NH₃·H₂O: The Simplest Nitrogen-Containing Ligand for Selective Aerobic Alcohol Oxidation to Aldehydes or Nitriles in Neat Water

Guofu Zhang,[a] Danting Ma,[a] Yiyong Zhao,[a] Guihua Zhang,[a] Guangyao Mei,[b] Jinghui Lyu,[a] Chengrong Ding,*[a] and Shang Shan*[a]

Aqueous ammonia (NH₃·H₂O) has been shown to serve as the simplest nitrogen-containing ligand to effectively promote copper-catalyzed selective alcohol oxidation under air in water. A series of alcohols with varying electronic and steric properties were selectively oxidized to aldehydes with up to 95% yield. Notably, by increasing the amount of aqueous ammonia in neat water, the exclusive formation of aryl nitriles was also accomplished with good-to-excellent yields. Additionally, the catalytic system exhibits a high level of functional group tolerance with −OH, −NO₂, esters, and heteroaryl groups all being amenable to the reaction conditions. This one-pot and green oxidation protocol provides an important synthetic route for the selective preparation of either aldehydes or nitriles from commercially available alcohols.

1. Introduction

The selective aerobic oxidation of alcohols to carbonyl compounds has emerged as one of the most important synthetic strategies in organic chemistry,[1] with significant effort being devoted to the development of new and efficient oxidative systems for effective transformations. Among these strategies, transition-metal-catalyzed selective alcohol oxidations have attracted much attention in the chemical community over the past few years. Generally, noble metal catalysts such as those based on palladium,[2] platinum,[3] gold,[4] ruthenium,[5] and rhodium,[6] together with various ligands, can effectively facilitate the oxidation of alcohols; however, their large-scale application has been hampered by the high cost and rarity of the metal species, as well as by their poor compatibility with heterocycles and other heteroatom-containing functional groups. Recently, inexpensive first-row transition metals such as Co,[7] Fe,[8] and Cu[9] have been shown to exhibit broader functional group tolerance in aerobic oxidations. A catalytic system consisting of a copper catalyst and TEMPO is an effective combination for alcohol oxidations, employing molecular oxygen or air as an ideal oxidant and a commercially available copper source as a catalyst. Since the earliest example of the use of a CuCl/TEMPO-catalytic system for the oxidation of benzylic and allylic alcohols reported by Semmelhack in 1984,[9a] significant progress has been made in this field. Due to the low electrode potential of copper (Cu/Cu²⁺ $E_{ox} = +0.34$ V),[10] ligands such as pyridine,[9a] 2,2-bipyridine,[9c,f] phenanthroline,[9b] N-heterocyclic carbene,[9d,i] and amino acids[9k,l] or their expensive derivatives,[9g,h] are usually required in order to promote smooth oxidative transformation. Generally, these ligands possess complex structures and most derivatives are not commercially available for direct use. Additionally, such ligands are not easily removed from the reaction and so complicate purification of the reaction mixture. To the best of our knowledge, aqueous ammonia, a readily available commodity source, has not been used as an N-containing ligand in aerobic oxidation reactions of alcohols. Its low boiling point and good solubility in water may allow it to be more easily removed from the reaction mixture and thus simplify the purification process.

In addition to the above, we were also interested in exploring whether it was possible to achieve a selective synthesis of aryl nitriles from commercially available aryl alcohols using ammonia as a potential nitrogen source and by carrying out the reaction in water. Although there are a considerable number of protocols that employ ammonia as a nitrogen source for cyanation reactions, only a few examples of the exclusive formation of both aryl aldehyde and aryl nitriles have been reported in aqueous media.[11] In this scenario, ammonia may act as an effective ligand to facilitate the copper-catalyzed aerobic oxidation, as well as function as a cyanide source for aryl nitrile formation. Herein, we report an efficient copper-catalyzed aerobic oxidative system for the selective preparation of both aldehydes and nitriles in water. By using ammonia as the sim-

[a] G. Zhang, D. Ma, Y. Zhao, G. Zhang, J. Lyu, Dr. C. Ding, Dr. S. Shan
College of Chemical Engineering
Zhejiang University of Technology
Hangzhou 310014 (P. R. China)
E-mail: dingcr@zjut.edu.cn
        shanshang2001@163.com

[b] G. Mei
Zhejiang Hongyuan Pharmaceutical Co. Ltd
Taizhou 317016 (P. R. China)
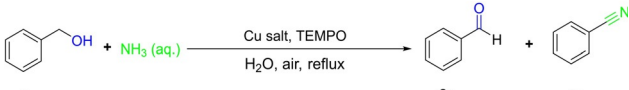
plest N-containing ligand, a series of alcohols could be reacted with excellent reactivity and selectivity. In addition, the demonstrated system exhibits a high level of functional group tolerance.

2. Results and Discussion

At the beginning of our studies, we embarked on reaction condition optimization using benzyl alcohol **1a** as a model substrate and by conducting the reaction in water under an air atmosphere (Table 1). Initial studies showed that only 39% benzyl alcohol was converted to the desired aldehyde using CuI/TEMPO in the absence of any additive and heating under reflux conditions in water (Table 1, entry 1). Gratifyingly, the conversion was significantly increased to 75% via the addition of 1.98 equiv of ammonia as a ligand. Notably, the side-product, benzonitrile, was also produced in the reaction, implying the high possibility of nitrile formation using ammonia as a sole ligand (Table 1, entry 2). The ammonia loading was further decreased in order to further improve the reactivity and selectivity of aldehyde formation (Table 1, entries 3–10). With 7.9 mol% ammonia, the desired product **2a** was exclusively formed and no benzonitrile was detected (Table 1, entry 8).

Considering ammonia can be formed in situ via the decomposition of ammonium salts at high temperature, the influence of ammonium acetate on the catalytic reaction was investigated. However, the aldehyde was obtained with 77% conversion and was accompanied by 2% of the corresponding benzonitrile (Table 1, entry 11). The effect of different copper salts was next examined (Table 1, entries 12–20). The results show that almost all of the copper salts, besides CuO, were effective in the reaction. CuI proved to be the optimal copper source giving the desired aldehyde with quantitative conversion. The conversion decreased when the catalyst loading was reduced to 3 mol% (Table 1, entry 21). Control experiments showed that both the copper catalyst and TEMPO are essential for this oxidative reaction (Table 1, entries 22, 23). Thus, the optimal reaction conditions for the aerobic alcohol oxidation to aldehydes were established as the following: alcohol (1.0 mmol), ammonia (7.9 mol%), catalyzed by CuI (5 mol%)/TEMPO (5 mol%), heating at reflux condition in water under an air atmosphere. Notably, by simply increasing the amount of ammonia to 8.0 equiv, we were excited to see that the benzonitrile was formed exclusively (see the SI).

Under the optimal conditions, we investigated the generality of our aerobic alcohol oxidation (Table 2). Generally, all the aryl alcohols bearing various electron-donating or electron-withdrawing groups on the aromatic rings, were oxidized selectively to the corresponding aldehydes with almost quantitative conversion and up to 95% isolated yield (Table 2, **2a–k** and **2r**). Compared to electronic-deficient substrates, electronic-rich substrates were more efficient and able to complete the transformation in a shorter time. Notably, the system exhibited a high level of chemoselectivity. For temperature-sensitive substrates such as 4-(hydroxymethyl)benzoic acid, methyl 4-(hy-

Table 1. Reaction condition optimization for selective aerobic alcohol oxidation of benzyl alcohol to benzaldehyde.[a]
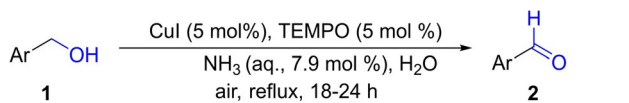

Entry	NH₃·H₂O [x mmol]	Catalyst	Conv.[b] [%]	Yield[b] [%] 2a	3a
1	–	CuI	39	39	–
2	1.98	CuI	75	55	20
3	1.32	CuI	70	60	10
4	0.79	CuI	64	60	4
5	0.66	CuI	72	69	3
6	0.39	CuI	65	65	–
7	0.15	CuI	97	97	<1
8[c]	**0.079**	**CuI**	**100**	**100 (94)**	**–**
9	0.039	CuI	87	87	–
10	0.016	CuI	65	65	–
11[d]	1.5	CuI	79	77	2
12	0.079	CuBr	81	81	–
13	0.079	CuBr₂	89	89	–
14	0.079	CuCl	88	88	–
15	0.079	CuCl₂	92	92	–
16	0.079	CuSO₄	73	73	–
17	0.079	Cu(NO₃)₂	74	74	–
18	0.079	Cu(OTf)₂	72	72	–
19	0.079	Cu(OAc)₂	92	91	–
20	0.079	CuO	14	14	–
21[e]	0.079	CuI	97	97	–
22[f]	0.079	–	trace	trace	–
23[g]	0.079	CuI	trace	trace	–

[a] Reaction conditions: benzyl alcohol **1a** (1.0 mmol), copper salt (5 mol%), TEMPO (5 mol%), NH₃·H₂O (aq., 25–28% w/w, x mmol), H₂O (3.0 mL), air, reflux, 18 h. [b] Determined by GC–MS. [c] Isolated yield in parentheses. [d] Using CH₃COONH₄ in place of NH₃·H₂O. [e] Using CuI (3 mol%). [f] Copper salt was omitted. [g] In the absence of TEMPO.

Table 2. Direct conversion of primary alcohols into aldehydes.[a]
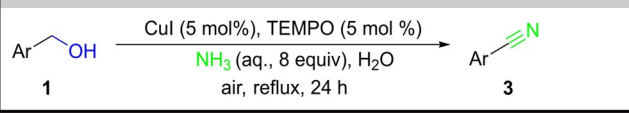
[a] Reaction conditions: alcohol 1 (1.0 mmol), CuI (5 mol%), TEMPO (5 mol%), NH₃ (aq., 25–28% w/w, 7.9 mmol%), H₂O (3.0 mL), air, reflux, 18–24 h; determined by GC, isolated yields in parentheses.

droxymethyl)benzoate and (4-morpholinophenyl)methanol, no coupling reactions were observed (Table 2, **2u–w**). In addition, alcohols bearing oxidation-sensitive group such as −OH, −SMe, and alkenyl functionalities, were selectively converted into the corresponding aldehydes as the exclusive products (Table 2, **2l–n**, **2s** and **2t**). This copper-based system has also shown high compatibility with N/O/S-containing heterocyclic functionalities, and the desired heteroaryl aldehydes were obtained in good yields (Table 2, **2o–q**). This remarkable feature further inspired us to apply our CuI/TEMPO/NH₃ oxidative protocol to the synthesis of pharmacologically active intermediates. As demonstrated by the oxidation of sterically demanding alcohol **1x**, an important intermediate in the synthesis of Rosuvastatin Calcium,[12] the desired aldehyde was isolated with a synthetically useful yield (Table 2, **2x**).

With a useful and highly selective synthesis of benzaldehydes in hand, we turned our attention to the preparation of nitrile derivatives from aryl alcohols (Table 3). To our delight,

bly, the derivatives bearing oxidation-sensitive groups (−OH, −SMe and alkenyl functionalities) also reacted smoothly, providing satisfying yields of the desired nitriles without the generation other side products (Table 3, **3o**, **3p** and **3u**, **3v**). It is noteworthy that the protocol could also be extended to the efficient cyanation of hetero-aromatic compounds (Table 3, **3q–s**).

The catalyst CuI has shown catalytic efficiency during the transformation, whose TONs and TOFs could reach up to 19.2 and 1.04 h⁻¹ (see Table S2 and Table S3).Considering that the use of a large excess of aqueous ammonia is undesirable, further experiments were conducted to investigate if it was possible to recycle the excessive amounts of ammonia (Table 4).

Table 4. Recycling of excess ammonia for cyanation of benzylalcohol derivative **1c**.[a*]

CuI (5 mol%), TEMPO
NH₃·H₂O
H₂O, air
reflux, 24 h

Cycle	Aqua ammonia [equiv]	TEMPO [mol%]	conv.[b] [%]
	1c		**3c**
1	8.0	5	> 99
2	3.0[c]	1	98
3	3.0[c]	1	98
4	3.0[c]	1	97
5	3.0[c]	1	96
6	3.0[c]	1	96

[a] Reaction conditions: 4-methoxybenzyl alcohol **1c** (1.0 mmol), CuI (5 mol%), TEMPO (1 mol%), NH₃ (aq., 25–28% w/w, 3 equiv), H₂O (3.0 mL), in air, refluxing for 24 h. [b] Determined by GC. [c] The amount of ammonia/TEMPO freshly added after the previous cycle.

Table 3. Direct conversion of primary alcohols into nitriles.[a]

Ar—OH → Ar—CN
CuI (5 mol%), TEMPO (5 mol%)
NH₃ (aq., 8 equiv), H₂O
air, reflux, 24 h
1 → **3**

3a, R = H, 99% (93%)
3b, R = 4-Me, 99% (91%)
3c, R = 4-MeO, 99% (96%)
3d, R = 3,4,5-MeO, 99% (95%)
3e, R = 3,4-Me, 99% (93%)
3f, R = 2-MeO, 95% (88%)
3g, R = 4-BnO, 99% (94%)
3h, R = 4-Cl, 99% (94%)
3i, R = 4-Br, 98% (93%)
3j, R = 4-F, 96% (90%)
3k, R= 2-I, 94% (89%)
3l, R = 4-NO₂, 98% (92%)
3m, R = 2-CN, 97% (90%)
3n, R = 2,4-Cl, 97% (92%)
3o, R = 4-OH, 97% (90%)
3p, R = 4-SMe, 98%(90%)

3q, 90% (85%)
3r, 98% (92%)
3s, 97% (90%)
3t, 99% (92%)
3u, 98% (90%)
3v, 96% (90%)
3w, 95% (89%)
3x, 98% (92%)

[a] Reaction conditions: substrate (1.0 mmol), CuI (5 mol%), TEMPO (5 mol%), NH₃ (aq., 25–28% w/w, 8 equiv), H₂O (3 mL), refluxing under air for 24 h, determined by GC, isolated yields in parentheses.

the copper-based catalytic system showed excellent reactivity, selectivity and functional groups compatibility. A plethora of aromatic primary alcohols underwent selective oxidative conversions to afford the corresponding nitriles in good to excellent isolated yields. Benzyl alcohol and its derivatives bearing electron-donating groups such as MeO, Me, and BnO, exhibited good reactivity with almost quantitative conversions to the corresponding products (Table 3, **3a--g**). Similar reactivities were also observed with substrates bearing electron-withdrawing groups, including halogen and nitro substituents (Table 3, **3h–n** and **3t**) which could be further derivatized. Moreover, substrates bearing p-COOH or p-CO₂Me groups, which exhibit lower activity in other systems, were also effectively transformed into 4-cyanobenzoic acid and methyl 4-cyanobenzoate, respectively, as the only products (Table 3, **3w** and **3x**). Nota-

Gratifyingly, the employment of water as a green solvent in our system greatly facilitates the separation of organic compounds (using ethyl acetate as an extraction solvent) from the reaction system. The recyclability of our catalyst system was tested using 4-methoxybenzyl alcohol **1c** as a model substrate. The separated aqueous phase was charged with fresh alcohol, 3.0 equiv aqueous ammonia and 1.0 mol% TEMPO in the residual aqueous solution after each cycle. To our delight, the recovered system was still highly effective for the conversion of alcohol into the desired nitrile compound with excellent yield and selectivity (Table 4, entries 2–6). The reusability of the catalyst system using excess aqueous ammonia makes this protocol more practically valuable.

On the basis of preliminary mechanistic studies[11b, 13] and our previous work,[9k,m] we propose the CuI mediated TEMPO oxidation mechanism shown in Scheme 1. Initially, CuI coordinates with NH₃ and H₂O to form Cu^I intermediate A, which after oxidation with TEMPOH and O₂, generates the Cu^II intermediate **B**. Metallization of the OH group of alcohol **1** with Cu^II intermediate **B** leads to Cu^II–OR intermediate **C**, which is subsequently reduction by TEMPO to give the Cu^I intermediate **A** meanwhile the -OR group undergoes a hydrogen abstraction mechanism to give the corresponding aldehyde **2**. The aldehyde proceeds a rapid conversion to the imine in the presence of 8.0 equiv
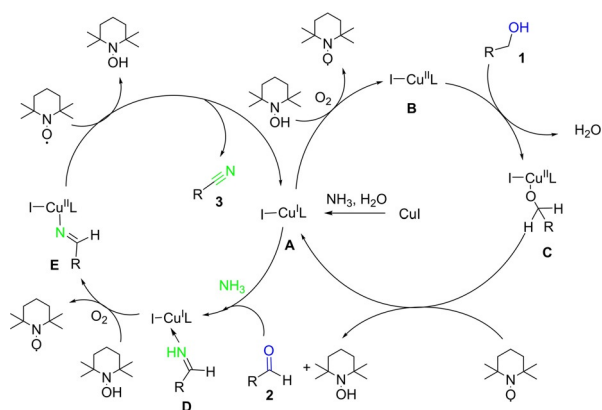
Scheme 1. The proposed mechanism for the reaction.

ammonia. The transient imine intermediate, being a better ligand than either the aldehyde, forms the favored Cu^I-imine intermediate **D**, which may trigger the second oxidation cycle leading to the corresponding nitrile **3**.

3. Conclusions

In conclusion, a novel, environmentally benign and efficient copper-catalyzed selective alcohol oxidation and cyanation has been developed in neat water under air. The transformation is effectively facilitated by aqueous ammonia (NH$_3$·H$_2$O) as the simplest N-containing ligand. Notably, by tuning the amount of aqueous ammonia in neat water, the exclusive formation of both aldehydes and aryl nitriles was accomplished with good to excellent yields. Additionally, the catalytic system exhibits a high level of functional group tolerance, being suitable for —OH, —NO$_2$, esters and other heteroaryl functionalities. This one-pot green oxidation protocol provides an important synthetic route for the selective preparation of either aldehydes or nitriles from commercially available alcohols, a copper source and ammonia.

Experimental Section

General Procedure for Direct Conversion of Primary Alcohols into Aldehydes

A mixture of alcohol (1.0 mmol), CuI (0.0095 g, 0.05 mmol), TEMPO (0.0078 g, 0.05 mmol), aqueous ammonia (2.6×10^{-2} mol L^{-1}, 3.0 mL) were added to a 150 mL seal tube. The resulting deep blue solution was vigorously stirred in air atmosphere at reflux temperature for 18–24 h. After the reaction, the residue was extracted with ethyl acetate (3×5.0 mL). Combined organic phase and the solvent were removed under vacuum to afford the crude product, which was purified by column chromatography on silica gel to give the pure product.

General Procedure for Direct Conversion of Primary Alcohols into Nitriles

A mixture of alcohol (1.0 mmol), CuI (0.0095 g, 0.05 mmol), TEMPO (0.0078 g, 0.05 mmol), NH$_3$ (aq., 25–28 % w/w, 600 μL, 8.0 mmol),

H$_2$O (3.0 mL) were added to a 150 mL seal tube. The resulting deep blue solution was vigorously stirred in air atmosphere at reflux temperature for 24 h. After the reaction, the residue was extracted with ethyl acetate (3×5.0 mL). Combined organic phase and the solvent were removed under vacuum to afford the crude product, which was purified by column chromatography on silica gel to give the pure product.

The experiments of excess ammonia reused. After the reaction, the product was separated from reaction system and the organic phase was detected by GC-MS, using ethyl acetate (3 ×10.0 mL) as extraction agent. Then, charging fresh 4-methoxybenzyl alcohol (0.1382 g, 1.0 mmol), TEMPO (0.0016 g, 0.01 mmol), NH$_3$ (aq., 25–28 % w/w, 230 μL, 3.0 mmol), in the residual aqueous solution. The solution was vigorously stirred in air atmosphere at reflux temperature for 24 h. The operation was repeated for 5 times.

Conflict of Interest

The authors declare no conflict of interest.

[1] a) M. Hudlicky, *Anal. Chem.* **1990**, *200*, 187–195; b) R. W. Dugger, J. A. Ragan, D. H. B. Ripin, *Org. Process Res. Dev.* **2005**, *9*, 253–258; c) J. S. Carey, D. Laffan, C. Thomson, M. T. Williams, *Org. Biomol. Chem.* **2006**, *4*, 2337–2347.

[2] a) M. S. Sigman, D. R. Jensen, *Acc. Chem. Res.* **2006**, *39*, 221–229; b) K. Karimi, S. Abedi, J. H. Clark, V. Budarin, *Angew. Chem. Int. Ed.* **2006**, *45*, 4776–4779; *Angew. Chem.* **2006**, *118*, 4894–4897; c) S. F. J. Hackett, R. M. Brydson, M. H. Gass, I. Harvey, A. D. Newman, K. Wilson, A. F. Lee, *Angew. Chem. Int. Ed.* **2007**, *46*, 8593–8596; *Angew. Chem.* **2007**, *119*, 8747–8750; d) E. V. Chubarova, M. H. Dickman, B. Keita, L. Nadjo, F. Miserque, M. Mifsud, I. W. C. E. Arends, U. Kortz, *Angew. Chem. Int. Ed.* **2008**, *47*, 9542–9546; *Angew. Chem.* **2008**, *120*, 9685–9689; e) B. Karimi, A. Zamani, S. Abedi, J. H. Clark, *Green Chem.* **2009**, *11*, 109–119; f) D. Barats, R. Neumann, *Adv. Synth. Catal.* **2010**, *352*, 293–298; g) G. Z. Chen, S. J. Wu, H. L. Liu, H. F. Jiang, Y. W. Li, *Green Chem.* **2013**, *15*, 230–235; h) B. Karimi, M. Khorasani, H. Vali, C. Vargas, R. Luque, *ACS Catal.* **2015**, *5*, 4189–4200.

[3] a) Y. M. A. Yamada, T. Arakawa, H. Hocke, Y. Uozumi, *Angew. Chem. Int. Ed.* **2007**, *46*, 704–706; *Angew. Chem.* **2007**, *119*, 718–720; b) T. Wang, C. X. Xiao, L. Yan, L. Xu, J. Luo, H. Shou, Y. Kou, H. Liu, *Chem. Commun.* **2007**, *39*, 4375–4377; c) C. Miyamura, R. Matsubara, S. Kobayashi, *Chem. Commun.* **2008**, *39*, 2031–2033; d) Y. H. Ng, S. Ikeda, Y. Morita, T. Harada, K. Ikeue, M. Matsumura, *J. Phys. Chem. C* **2009**, *113*, 12799–12805.

[4] a) A. Abad, C. Concepcion, A. Corma, H. Garcia, *Angew. Chem. Int. Ed.* **2005**, *44*, 4066–4069; *Angew. Chem.* **2005**, *117*, 4134–4137; b) F. Z. Su, Y. M. Liu, L. C. Wang, Y. Cao, H. Y. He, K. N. Fan, *Angew. Chem. Int. Ed.* **2008**, *47*, 334–337; *Angew. Chem.* **2008**, *120*, 340–343; c) K. Kaizuka, H. Miyamura, S. Kobayashi, *J. Am. Chem. Soc.* **2010**, *132*, 15096–15098; d) B. Karimi, F. K. Esfahani, *Adv. Synth. Catal.* **2012**, *354*, 1319–1326; e) S. Yamazoe, K. Koyasu, T. Tsukuda, *Acc. Chem. Res.* **2014**, *47*, 816–824; f) J. Yu, J. Y. Li, H. L. Wei, J. W. Zheng, H. Q. Su, X. J. Wang, *J. Mol. Catal. A:*

Chem. **2014**, *395*, 128–136; g) L. Han, P. Xing, B. Jiang, *Org. Lett.* **2014**, *16*, 3428–3431; h) Y. X. Li, Y. Gao, C. Yang, *Chem. Commun.* **2015**, *51*, 7721–7724.

[5] a) K. Yamaguchi, K. Mori, T. Mizugaki, K. Ebitani, K. Kaneda, *J. Am. Chem. Soc.* **2000**, *122*, 7144–7145; b) K. Yamaguchi, N. Mizuno, *Angew. Chem. Int. Ed.* **2002**, *41*, 4538–4542; *Angew. Chem.* **2002**, *114*, 4720–4724; c) M. Kotani, T. Koike, K. Yamaguchi, N. Mizuno, *Green Chem.* **2006**, *8*, 735–741; d) N. Zotova, K. Hellgardt, G. H. Kelsall, A. S. Jessimanc, K. K. Hii, *Green Chem.* **2010**, *12*, 2157–2163; e) Y. J. Zhang, J. H. Wang, T. Zhang, *Chem. Commun.* **2011**, *47*, 5307–5309; f) D. S. Mannel, S. S. Stahl, T. W. Root, *Org. Process Res. Dev.* **2014**, *18*, 1503–1508.

[6] a) L. H. Liu, M. Yu, B. B. Wayland, X. F. Fu, *Chem. Commun.* **2010**, *46*, 6353–6355; b) S. Muratsugu, S. Tajima, M. Tada, *Chem. Lett.* **2014**, *43*, 1321–1323; c) Y. Sawama, K. Morita, T. Yamada, S. Nagata, Y. Yabe, Y. Monguchi, H. Sajiki, *Green Chem.* **2014**, *16*, 3439–3443; d) F. Saleem, G. K. Rao, A. Kumar, G. Mukherjee, A. K. Singh, *Organometallics* **2014**, *33*, 2341–2351.

[7] a) T. Iwahama, Y. Yoshino, T. Keitoku, S. Sakaguchi, Y. Ishii, *J. Org. Chem.* **2000**, *65*, 6502–6507; b) V. B. Sharma, S. L. Jain, B. Sain, *J. Mol. Catal. A: Chem.* **2004**, *212*, 55–59; c) V. B. Sharma, S. L. Jain, B. Sain, *Tetrahedron Lett.* **2003**, *44*, 383–386; d) V. Panwar, P. Kumar, S. S. Ray, S. L. Jain, *Tetrahedron Lett.* **2015**, *56*, 3948–3953; e) A. Mon-dal, D. Mukherjee, B. Adhikary, M. A. Ahmed, *J. Nanopart. Res.* **2016**, *18*, 117.

[8] a) S. E. Martin, D. F. Suarez, *Tetrahedron Lett.* **2002**, *43*, 4475–4479; b) N. Wang, R. Liu, J. Chen, X. Liang, *Chem. Commun.* **2005**, *41*, 5322; c) L. Wang, S. S. Shang, G. Li, L. Ren, Y. Lv, S. Gao, *J. Org. Chem.* **2016**, *81*, 2189–2193.

[9] a) M. F. Semmelhack, C. R. Schmid, D. A. Cortés, C. S. Chou, *J. Am. Chem. Soc.* **1984**, *106*, 3374–3376; b) I. E. Marko, P. R. Giles, M. Tsukazaki, S. M. Brown, C. J. Urch, *Science* **1996**, *274*, 2044–2046; c) P. Gamez, I. W. C. E. Arends, J. Reedijka, R. A. Sheldon, *Chem. Commun.* **2003**, *39*, 2414–2415; d) J. M. Hoover, S. S. Stahl, *J. Am. Chem. Soc.* **2011**, *133*, 16901–16910; e) J. E. Steves, S. S. Stahl, *J. Am. Chem. Soc.* **2013**, *135*, 15742–

15745; f) J. F. Greene, J. M. Hoover, D. S. Mannel, T. W. Root, S. S. Stahl, *Org. Process Res. Dev.* **2013**, *17*, 1247–1251; g) L. M. Dornan, Q. Cao, J. C. A. Flanagan, J. J. Crawford, M. J. Cook, M. J. Muldoon, *Chem. Commun.* **2013**, *49*, 6030–6032; h) J. E. Steves, S. S. Stahl, *J. Org. Chem.* **2015**, *80*, 11184–11188; i) X. Xie, S. S. Stahl, *J. Am. Chem. Soc.* **2015**, *137*, 3767–3770; j) S. L. Zultanski, J. Zhao, S. S. Stahl, *J. Am. Chem. Soc.* **2016**, *138*, 6416–6419; k) G. F. Zhang, X. W. Han, Y. X. Luan, Y. Wang, X. Wen, C. R. Ding, *Chem. Commun.* **2013**, *49*, 7908–7910; l) G. F. Zhang, J. Lei, X. W. Han, Y. X. Luan, C. R. Ding, S. Shan, *Synlett* **2015**, *26*, 779–784; m) G. F. Zhang, X. W. Han, Y. X. Luan, Y. Wang, X. Wen, L. Xu, C. R. Ding, J. R. Gao, *RSC Adv.* **2013**, *3*, 19255–19258.

[10] a) K. T. Mahmudov, M. N. Kopylovich, M. F. C. D. Silva, P. J. Figiel, Y. Y. Karabach, A. J. L. Pombeiro, *J. Mol. Catal. A: Chem.* **2010**, *318*, 44–50; b) Z. Z. Hu, F. M. Kerton, *Appl. Catal. A* **2012**, *413*, 332–339.

[11] a) D. K. T. Yadav, B. M. Bhanage, *Eur. J. Org. Chem.* **2013**, *78*, 5106–5110; b) W. Y. Yin, C. M. Wang, Y. Huang, *Org. Lett.* **2013**, *15*, 1850–1853; c) D. W. Tan, J. B. Xie, Q. Li, H. X. Li, J. C. Li, H. Y. Li, J. P. Lang, *Dalton Trans.* **2014**, *43*, 14061–14071; d) J. B. Xie, J. J. Bao, H. X. Li, D. W. Tan, H. Y. Li, J. P. Lang, *RSC Adv.* **2014**, *4*, 54007–54017; e) D. Azarifar, H. Najminejad, *J. Iran. Chem. Soc.* **2015**, *12*, 107–111; f) G. F. Zhang, G. H. Zhang, J. Lei, S. S. Li, S. J. Xu, C. R. Ding, S. Shan, *Chem. Res. Chin. Univ.* **2016**, *32*, 586–593; g) S. S. Shang, L. Y. Wang, W. Dai, B. Chen, Y. Lv, S. Gao, *Catal. Sci. Technol.* **2016**, *6*, 5746–5753.

[12] J. Quirk, M. Thornton, P. Kirkpatrick, *Nat. Rev. Drug. Discov.* **2003**, *2*, 769–770.

[13] a) J. M. Hoover, B. L. Ryland, S. S. Stahl, *J. Am. Chem. Soc.* **2011**, *135*, 2357–2367; b) J. M. Hoover, B. L. Ryland, S. S. Stahl, *ACS Catal.* **2013**, *3*, 2599–2605; c) B. L. Ryland, S. D. McCann, T. C. Brunold, S. S. Stahl, *J. Am. Chem. Soc.* **2014**, *136*, 12166–12173; d) S. D. McCann, S. S. Stahl, *J. Am. Chem. Soc.* **2015**, *138*, 199–206.