *Synthesis* **2011**, 1321. (m) Nielsen, M.; Worgull, D.; Zweifel, T.; Gschwend, B.; Bertelsen, S.; Jøgensen, K. A. *Chem. Commun.* **2011**, *47*, 632.

(2) (a) Schiff, H. *Justus Liebigs Ann. Chem.* **1864**, *131*, 118. (b) Sprung, M. M. *Chem. Rev.* **1940**, *26*, 297. (c) Layer, R. W. *Chem. Rev.* **1963**, *63*, 489.

(3) For aza-Wittig methods: (a) Palacios, F.; Alonso, C.; Aparicio, D.; Rubiales, G.; de los Santos, J. M. *Tetrahedron* **2007**, *63*, 523. (b) Fresneda, P. M.; Molina, P. *Synlett* **2004**, 1.

(4) (a) Blackburn, L.; Taylor, R. J. K. *Org. Lett.* **2001**, *3*, 1637. (b) Medvedeva, A. S.; Mareev, A. V.; Borisova, A. I.; Afonin, A. V. *ARKIVOC* **2003**, *13*, 157. (c) Yusubov, M. S.; Chi, K.-W.; Park, J. Y.; Karimovc, R.; Zhdankinc, V. V. *Tetrahedron Lett.* **2006**, *47*, 6305.

(5) (a) Murahashi, S.-I.; Naota, T.; Taki, H. *Chem. Commun.* **1985**, 613. (b) Müller, F.; Gilabert, D. M. *Tetrahedron* **1988**, *44*, 7171. (c) Éll, A. H.; Samec, J. S.; Brasse, C.; Bäckvall, J.-E. *Chem. Commun.* **2002**, 1144. (d) Nicolaou, K. C.; Mathison, C. J. N.; Montagnon, T. *Angew. Chem., Int. Ed.* **2003**, *42*, 4077. (e) Nicolaou, K. C.; Mathison, C. J. N.; Montagnon, T. *J. Am. Chem. Soc.* **2004**, *126*, 5192. (f) Choi, H.; Doyle, M. P. *Chem. Commun.* **2007**, 745.

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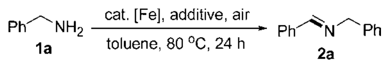
or dangerous pure oxygen as the oxidant.[10,11] To our knowledge, the cheaper, more available, and nontoxic metals such as iron have not been successfully used in the methods yet.[12] Herein we report that a general $Fe(NO_3)_3$/TEMPO system can readily catalyze the aerobic oxidative reactions of 1° and 2° amines, different amines, and alcohols with amines by using air as the oxidant, providing several greener and more practical approaches for the preparation of useful imines.

In previous stuides on aerobic oxidative reactions of alcohols with amides and amines,[8,9d,10c,13] we noticed that the versatile metal Fe[14] is also a good catalyst for the aerobic oxidation of alcohols.[15] Since an Fe-catalyzed method was not known yet, we envisoned that, if Fe is also a good catalyst for imine synthesis through aerobic oxidative reactions of alcohols and amines or directly the amines, it may become a potentially more advantageous and more practical catalyst than other metals due to its abundance in the Earth's crust, high availability, low price, and also possibly its nontoxic and biofriendly properties.

Thus, the Fe-catalyzed oxidation of primary amine **1a** was first investigated under air (Table 1). Preliminary screening on Fe catalysts and reaction temperatures showed that various Fe catalysts [$FeCl_3$, $FeBr_3$, Fe_2O_3, $Fe_2(SO_4)_3$, $Fe(NO_3)_3$] (5 mol %) could catalyze the reaction alone without any ligands, bases, or additives.[16] $Fe(NO_3)_3$ was in comparison the best catalyst and 80 °C an appropriate temperature for the reaction, giving an accepatble yield of target imine **2a** (run 1).[17] Additives were then employed to improve the reaction efficiency.[16] We were pleased to find that the addition of TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxyl, 3 mol %) could greatly enhance the product yield to 85% (run 2) as in other catalytic systems.[8-11] In contrast, the reaction with 3 mol % of TEMPO alone was rather ineffective under the same conditions (run 3), indicating the key role of Fe in catalyzing the reaction.[17] Further condition screening by investigating the effects of catalyst loadings, Fe catalyst and TEMPO combinations, solvents, and temperatures[16] revealed that xylene and dioxane are also suitable solvents, and using both 5 mol % of $Fe(NO_3)_3$ and TEMPO in toluene at 80 °C was optimal for the reaction, giving almost full conversion of **1a** and a good isolated yield of **2a** (run 4).

Table 1. Condition Optimization for Fe-Catalyzed Aerobic Oxidation of Benzylamine to Imine under Air[a,16]



run	[Fe] (mol %)[b]	additive (mol %)	**2a** %[c]
1	$Fe(NO_3)_3$ (5)	–	66
2	$Fe(NO_3)_3$ (5)	TEMPO (3)	85
3	–	TEMPO (3)	8
4	$Fe(NO_3)_3$ (5)	TEMPO (5)	97 (82)

[a] The mixture of **1a** (2 mmol), Fe catalyst, and additives in toluene (0.5 mL) was heated under air in a 100 mL tube at 80 °C for 24 h and then monitored by TLC and/or GC-MS. [b] $Fe(NO_3)_3\cdot 9H_2O$ was used and abbreviated. [c] GC yields (isolated yields in parentheses) based on **1a**.

The optimized conditions (Table 1, run 4) were then applied to various primary and secondary amines by using the $Fe(NO_3)_3$/TEMPO catalyst system (Table 2). The results showed that the method tolerates various functional groups. It should be mentioned that nitriles and amides, which might be generated as the byproducts in other catalytic systems,[5,7,9,11] were not detected at all in the present reactions, revealing the high imine selectivity and another advantage of using $Fe(NO_3)_3$/TEMPO as the catalyst. Thus, both electron-rich (runs 1–6) and -deficient (runs 7–13) benzylamines, including the sterically more

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(6) (a) Gnanaprakasam, B.; Zhang, J.; Milstein, D. *Angew. Chem., Int. Ed.* **2010**, *49*, 1468. (b) Esteruelas, M. A.; Honczek, N.; Oliván, M.; Onate, E.; Valencia, M. *Organometallics* **2011**, *30*, 2468. (c) Cano, R.; Ramón, D. J.; Yus, M. *J. Org. Chem.* **2011**, *76*, 5547. (d) Maggi, A.; Madsen, R. *Organometallics* **2012**, *31*, 451. (e) Zhang, G.; Hanson, S. K. *Org. Lett.* **2013**, *15*, 650.

(7) (a) Muthaiah, S.; Hong, S. K. *Adv. Synth. Catal.* **2012**, *354*, 3045. (b) Prades, A.; Peris, E.; Albrecht, M. *Organometallics* **2011**, *30*, 1162. (c) Yi, C. S.; Lee, D. W. *Organometallics* **2009**, *28*, 947.

(8) Tian, H.; Yu, X.; Li, Q.; Wang, J.; Xu, Q. *Adv. Synth. Catal.* **2012**, *354*, 2671.

(9) (a) For a recent perspective on amine oxidation: Largeron, M.; Fleury, M. B. *Science* **2013**, *339*, 43. (b) Hu, Z.; Kerton, F. M. *Org. Biomol. Chem.* **2012**, *10*, 1618. (c) Largeron, M.; Fleury, M. B. *Angew. Chem., Int. Ed.* **2012**, *51*, 5409. (d) Huang, B.; Tian, H.; Lin, S.; Xie, M.; Yu, X.; Xu, Q. *Tetrahedron Lett.* **2013**, *54*, 2861.

(10) (a) Kwon, M. S.; Kim, S.; Park, S.; Bosco, W.; Chidrala, R. K.; Park, J. *J. Org. Chem.* **2009**, *74*, 2877. (b) Sun, H.; Su, F.-Z.; Ni, J.; Cao, Y.; He, H.-Y.; Fan, K.-N. *Angew. Chem., Int. Ed.* **2009**, *48*, 4390. (c) Jiang, L.; Jin, L.; Tian, H.; Yuan, X.; Yu, X.; Xu, Q. *Chem. Commun.* **2011**, *47*, 10833. (d) Kang, Q.; Zhang, Y. *Green Chem.* **2012**, *14*, 1016. (e) Xu, J.; Zuang, R.; Bao, L.; Tang, G.; Zhao, Y. *Green Chem.* **2012**, *14*, 2384. (f) Donthiri, R. D.; Patil, R. D.; Adimurthy, S. *Eur. J. Org. Chem.* **2012**, 4457. (g) Soulé, J.-F.; Miyamura, H.; Kobayashi, S. *Chem. Commun.* **2013**, *49*, 355.

(11) (a) Yuan, H.; Yoo, W.-J.; Miyamura, H.; Kobayashi, S. *J. Am. Chem. Soc.* **2012**, *134*, 13790. (b) Sonobe, T.; Oisaki, K.; Kanai, M. *Chem. Sci.* **2012**, *3*, 3249. (c) Wendlandt, A. E.; Stahl, S. S. *Org. Lett.* **2012**, *14*, 2850. (d) Liu, L.; Wang, Z.; Fu, X.; Yan, C. *Org. Lett.* **2012**, *14*, 5692. (e) Lang, X.; Ji, H.; Chen, C.; Ma, W.; Zhao, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 3934. (f) Patil, R. D.; Adimurthy, S. *Adv. Synth. Catal.* **2011**, *353*, 1695. (g) Aschwanden, L.; Mallat, T.; Maciejewski, M.; Krumeich, F.; Baiker, A. *ChemCatChem* **2010**, *2*, 666. (h) Dhakshinamoorthy, A.; Alvaro, M.; Garcia, H. *ChemCatChem* **2010**, *2*, 1438. (i) Liang, G.; Chen, J.; Huang, J.-S.; Che, C.-M. *Org. Lett.* **2009**, *11*, 4568. (j) Murahashi, S.-I.; Okano, Y.; Sato, H.; Nakae, T.; Komiya, N. *Synlett* **2007**, 1675. (k) Samec, J. S.; Éll, A. H.; Bäckvall, J.-E. *Chem.—Eur. J.* **2005**, *11*, 2327.

(12) Recently Zhang and Hanson reported a cobalt-complex-catalyzed anaerobic alcohol dehydrogenation method and applied it in the synthesis of imines (ref 6e), which may still suffer from cobalt's toxicity and the catalyst's sensitivity, availability, and price.

(13) (a) Liu, C.; Liao, S.; Li, Q.; Feng, S.; Sun, Q.; Yu, X.; Xu, Q. *J. Org. Chem.* **2011**, *76*, 5759. (b) Yu, X.; Liu, C.; Jiang, L.; Xu, Q. *Org. Lett.* **2011**, *13*, 6184. (c) Li, Q.; Fan, S.; Sun, Q.; Tian, H.; Yu, X.; Xu, Q. *Org. Biomol. Chem.* **2012**, *10*, 2966.

(14) (a) Bolm, C.; Legros, J.; Paih, J. L.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217. (b) Sherry, B. D.; Fürstner, A. *Acc. Chem. Res.* **2008**, *41*, 1500. (c) Enthaler, S.; Junge, K.; Beller, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 3317. (d) Correa, A.; Mancheno, O. G.; Bolm, C. *Chem. Rev.* **2008**, *37*, 1108. (e) Czaplik, W. M.; Mayer, M.; Cvengroš, J.; von Wangelin, A. J. *ChemSusChem* **2009**, *2*, 396. (f) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2011**, *111*, 1293.

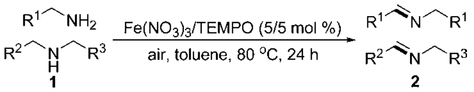
(15) (a) Ma, S.; Liu, J.; Li, S.; Chen, B.; Cheng, J.; Kuang, J.; Liu, Y.; Wan, B.; Wang, Y.; Ye, J.; Yu, Q.; Yuan, W.; Yu, S. *Adv. Synth. Catal.* **2011**, *353*, 1005. (b) Xue, G.; Pokutsa, A.; Que, L., Jr. *J. Am. Chem. Soc.* **2011**, *133*, 16657. (c) Miao, C.-X.; Wang, J.-Q.; Yu, B.; Cheng, W.-G.; Sun, J.; Chanfreau, S.; He, L.-N.; Zhang, S.-J. *Chem. Commun.* **2011**, *47*, 2697. (d) Al-Hunaiti, A.; Niemi, T.; Sibaouih, A.; Pihko, P.; Leskelä, M.; Repo, T. *Chem. Commun.* **2010**, *46*, 9250. (e) Yin, W.; Chu, C.; Lu, Q.; Tao, J.; Liang, X.; Liu, R. *Adv. Synth. Catal.* **2010**, *352*, 113.

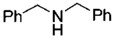
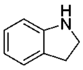
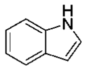
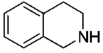
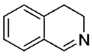
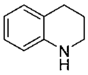
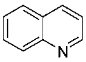
(16) See Supporting Information for details.

(17) $Fe(NO_3)_3$ alone could give >99% GC yield of **2a** under O_2.

hindered *ortho*-substituted ones (runs 3, 6, 9, 11, 13), reacted efficiently to give the target imines in good yields. The halo-substituted imines **2h**−**n** are potentially useful in the synthesis, as they bear fluoro and chloro groups and the reactive C=N bond. In contrast to benzylamines, the reaction of a heterobenzylamine **1o** was not efficient (run 14), and the product could not be isolated in pure form due to easy hydrolysis during purification, even with the use preneutralized silica gel.[18] Similarly, aliphatic amines are also not suitable substrates, and only trace products were detected (runs 15−16).[18]

Table 2. Fe-Catalyzed Aerobic Oxidation of Primary and Secondary Amines to Imines under Air[a]



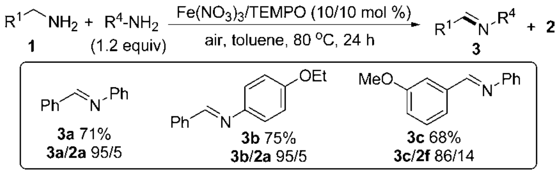
run	1	2: yield %[b]
1	*p*-$MeC_6H_4CH_2NH_2$ (**1b**)	**2b**: 91 (77)
2	*m*-$MeC_6H_4CH_2NH_2$ (**1c**)	**2c**: 94 (76)
3	*o*-$MeC_6H_4CH_2NH_2$ (**1d**)	**2d**: 77 (62)
4	*p*-$MeOC_6H_4CH_2NH_2$ (**1e**)	**2e**: 93 (78)
5	*m*-$MeOC_6H_4CH_2NH_2$ (**1f**)	**2f**: 78 (62)
6	*o*-$MeOC_6H_4CH_2NH_2$ (**1g**)	**2g**: 80 (65)
7	*p*-$FC_6H_4CH_2NH_2$ (**1h**)	**2h**: 95 (80)
8	*m*-$FC_6H_4CH_2NH_2$ (**1i**)	**2i**: 95 (83)
9	*o*-$FC_6H_4CH_2NH_2$ (**1j**)	**2j**: 93 (79)
10	*p*-$ClC_6H_4CH_2NH_2$ (**1k**)	**2k**: 94 (74)
11	*m*-$ClC_6H_4CH_2NH_2$ (**1l**)	**2l**: 96 (81)
12	*o*-$ClC_6H_4CH_2NH_2$ (**1m**)	**2m**: 84 (67)
13	2,4-$Cl_2C_6H_3CH_2NH_2$ (**1n**)	**2n**: 90 (71)
14	2-furanmethyamine (**1o**)	**2o**: 45
15	$PhCH_2CH_2NH_2$	trace
16	*n*-$C_8H_{17}NH_2$	trace
17[c]	 (**1p**)	**2a**: 44 (33)
18	 (**1q**)	**2q**:  77 (64)
19	 (**1r**)	**2r**:  63 (47)
20	 (**1s**)	**2s**:  45 (27)

[a] The mixture of **1** (2 mmol), $Fe(NO_3)_3 \cdot 9H_2O$ (5 mol %), TEMPO (5 mol %) in toluene (0.5 mL) was heated under air in a 100 mL tube at 80 °C for 24 h and then monitored by TLC and/or GC-MS. [b] GC yields (isolated yields in parentheses) based on **1**. [c] $Fe(NO_3)_3 \cdot 9H_2O$ (10 mol %), TEMPO (10 mol %), 120 °C, 24 h.

The Fe-catalyzed aerobic oxidation method was then applied to secondary amines. It seemed the present method was not suitable for simple secondary amines such as dibenzyl amine (**1p**), for only a low yield of the product was obtained under harsher reaction conditions (run 17). Contrarily, cyclic secondary amines such as indoline (**1q**) and 1,2,3,4-tetrahydroisoquinoline (**1r**) could be readily oxidized to indole (**2q**) and 3,4-dihydroisoquinoline (**2r**) in moderate yields, respectively (runs 18, 19). In contrast, the oxidation of 1,2,3,4-tetrahydroquinoline (**1s**) was more difficult, giving aromatized quinoline (**2s**) in only a low yield (run 20).

The similar method could also be applied to the reactions of benzylamines and anilines to synthesize the cross imines. Condition screening showed that 5 mol % of either Fe or TEMPO, or both 5 mol % of Fe and TEMPO, and a 1/1 molar ratio of **1a** and aniline only resulted in incomplete conversion of the substrates and formation of the undesired byproduct **2a** in large amounts.[16] Then, by using both 10 mol % of Fe and TEMPO and slight excess amounts of aniline (1.2 equiv), the full conversion of **1a**, with high selectivity (95%) and a good isolated yield (71%), to the target imine **3a** was achieved (Scheme 1). This method can be extended to different benzylamines and anilines. Thus, under the same conditions, cross imines **3b**−**c** were also obtained in high selectivities and good yields from the reactions of corresponding benzylamines and anilines (Scheme 1).

Scheme 1. Fe-Catalyzed Aerobic Oxidation of Benzylamines and Anilines to Cross Imines under Air[16]



Since alcohols are generally known as much greener chemicals due to their wide scope, high availability, low price, and low toxicity,[19] we then turned to investigate the Fe-catalyzed aerobic reactions of alcohols and amines under air, which, if achieved, should be a comparatively more advantageous method than the above cross reactions of different amines. Therefore, the same catalyst was first applied to the reaction of **1a** and benzyl alcohol (**4a**) to optimize the condition (Table 3). However, only a low yield of the target imines **2a** was detected along with large amounts of unreacted **4a** and the formation of benzaldehyde as the byproduct (run 1). Like most of the known imination reactions of alcohols and amines,[6,10] it was then found that the base played a crucial role in the reaction. As shown in Table 3, the reaction was initially tested at room temperature with a catalytic amount of KOH added, but only a low yield of **2a** was detected (run 2). This result was then gradually improved by heating the reaction at higher temperatures or adding more KOH (runs 3−5). Thus, nearly full conversion of **1a** (97%) and a good isolated

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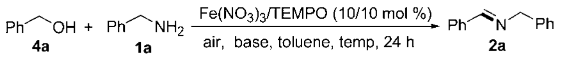
(18) Despite that we tried many attempts, these imines could not be isolated in pure form due to easy hydrolysis during purification. See: (a) Li, C.; Thomson, R. K.; Gillon, B.; Patrick, B. O.; Schafer, L. L. *Chem. Commun.* **2003**, 2462. (b) Lee, A. V.; Schafer, L. L. *Organometallics* **2006**, *25*, 5249. (c) Burland, P. A.; Coisson, D.; Osborn, H. M. I. *J. Org. Chem.* **2010**, *75*, 7210. (d) Monnereau, L.; Sémeril, D.; Matt, D. *Green Chem.* **2010**, *12*, 1670. (e) References 9 and 11.

(19) (a) Watson, A. J. A.; Williams, J. M. J. *Science* **2010**, *329*, 635. (b) Dobereiner, G. E.; Crabtree, R. H. *Chem. Rev.* **2010**, *110*, 681. (c) Guillena, G.; Ramón, D. J.; Yus, M. *Chem. Rev.* **2010**, *110*, 1611. (d) Emer, E.; Sinisi, R.; Capdevila, M. G.; Petruzziello, D.; De Vincentiis, F.; Cozzi, P. G. *Eur. J. Org. Chem.* **2011**, 647. (e) Zhang, S.-Y.; Zhang, F.-M.; Tu, Y.-Q. *Chem. Soc. Rev.* **2011**, *40*, 1937. (f) Xu, Q.; Li, Q. *Chin. J. Org. Chem.* **2013**, *33*, 18.

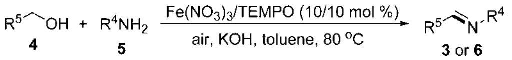
Table 3. Condition Optimization for Fe-Catalyzed Aerobic Oxidation of Benzyl Alcohol and Benzylamine under Air[a]



run	base (mol %)	temp	**2a** %[b]
1[c]	–	80 °C	45
2	KOH (10)	rt[d]	29
3	KOH (10)	50 °C	53
4	KOH (10)	80 °C	70
5	KOH (20)	80 °C	97 (78)

[a] The mixture of **1a** (1 mmol), **4a** (1.2 mmol), $Fe(NO_3)_3 \cdot 9H_2O$ (10 mol %), TEMPO (10 mol %), and the base in toluene (0.5 mL) was heated under air in a 100 mL tube for 24 h and then monitored by TLC and/or GC-MS. [b] GC yields (isolated yields in parentheses) based on **1a**. [c] ∼10% PhCHO (based on **4a**) was detected as the byproduct. A large amount of **4a** remained unreacted. [d] Ca. ∼30 °C.

Table 4. Fe-Catalyzed Aerobic Oxidative Reactions of Alcohols and Amines to Imines under Air[a]



run	**4**, **5**	**3** or **6**: yield %[b]
1[c]	**4a**, $PhCH_2CH_2NH_2$ (**5a**)	**6aa**: 84 (61)
2[c,d]	**4a**, *n*-$C_4H_9NH_2$ (**5b**)	**6ab**: (32)
3[c,d]	**4a**, *c*-$C_6H_{12}NH_2$ (**5c**)	**6ac**: (41)
4[c,d]	**4a**, *t*-$C_4H_9NH_2$ (**5d**)	**6ad**: 19
5[e]	**4a**, $PhNH_2$ (**5e**)	**3a**: 96 (75)
6[e]	*p*-$MeC_6H_4CH_2OH$ (**4b**), **5e**	**6be**: 91 (77)
7[e]	*m*-$MeOC_6H_4CH_2OH$ (**4c**), **5e**	**3c**: 94 (83)
8[e]	*p*-$FC_6H_4CH_2OH$ (**4d**), **5e**	**6de**: 83 (67)
9[e]	*p*-$ClC_6H_4CH_2OH$ (**4e**), **5e**	**6ee**: 89 (70)
10[e]	*m*-$ClC_6H_4CH_2OH$ (**4f**), **5e**	**6fe**: 92 (76)
11[e]	*o*-$ClC_6H_4CH_2OH$ (**4g**), **5e**	**6ge**: 98 (81)
12[e]	*p*-$BrC_6H_4CH_2OH$ (**4h**), **5e**	**6he**: 96 (82)
13[e]	*p*-$NO_2C_6H_4CH_2OH$ (**4i**), **5e**	**6ie**: 80 (62)
14[e]	2-thiophenemethanol (**4j**), **5e**	**6je**: 90 (78)
15[e]	*n*-$C_6H_{13}OH$ (**4k**), **5e**	–
16[e]	$PhCH(CH_3)OH$ (**4l**), **5e**	–
17[e]	**4a**, *p*-$MeC_6H_4NH_2$ (**5f**)	**6af**: 75 (58)
18[e]	**4a**, *m*-$MeC_6H_4NH_2$ (**5g**)	**6ag**: 76 (61)
19[e]	**4a**, *o*-$MeC_6H_4NH_2$ (**5h**)	**6ah**: 70 (63)
20[e]	**4a**, *p*-$EtOC_6H_4NH_2$ (**5i**)	**3b**: 95 (82)
21[e]	**4b**, **5i**	**6bi**: 99 (75)
22[e]	**4e**, **5i**	**6ei**: 91(78)
23[e]	**4g**, **5i**	**6gi**: 95 (85)
24[e]	**4h**, **5i**	**6hi**: 81 (64)
25[e]	**4j**, **5i**	**6ji**: 71 (57)
26[e]	**4a**, *p*-$ClC_6H_4NH_2$ (**5j**)	**6aj**: 70 (56)
27[e,f]	**4a**, 1-naphthylamine (**5k**)	**6ak**: 59 (43)

[a] Unless otherwise noted, the mixture of **4** (1.2 mmol), **5** (1 mmol), $Fe(NO_3)_3 \cdot 9H_2O$ (10 mol %), TEMPO (10 mol %), and KOH in toluene (0.5 mL) was heated under air in a 100 mL tube at 80 °C and then monitored by TLC and/or GC-MS. [b] GC yields (isolated yields in parentheses) based on **5**. [c] 20 mol % KOH, 24 h. [d] 1 mmol **4** and 2 mmol **5** were used; yields were based on **4**. [e] 50 mol % KOH, 36 h. [f] CsOH (50 mol %) used instead of KOH.

yield of **2a** (78%) could be achieved at 80 °C by using 20 mol % of KOH as the base (run 5).

The optimized conditions were then applied to various alcohols and amines to extend the scope of the method (Table 4). Similar to **1a**, the reaction of 2-phenylethylamine (**5a**) was also efficient under the same conditions and gave a moderate yield of the target imine **6aa** (run 1). In contrast, the reactions of aliphatic amines were not efficient, affording only low yields of the products under similar conditions (runs 2–4). We then focused on the reactions of anilines to synthesize useful aromatic imines. However, possibly because the anilines are less basic and less nucleopilic, only a 36% yield of **3a** was detected under the conditions for benzylamine.[16] Further condition screening showed that 30–50 mol % of KOH, CsOH, and *t*-BuOK were the most effective for the reaction (e.g., 91–96% GC yields of **3a**),[16] and a good isolated yield of **3a** could be obtained (run 5). Similarly, both electron-rich and -deficient benzylic alcohols, including a sterically more bulky *ortho*-substituted **4g** (run 11) and a heterobenzylic alcohol **4j** (run 14), reacted efficiently with **5e** to afford the target imines in moderate to good yields (runs 6–14). The reactions of an aliphatic alcohol and a secondary benzilic alcohol were also tested under the same condtions, but they were not successful (runs 15, 16). Besides, this method is applicable to various electron-rich and -deficient anilines, including sterically more bulky *ortho*-subsituted **5h** (run 19) and 1-naphthylamine **5k** (run 27), giving moderate to good yields of the products (runs 17–27). It seemed the electron-rich anilines were better substrates, for they generally gave higher yields of the products (runs 17–25) than the electron-deficient one (run 26). The reaction of 1-naphthylamine **5k** was less efficient than the anilines under the same conditions, and CsOH had to be used as the base instead of KOH (run 27).

In summary, by using the general $Fe(NO_3)_3$/TEMPO catalyst system, we developed several Fe-catalyzed methods for the preparation of useful imines by aerobic oxidation reactions of primary amines, secondary amines, benzylamines with anilines, and alcohols with amines. Since abundant, cheap, and relatively more biofriendly iron can be readily used as the catalyst and air as the economic and safe oxidant, these aerobic methods may become green and practical alternatives for the direct synthesis of imines from amines and alcohols. Further extension of the Fe-catalyzed aerobic oxidative method and mechanistic studies of the reactions are underway.

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Supporting Information Available. Experimental procedures, detailed condition screening tables, product characterization, and ^1H and ^{13}C NMR spectra of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.