

Iron(III)-Catalyzed Synthesis of 1,2,4-Trisubstituted Imidazoles through the Reactions of Amidines and Aldehydes in Air

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Abstract: A novel and efficient iron(III)-catalyzed synthesis of 1,2,4-trisubstituted imidazoles through the reactions of amidines and aldehydes in air has been developed. Five hydrogen dissociations involving C–H and N–H bond activation are realized under mild conditions in this approach. The procedure is sustainable, simple and environmentally friendly.

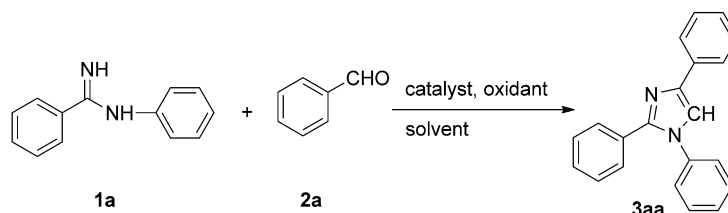
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1,2,4-Trisubstituted imidazoles are one of the most important classes of *N*-containing heterocyclic compounds, they have been found in a lot of biologically active drugs^[1] and functional materials.^[2] In addition, they are of interest in the synthesis of organic semiconductors,^[3] dyes,^[4] dehydroannulenes,^[5] and electroluminescent materials.^[6] During the last decades, many methodologies have been developed for the synthesis of multi-substituted imidazoles. Among them, the general one is the reaction of an α -hydroxy ketone/1,2-diketone, a primary amine, an aldehyde and ammonium acetate in one-pot.^[7] A number of catalysts for this process have been reported,^[8] such as silica gel/NaHSO₄, molecular iodine, HClO₄·SiO₂, BF₃·SiO₂, hetero-polyacids, Wells–Dawson acid, L-proline, FeCl₃·6H₂O. Very recently, another way to synthesize multi-substituted imidazoles through the functionalization of C–H/N–H bonds directly was developed. For example, Yan and co-workers^[9] reported the copper-catalyzed synthesis of imidazo[1,2-*a*] pyridines *via* oxidative activation of C–H and N–H bonds from aminopyridines and nitroolefins. Neuville and co-workers^[10] developed an efficient copper-catalyzed synthesis of 1,2,4-trisubstituted imidazoles using ami-

dines and terminal alkynes. Despite the advances of these methods for multisubstituted imidazoles, most of them require strong bases, long reaction times and an oxygen atmosphere, but only provide low yields. Therefore, the development of improved ways for the synthesis of multi-substituted imidazoles continues to be a challenging goal.

Amidines, as easily available and versatile structures, play an important role as precursors for the synthesis of *N*-containing heterocyclic compounds such as quinazolines, benzimidazoles, pyrimidines or imidazoles.^[11] Earlier in this year, our group reported a novel and efficient strategy for the synthesis of tri- or tetrasubstituted imidazoles *via* copper-catalyzed [3+2] cycloaddition reactions of nitroolefins with amidines.^[12] As a part of our current studies on the development of new routes in multisubstituted imidazoles synthesis, herein, we first present a new and efficient iron(III)-catalyzed synthesis of 1,2,4-trisubstituted imidazoles *via* oxidative activation of C–H and N–H bonds from amidines and aldehydes.

First, the reaction conditions were optimized using *N*-phenylbenzamidinium **1a** and benzaldehyde **2a** as model substrates. As shown in Table 1, the reaction was carried out with *N*-phenylbenzamidinium **1a** (0.24 mmol), benzaldehyde **2a** (0.20 mmol) in the presence of FeCl₃ (10% mmol) in CH₃NO₂ (2 mL) at 90 °C under an atmosphere of O₂ for 8 h. The desired product **3aa** was obtained in only 5% yield (Table 1, entry 1). When the reactions were carried out in different solvents including THF, DMF and DMSO, they did not give the expected product **3aa** (entries 2–4). The yield of **3aa** was increased to 42% by using a mixture of DMF and CH₃NO₂ as solvent (entry 5). Then, the cyclization reactions were conducted in different solvent mixtures, such as CH₃NO₂/DMSO, CH₃NO₂/toluene, CH₃NO₂/DMA and CH₃NO₂/1,4-dioxane, and the reactions did not provide higher yields (entries 6–9). Based on the above-studied results, we

Table 1. Optimization of the reaction conditions.^[a]

Entry	Catalyst	Oxidant	Solvent	Yield ^[b]
1	FeCl ₃ (10%)	O ₂	CH ₃ NO ₂	5%
2	FeCl ₃ (10%)	O ₂	THF	0%
3	FeCl ₃ (10%)	O ₂	DMF	0%
4	FeCl ₃ (10%)	O ₂	DMSO	0%
5	FeCl ₃ (10%)	O ₂	CH ₃ NO ₂ /DMF	42%
6	FeCl ₃ (10%)	O ₂	CH ₃ NO ₂ /DMSO	40%
7	FeCl ₃ (10%)	O ₂	CH ₃ NO ₂ /DMA	12%
8	FeCl ₃ (10%)	O ₂	CH ₃ NO ₂ /toluene	trace
9	FeCl ₃ (10%)	O ₂	CH ₃ NO ₂ /dioxane	trace
10	FeCl ₃ (10%)	TBHP	CH ₃ NO ₂ /DMF	12%
11	FeCl ₃ (10%)	DDQ	CH ₃ NO ₂ /DMF	trace
12	FeCl ₃ (10%)	Ag ₂ CO ₃	CH ₃ NO ₂ /DMF	5%
13	FeCl ₃ (10%)	<i>t</i> -BuOOBu- <i>t</i>	CH ₃ NO ₂ /DMF	trace
14	FeCl ₃ (10%)	BPO	CH ₃ NO ₂ /DMF	4%
15	FeCl ₃ (30%)	CO(NH ₂) ₂ ·H ₂ O ₂	CH ₃ NO ₂ /DMF	55%
16	FeCl ₃ (10%)	air	CH ₃ NO ₂ /DMF	42%
17	FeCl ₃ (20%)	air	CH ₃ NO ₂ /DMF	45%
18	FeCl₃ (30%)	air	CH₃NO₂/DMF	62%
19	FeCl ₃ (50%)	air	CH ₃ NO ₂ /DMF	54%
20	FeBr ₃ (30%)	air	CH ₃ NO ₂ /DMF	55%
21	Fe(OTf) ₃ (30%)	air	CH ₃ NO ₂ /DMF	45%
22	Fe(acac) ₃ (30%)	air	CH ₃ NO ₂ /DMF	12%
23	CuI (30%)	air	CH ₃ NO ₂ /DMF	0%
24 ^[c]	FeCl ₃ (30%)	air	CH ₃ NO ₂ /DMF	44%
25 ^[d]	FeCl ₃ (30%)	air	CH ₃ NO ₂ /DMF	62%

^[a] Reaction conditions: **1a** (0.24 mmol), **2a** (0.2 mmol), catalyst, oxidant (2 equiv), solvent (2 mL), CH₃NO₂:other solvents = 0.5:1.5 mL, 90°C, 8 h.

^[b] Isolated yield.

^[c] The reaction was carried out at 70°C.

^[d] The reaction was carried out at 110°C.

chose the mixture CH₃NO₂/DMF as the reaction solvent. Next, the reactions were carried out with different oxidants. Ag₂CO₃, BPO and *t*-BuOOBu-*t*, 6-dicyanobenzoquinone (DDQ), CO(NH₂)₂·H₂O₂, and TBHP showed no or slight effects to promote the reaction, but using air gave the same yield as what was got under O₂ (entries 10–16). Then, we investigated the reactions at different loadings of FeCl₃. The yield of **3aa** was further improved by increasing the amount of FeCl₃ gradually. When the reaction was carried out with 30 mol% FeCl₃, the yield of **3aa** was increased to 62%, but the higher loading (>30 mol%) resulted in reduced yield (entries 16–19). Finally, the catalysts screening was done. Some generally used catalysts including CuI, FeBr₃, Fe(OTf)₃, FeCl₃ and Fe(acac)₃ were tested, and FeCl₃ was found to be the best one (entries 20–23). Besides, increasing the temperature

to 110°C did not enhance the yield. At the temperature of 70°C, the yield decreased sharply (entries 24 and 25). Increasing the reaction time also did not enhance the yield. Thus, 30 mol% FeCl₃, 90°C and CH₃NO₂/DMF are the optimal conditions for this reaction.

Under the optimized reaction conditions, various aldehydes **2** were found to be suitable reaction partners with *N*-phenylbenzamidinium **1a** to provide the corresponding 1,2,4-trisubstituted imidazoles derivatives **3** (Table 2). It could be seen that electronic effects played a significant role: benzaldehydes with electron-donating groups such as methyl and methoxy proceeded with good yields (entries 1–6), but the dimethylamino did not give the expected product (entry 15). Benzaldehydes with electron-withdrawing groups such as chloro, fluoro, cyano and trifluoro-

Table 2. Reactions of *N*-phenylbenzamidines with various aldehydes.^[a]

$\text{Ph}-\text{NH}-\text{C}(\text{NH})=\text{Ph} + \text{R}^1-\text{CHO} \xrightarrow[\text{CH}_3\text{NO}_2/\text{DMF}, 8\text{ h}]{\text{FeCl}_3 (30\%), 90^\circ\text{C}}$			
Entry	R ¹	Product	Yield ^b
1	C ₆ H ₅ (2a)	3aa	62%
2	4-CH ₃ C ₆ H ₄ (2b)	3ab	64%
3	4-CH ₃ OC ₆ H ₄ (2c)	3ac	70%
4	2-CH ₃ OC ₆ H ₄ (2d)	3ad	61%
5	3,4-CH ₃ OC ₆ H ₃ (2e)	3ae	66%
6	3,4-CH ₃ C ₆ H ₃ (2f)	3af	59%
7	4-ClC ₆ H ₄ (2g)	3ag	57%
8	2-ClC ₆ H ₄ (2h)	3ah	52%
9	4-F C ₆ H ₄ (2i)	3ai	60%
10	3-F C ₆ H ₄ (2j)	3aj	61%
11	4-CF ₃ C ₆ H ₄ (2k)	3ak	56%
12	4-CN C ₆ H ₄ (2l)	3al	40%
13	4-NO ₂ C ₆ H ₄ (2m)	3am	0%
14	2-NO ₂ C ₆ H ₄ (2n)	3an	0%
15	4-NMe ₂ C ₆ H ₄ (2o)	3ao	0%
16	<i>n</i> -C ₃ H ₇ (2p)	3ap	57%
17	<i>n</i> -C ₅ H ₁₁ (2q)	3aq	55%
18	<i>n</i> -C ₁₁ H ₂₃ (2r)	3ar	51%
19	2,6-dimethylhept-5-enyl (2s)	3as	41%

^[a] Reaction conditions: **1a** (0.24 mmol), **2a–s** (0.2 mmol), FeCl₃ (30% mmol), CH₃NO₂: DMF = 0.5:1.5 mL, 90 °C, 8 h.

^[b] Isolated yield.

methyl groups gave lower but still acceptable yields (entries 7–12). However, the desired product could not be obtained when a strong electron-withdrawing group such as nitro was present (entries 13 and 14). Aliphatic aldehydes were suitable substrates to produce 1,2,4-trisubstituted imidazoles in good yield (entry 16–19). Besides, the 2-substituted benzaldehydes showed slightly lower yields than the 4-substituted ones (entries 3, 4, 7 and 8), which was probably caused by steric effects.

To study the scope and generality of the present protocol, various *N*-arylbenzamidines were studied for the oxidative C–H/N–H bond cycloaddition reactions with benzaldehyde under the above optimized reaction conditions. As shown in Table 3, the most of investigated *N*-arylbenzamidines were suitable partners for the oxidative C–H/N–H bond cycloaddition reactions and provided the corresponding products in moderate yields. In general, *N*-arylbenzamidines with electron-donating groups (such as methyl, methoxy and ethyl) on R² and/or R³ provided higher yields of the desired product (entries 1–6). Especially, when the *N*-arylbenzamidines bearing two electron-donating groups were employed, the yields were up to 76%

Table 3. Reactions of benzaldehyde with various *N*-arylbenzamidines.^[a]

$\text{R}^2-\text{NH}-\text{C}(\text{NH})=\text{R}^3 + \text{Ph}-\text{CHO} \xrightarrow[\text{CH}_3\text{NO}_2/\text{DMF}, 8\text{ h}]{\text{FeCl}_3 (30\%), 90^\circ\text{C}}$				
Entry	R ²	R ³	Product	Yield ^[b]
1	C ₆ H ₅	C ₆ H ₅	3aa	62%
2	C ₆ H ₅	4-CH ₃ C ₆ H ₄	3ba	72%
3	4-CH ₃ C ₆ H ₄	C ₆ H ₅	3ca	71%
4	C ₆ H ₅	3-CH ₃ C ₆ H ₄	3da	62%
5	C ₆ H ₅	4-CH ₃ OC ₆ H ₄	3ea	75%
6	C ₆ H ₅	2-C ₂ H ₅ C ₆ H ₄	3fa	61%
7	C ₆ H ₅	4-ClC ₆ H ₄	3ga	58%
8	C ₆ H ₅	3-ClC ₆ H ₄	3ha	54%
9	2-ClC ₆ H ₄	C ₆ H ₅	3ia	52%
10	4-CH ₃ C ₆ H ₄	4-CH ₃ C ₆ H ₄	3ja	71%
11	4-CH ₃ OC ₆ H ₄	4-CH ₃ C ₆ H ₄	3ka	76%
12	3-pyridinyl	C ₆ H ₅	3la	57%
13	<i>t</i> -Bu	C ₆ H ₅	3ma	0%
14	C ₆ H ₅	C ₂ H ₅	3na	0%
15	C ₆ H ₅	4-NO ₂ C ₆ H ₄	3oa	0%

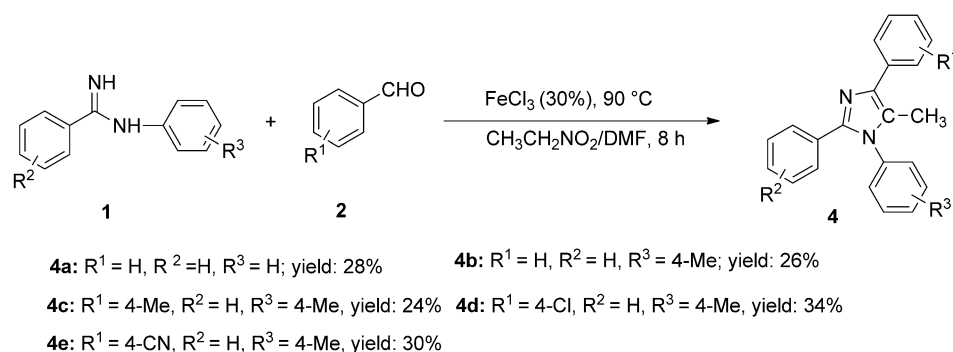
^[a] Reaction conditions: **1a–o** (0.24 mmol), **2a** (0.2 mmol), FeCl₃ (30% mmol), CH₃NO₂: DMF = 0.5:1.5 mL, 90 °C, 8 h.

^[b] Isolated yield

(entries 10 and 11). Benzamidines with electron-withdrawing groups (such as chloro) gave lower but still acceptable yields (entries 7–9), but the strongly electron-withdrawing substituted *N*-arylbenzamidines [such as *N*-(4-nitrophenyl)benzamidines, **1o**] did not give the expected product (entry 15). Moreover, the amidines with aliphatic groups, such as *N*-phenylpivalamidines **1m** and *N*-ethylbenzamidines **1n** did not give the expected product (entries 13 and 14). The 4-substituted benzamidines showed slightly higher yields than the 3-substituted ones (entries 3, 4, 7 and 8). Notably, *N*-phenylnicotinamidines **2l** could also be suitable for the cycloaddition reactions and provided the corresponding product **3la** with 57% yield (entry 12).

The synthesis of 1,2,4,5-tetrasubstituted imidazoles through the reactions of amidines and aldehydes was performed in CH₃CH₂NO₂/DMF (1:3), with FeCl₃ (30%) as catalyst at 90 °C for 8 h (Scheme 1). It was found that the corresponding 1,2,4,5-tetrasubstituted imidazoles **4a**, **4b**, **4c**, **4d**, **4e** were obtained in only 24–34% yield. This was probably due to steric effects.

To probe the mechanism of the reactions, several control experiments were performed. While the reaction was carried out with *N*-phenylbenzamidines **1a** (0.24 mmol), benzaldehyde **2a** (0.20 mmol), CH₃NO₂ (0.40 mmol) in the presence of FeCl₃ (30 mol%) in DMF at 90 °C under an atmosphere of air for 8 h, the desired product **3aa** was obtained in 25% yield. The

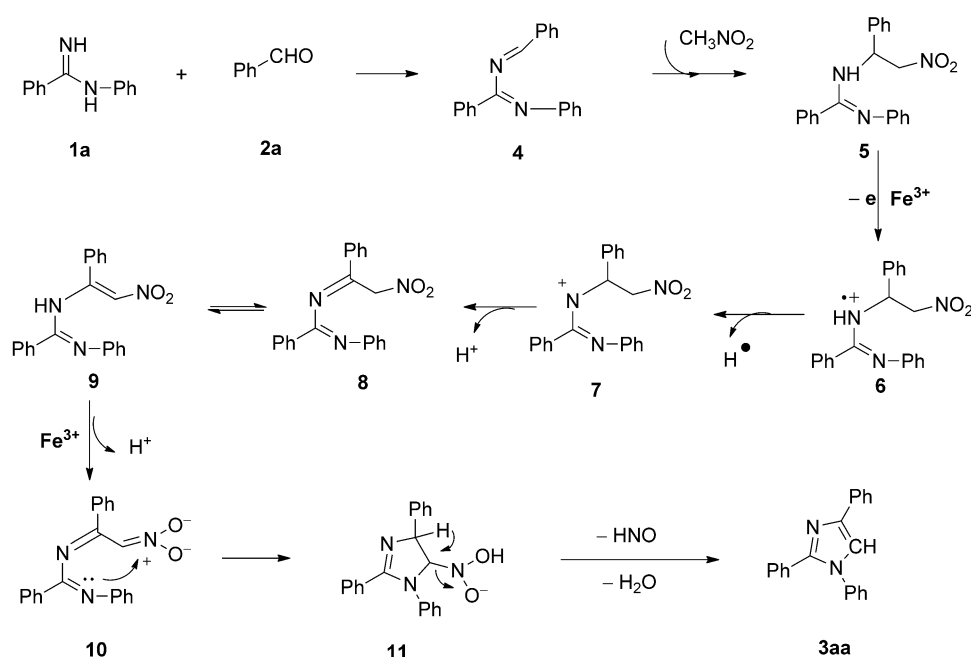


Scheme 1. Synthesis of 1,2,4,5-tetrasubstituted imidazoles.

cycloaddition reaction did not occur without participation of CH_3NO_2 . Therefore, nitromethane could provide a carbon atom for the reaction. Imidazole **3aa** was also obtained in 62% yield *via* reaction of **1a** with **2a** under N_2 -protected conditions. Thus, we speculate the NO_2 group was the terminal oxidant in this process. Based on the above observations and the analogous mechanisms discussed in the literature,^[13] a plausible mechanism was proposed as shown in Scheme 2. First, the intermediate **4** was produced by the condensation reaction of *N*-phenylbenzamidine **1a** with benzaldehyde **2a**. Then the intermediate **5** was produced from Michael addition of intermediate **4** with CH_3NO_2 . Subsequently, the iron catalyst oxidized the intermediate **5** into the radical cation **6**, and the intermediate **7** was obtained from intermediate **6** after subsequent removal of a hydrogen radical. Next, the intermediate **7** underwent proton abstraction with the oxidant forming intermediate **8**, which further iso-

merized into enamine **9** smoothly. Then, iron-catalyzed synthesis of radical cation **10** from **9** occurred *via* loss of a proton. Finally, the product **3aa** was obtained *via* the intramolecular Michael addition with removal of nitroxyl (HNO) and H_2O abstraction from intermediate **11**, which was produced from **10**.

In conclusion, we have developed an efficient iron(III)-catalyzed synthesis of 1,2,4-trisubstituted imidazoles through the reactions of amidines and aldehydes in air. Five hydrogen dissociations involving C–H and N–H bonds activation are realized under mild conditions in this approach. The procedure is sustainable, simple and economic. This procedure uses FeCl_3 as the catalyst which is less toxic than the copper catalyst. Comparing with the literature methods, this methodology has several advantages, such as commercial starting materials, multicomponent reaction in one-pot, use of base-free and ligand-free conditions, under air.



Scheme 2. A plausible reaction mechanism.

Experimental Section

Typical Procedure for the Reaction between Amidines and Benzaldehydes: Synthesis of 1,2,4-Triphenyl-1H-imidazole (3aa)

All reactions were performed on a 0.20-mmol scale relative to aldehydes. The *N*-phenylbenzamidine (**1a**, 0.24 mmol), benzaldehyde (**2a**, 0.2 mmol), FeCl₃ (0.060 mmol) and 2 mL MeNO₂/DMF (1:3) were charged in a round-bottom flask equipped with a stirrer. The resulting mixture was stirred for 8 h at 90 °C. After cooling to room temperature, the reaction mixture was treated with water (2 mL), and extracted with ethyl acetate (3 × 10 mL). The combined organic phases were washed with brine (2 × 5 mL), dried over anhydrous MgSO₄ and concentrated under vacuum. The residue was subjected to flash column chromatography with hexanes/EtOAc (20/1) as eluent to obtain the desired **3aa** as a light yellow oil; yield: 62%. ¹H NMR (300 MHz, CDCl₃): δ = 7.87–7.90 (d, *J* = 9.0 Hz, 2H), 7.21–7.45 (m, 14H); ¹³C NMR (100 MHz, CDCl₃): δ = 146.9, 141.6, 138.4, 133.8, 130.2, 129.4, 129.1, 128.7, 128.5, 128.4, 128.1, 126.9, 125.7, 125.0, 118.5. ESI HR-MS: *m/z* = 296.1316, calcd. for C₂₁H₁₆N₂ [M+H]⁺: 296.1313.

The remaining 1,2,4-trisubstituted imidazoles were prepared in a similar manner.

Acknowledgements

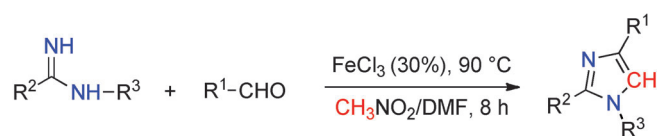
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References

- [1] a) A. Gazit, H. App, G. McMahon, J. Chen, A. Levitzki, F. D. Bohmer, *J. Med. Chem.* **1996**, 39, 2170; b) G. Sakata, K. Makino, Y. Kurasawa, *Heterocycles* **1988**, 27, 2481; c) W. He, M. R. Myers, B. Hanney, A. P. Sapada, G. Bilder, H. Galz-cinski, D. Amin, S. Needle, K. Page, Z. Jayyosi, M. H. Perrone, *Bioorg. Med. Chem. Lett.* **2003**, 13, 3097; d) Y. B. Kim, Y. H. Kim, J. Y. Park, S. K. Kim, *Bioorg. Med. Chem. Lett.* **2004**, 14, 541; e) U. Sehlstedt, P. Aich, J. Bergman, H. Vallberg, B. Norden, A. Graslund, *J. Mol. Biol.* **1998**, 278, 31.
- [2] R. H. Sarges, R. Howard, R. G. Browne, L. A. Lebel, P. A. Seymour, *J. Med. Chem.* **1990**, 33, 2240.
- [3] a) D. T. Mowry, *Chem. Rev.* **1948**, 43, 189; b) G. P. Ellis, T. M. Romney-Alexandar, *Chem. Rev.* **1987**, 87, 779; c) R. G. R. Bacon, H. A. O. Hill, *J. Chem. Soc.* **1964**, 1097; d) T. Sandmeyer, *Ber. Dtsch. Chem. Ges.* **1884**, 17, 2650; e) C. F. Koelsch, A. G. Whitney, *J. Org. Chem.* **1941**, 6, 795.
- [4] a) K. Mori, K. Yamaguchi, T. Mizugaki, K. Ebitani, K. Kaneda, *Chem. Commun.* **2001**, 461; b) K. Yamaguchi, N. Mizuno, *Angew. Chem.* **2003**, 115, 1518; c) M. Kotani, T. Koike, K. Yamaguchi, N. Mizuno, *Green Chem.* **2006**, 8, 735; d) F. Li, J. Chen, Q. Zhang, Y. Wang, *Green Chem.* **2008**, 10, 553; e) Y. Zhang, K. Xu, X. Chen, T. Hu, Y. Yu, J. Zhang, J. Hung, *Catal. Commun.* **2010**, 11, 951.
- [5] a) M. L. Mihailović, A. Stojiljković, V. Andrewjević, *Tetrahedron Lett.* **1965**, 461; b) T. Kajimoto, H. Takahashi, J. Tsuji, *J. Org. Chem.* **1976**, 41, 1389; c) W. P. Griffith, B. Reddy, A. G. F. Shoir, M. Suriaatmaja, A. J. P. White, D. J. Williams, *J. Chem. Soc. Dalton Trans.* **1998**, 2819.
- [6] a) P. Capdevielle, A. Lavigne, D. Sparfel, J. Baranne-Lafont, M. Maumy, *Tetrahedron Lett.* **1990**, 31, 3305; b) R. Tang, S. E. Di-amond, N. Neary, F. Marks, *J. Chem. Soc. Perkin Trans. 1* **1978**, 562; c) F. Porta, C. Crotti, S. Cennini, *J. Mol. Catal.* **1989**, 50, 333; d) A. Bailey, B. R. James, *Chem. Commun.* **1996**, 2343; e) Y. Maeda, T. Nishimura, S. Uemura, *Bull. Chem. Soc. Jpn.* **2003**, 76, 2399.
- [7] a) A. R. Karimi, Z. Alimohammadi, J. Azizian, A. A. Mohammadi, M. R. Mohammadzadeh, *Catal. Commun.* **2006**, 7, 728; b) S. Samai, G. C. Nandi, P. Singh, M. S. Singh, *Tetrahedron* **2009**, 65, 10155; c) M. M. Heravi, F. Derikvand, M. Haghighi, *Monatsh.-Chem.* **2008**, 139, 31; d) B. Sadeghi, B. B. F. Mirjalili, M. M. Hashemi, *Tetrahedron Lett.* **2008**, 49, 2575.
- [8] a) S. Balalaie, A. Arabanian, *Green Chem.* **2000**, 2, 274; b) M. Kidwai, P. Mothra, V. Bansal, R. K. Somvanshi, A. S. Ethayathulla, S. Dey, T. P. Singh, *J. Mol. Catal. A: Chem.* **2007**, 265, 177; c) S. Kantevari, S. V. N. Vuppala-pati, D. O. Biradar, L. Nagarapu, *J. Mol. Catal. A: Chem.* **2007**, 266, 109; d) M. M. Heravi, F. Derikvand, F. F. Bamoharram, *J. Mol. Catal. A: Chem.* **2007**, 263, 112; e) L. agarapu, S. puri, S. Antevvari, *J. Mol. Catal. A: Chem.* **2007**, 266, 104.
- [9] R. L. Yan, H. Yan, C. Ma, Z. Y. Ren, X. A. Cao, G. S. Huang, Y. M. Liang, *J. Org. Chem.* **2012**, 77, 2024.
- [10] J. Li, L. Neuville, *Org. Lett.* **2013**, 15, 1752.
- [11] a) B. Chao, S. Lin, Q. Ma, D. Lu, Y. Hu, *Org. Lett.* **2012**, 14, 2398; b) X. Yang, Y. Jin, H. Liu, Y. Jiang, H. Fu, *RSC Adv.* **2012**, 2, 11061; c) L. Xu, Y. Jiang, D. Ma, *Org. Lett.* **2012**, 14, 1150; d) M. A. McGowan, C. Z. McAvoy, S. L. Buchwald, *Org. Lett.* **2012**, 14, 3800; e) S. Li, Z. Li, Y. Yuan, Y. Li, L. Zhang, Y. Wu, *Chem. Eur. J.* **2013**, 19, 1496; f) B. Li, L. Samp, J. Sagal, C. M. Hayward, C. Yang, Z. Zhang, *J. Org. Chem.* **2013**, 78, 1273.
- [12] D. Tang, P. Wu, X. Liu, Y. X. Chen, S. B. Guo, W. L. Chen, J. G. Li, B. Chen, *J. Org. Chem.* **2013**, 78, 2746.
- [13] a) H. Yan, S. Yang, X. Gao, K. Zhou, C. Ma, R. Yan, G. Huang, *Synlett* **2012**, 23, 2961; b) H. Shiraishi, T. Nishitani, S. Sakaguchi, Y. Ishii, *J. Org. Chem.* **1998**, 63, 6234; c) S. Maiti, S. Biswas, U. Jana, *J. Org. Chem.* **2010**, 75, 1674; d) D. K. Nair, S. M. Mobin, I. N. N. Namboothiri, *Tetrahedron Lett.* **2012**, 53, 3349; e) W. Y. Huang, Y. C. Chen, K. Chen, *Chem. Asian J.* **2012**, 7, 688.

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