DOI: 10.1002/cjoc.201400141

4-Benzamido-TEMPO Catalyzed Oxidation of a Broad Range of Alcohols to the Carbonyl Compounds with $NaBrO_3$ under Mild Conditions

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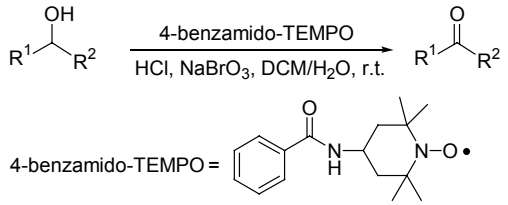
4-Benzamido-TEMPO catalyzed oxidation system for conversion of a wide range of alcohols to the aldehydes or ketones with $NaBrO_3$ under room temperature conditions has been developed. The credible, operationally convenient and economical, and condition mild oxidation protocol is particularly of interest in laboratory and in fine chemicals manufacture.

Keywords alcohols, oxidation, carbonyl compounds, sodium bromated, 4-benzamido-TEMPO

Introduction

The selective oxidation of alcohols into their corresponding aldehydes or ketones is a very important functional group transformation in organic synthesis.[1] In recent years, major efforts in the transformation have been devoted to the discovery and development of environmentally benign methods using O_2 or H_2O_2 as the terminal oxidant.[2] Although catalytic oxidation with O_2 or H_2O_2 is certainly of importance, there are also important advantages in the use of less toxic or nontoxic and easily available other oxidants. This is true especially for smaller scale operations such as in fine chemicals manufacture, where the credible, operationally convenient and economical, as well as condition mild oxidation methods are particularly of importance.[3] As such, one key criterion is the use of minimum quantities or total nonuse of auxiliary additives. Herein, we reported a 4-benzamido-TEMPO catalyst system for oxidation of a broad range of alcohols to the aldehydes or ketones with sodium bromate oxidant under mild conditions (Scheme 1).

Scheme 1 Oxidation of alcohols with 4-benzamido-TEMPO/HCl/$NaBrO_3$



Sodium bromate is a commercially available and inexpensive compound, and has been extensively used in organic synthesis. It can be used as an effective bromohydroxylation reagent for alkenes and alkynes.[4] It can also oxidize sulfides to the sulfoxides, thiols to the disulfides and hydroquinones to the quinones.[5] As the bromine of sodium bromate is a positive five-valence element, the oxidation of 1 mol of alcohols to the aldehydes or ketones only requires 1/3 mol sodium bromate in theory. In addition, the oxidative systems with $NaBrO_3$ oxidant are free of transition metals, therefore, the oxidative systems are intrinsically devoid of complications caused by transition metal oxidants. Sodium bromate had been previously employed in the presence of transition metals as catalysts to oxidize alcohols to aldehydes.[6] In addition, transition metal-free catalytic oxidations of alcohols with sodium bromate as oxidant or co-catalyst were also reported.[7,5c] However, a major drawback to these reported methods is their inability to oxidize primary aliphatic alcohols to the aldehydes.

We and other groups have recently reported a series of TEMPO-based catalyst systems for aerobic oxidation of alcohols to the aldehydes or ketones.[8] Based on our previous work,[8e,8f] we find the ability of 4-benzamido-TEMPO to catalytically oxidize primary aliphatic alcohols to the aldehydes with high effectiveness. We reasoned that 4-benzamido-TEMPO in combination with sodium bromate would be a competent catalytic system for oxidation of a wide range of alcohols to the carbonyl compounds.

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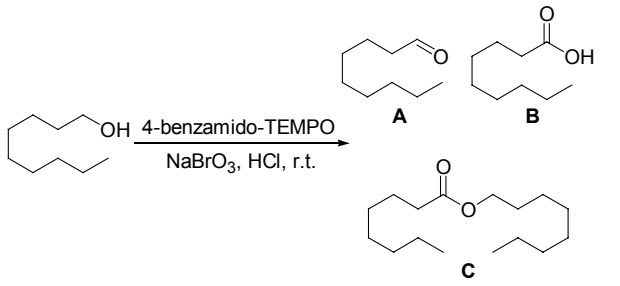
Received March 10, 2014; accepted April 15, 2014; published online May 22, 2014.
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/cjoc.201400141 or from the author.

Results and Discussion

The investigation began with 1-octyl alcohol (1 mmol) as a representative substrate, 4-benzamido-TEMPO as the catalyst, sodium bromate as the oxidant at room temperature for optimization of the reaction conditions (Table 1). As can be seen in Table 1, the catalytic system is applicable to a wide range of solvents with regard to the conversion (Table 1, Entries 1—10). The use of a mixture of H_2O and AcOH, H_2O and DMF, H_2O and dioxane as the solvents can provide high conversion. Fortunately, when a mixture of DCM and H_2O was used we obtained 69% of conversion and 93% of selectivity (Table 1, Entry 3). However, low conversion and selectivity were observed when DCM and H_2O were used as the solvent, separately (Table 1, Entries 9—10). We were pleased to find that 100% of conversion and 96% of selectivity were reached when 2 mol% of HCl were extra added to the catalytic system under standard reaction conditions (Table 1, Entry 11).

Table 1 Optimization of reaction conditions[a]



Entry	HCl/mol%	Solvent	Time/h	Conv.[b]/%	Select.[b]/% (A/B/C)
1	5	CH_3CN/H_2O	1	16	75/6/19
2	5	DCE/H_2O	1	85	78/4/18
3	5	DCM/H_2O	1	69	93/0/7
4	5	$PhMe/H_2O$	1	12	50/0/50
5	5	$AcOH/H_2O$	1	86	40/41/19
6	5	THF/H_2O	1	50	40/50/10
7	5	DMF/H_2O	1	70	30/64/6
8	5	$Dioxane/H_2O$	1	68	29/59/12
9[c]	5	DCM	1	57	14/0/86
10[c]	5	H_2O	1	15	0/0/100
11	**2**	**DCM/H_2O**	**2**	**100**	**96/0/4**
12	1	DCM/H_2O	2	0	0/0/0
13[d]	2	DCM/H_2O	2	90	72/0/28
14	0	DCM/H_2O	2	0	0/0/0
15[e]	2	DCM/H_2O	2	0	0/0/0
16[f]	2	DCM/H_2O	2	0	0/0/0
17[g]	2	DCM/H_2O	2	92	97/0/3

[a] The reactions were carried out with alcohols (1 mmol), 4-benzamido-TEMPO (2 mol%), $NaBrO_3$ (0.35 mmol, H_2O 0.5 mL), solvent (1.5 mL, 2∶1) at room temperature. [b] GC yield. [c] $NaBrO_3$ was added in solid. [d] 4-Benzamido-TEMPO (1 mol%). [e] 4-Benzamido-TEMPO (0 mol%). [f] $NaBrO_3$ (0 mmol). [g] $NaBrO_3$ (0.3 mmol, H_2O 0.5 mL).

The use amount of 4-benzamido-TEMPO greatly influenced the selectivity of the reaction. Decrease of the use amount of 4-benzamido-TEMPO to 1 mol% led to the generation of 28% of ester (Table 1, Entry13). All the HCl, $NaBrO_3$ and 4-benzamido-TEMPO are required, and if any additive is absent the reaction will not proceed (Table 1, Entries 14—16). As expected, only 33 mol% of $NaBrO_3$ was required for totall conversion of the substrate. Therefore, the optimal reaction conditions were considered as 2 mol% HCl, 35 mol% $NaBrO_3$, 2 mol% 4-benzamido-TEMPO and DCM/H_2O as the solvent at room temperature.

Having established the optimal conditions, we next examined the range of alcohols, and the results are summarized in Table 2. Several features of this simple yet robust catalytic system are worth noting. First, the catalytic system results in fairly efficient conversion of a broad spectrum of alcohols to the corresponding aldehydes or ketones under very mild conditions. The reaction tolerates both simple aliphatic alcohols (Table 2, Entries 14 and 17—20) and more hindered derivatives (Entries 11—12 and 21) as well as protecting groups (Entry 15). Most of the substrates employed were quantitatively converted into the corresponding aldehydes or ketones with 99% selectivity. The benzylic alcohols, including pyridine methanol, were converted into the corresponding benzaldehydes or ketones in very high isolated yields (Table 2, Entries 1—10). The electronic properties of the substituents on the benzene ring seldom interfered the high yields of reactions. Of particular interest is the oxidation of aliphatic primary alcohols under these conditions. Although several effective methods for oxidation of primary alcohols have been reported, the overoxidation and/or generation of esters has been a recurring problem toward oxidation of aliphatic primary alcohols. The present protocol for oxidation of aliphatic primary alcohols showed that carboxylic acid and esters generated less than 5% (Table 2, Entries 15—20). It is interesting to note that the alcohols, which remain difficult recalcitrant substrates in many anerobic and aerobic oxidation protocols, were smoothly oxidized to the ketones in more than 90% isolated yields (Table 2, Entries 21 and 22).

Conclusions

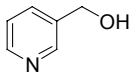
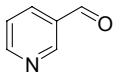
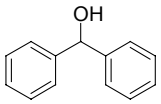
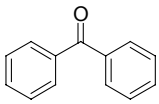
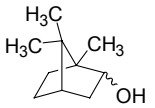
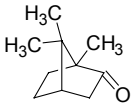
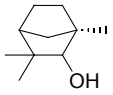
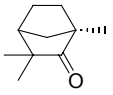
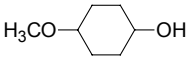
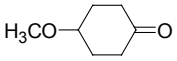
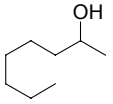
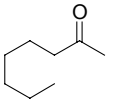
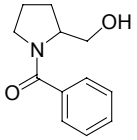
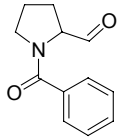
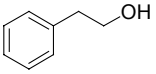
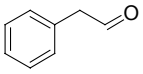
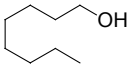
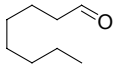
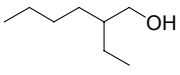
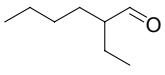
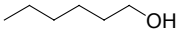
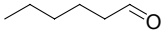
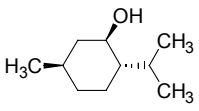
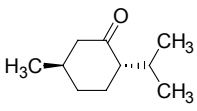
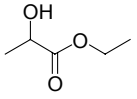
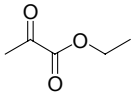
In conclusion, we have developed a highly efficient catalyst system for oxidation of a wide range of alcohols by using 4-benzamido-TEMPO as the catalyst and $NaBrO_3$ as the terminal oxidant under room temperature. This inexpensive and convenient catalytic system could be broadly used in laboratory and in fine chemicals manufacture.

Experimental

General experimental methods

All the chemical reagents were obtained from com-

Table 2 Scope of the 4-benzamido-TEMPO/HCl/$NaBrO_3$ system[a]

Entry	Alcohol	Product	Time/h	Conv.[b] /%	Yield[b]/%
1	$C_6H_5CH_2OH$	C_6H_5CHO	1	99	99
2	2-$MeC_6H_4CH_2OH$	2-MeC_6H_4CHO	1	99	99
3	4-$NO_2C_6H_4CH_2OH$	4-$NO_2C_6H_4CHO$	1	99	99 (99)
4	2-$ClC_6H_4CH_2OH$	2-ClC_6H_4CHO	1	99	99 (96)
5	4-$FC_6H_4CH_2OH$	4-FC_6H_4CHO	1	99	99
6	4-$BrC_6H_4CH_2OH$	4-BrC_6H_4CHO	1	99	99
7	4-$IC_6H_4CH_2OH$	4-IC_6H_4CHO	1	99	99
8	4-$MeOC_6H_4CH_2OH$	4-$MeOC_6H_4CHO$	1	99	99
9[c]			1	99	99 (93)
10			2	99	99 (93)
11			1.5	99	99 (92)
12			4	99	99 (93)
13			1.5	99	99 (94)
14			2	99	99
15			4	99	99 (93)
16			1	99	98 (91)
17			2	99	96 (90)
18			5	95	96
19			2	99	97
20	tetradecan-1-ol	tetradecanal	4	99	95
21[d]			9	99	99 (92)
22[d]			8	97	99 (90)

[a] The reactions were carried out with alcohols (1 mmol), 4-benzamido-TEMPO (2 mol%), $NaBrO_3$ (0.35 mmol, H_2O 0.5mL), HCl (2 mol%) at room temperature. [b] Detected by GC. Isolated yields are in parentheses. [c] 1 equiv. AcOH was added. [d] 4-Benzamido-TEMPO (10 mol%), $NaBrO_3$ (1 mmol, H_2O 0.5mL) were used.

mercial sources and used without further purification. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were obtained on a Bruker DRX-400 NMR using $CDCl_3$ as the solution with TMS as an internal reference. Column chromatography was performed with 300－400 mesh silica gel. GC analysis was measured on Agilent 7890N. General GC conditions: HP-5 column, 30 m×0.32 mm (id); FID detector; injection: 0.2 μL; carrier gas: N_2; carrier gas rate: 1.2 mL/min; area normalization. The reactions were detected under the conditions: column temperature: 75 ℃ for 2 min, rising to 300 ℃ at a rate of 10 ℃/min.

Procedure for the catalytic oxidation of alcohols

A mixture of alcohols (1 mmol), 4-benzamido-TEMPO (0.02 mmol, 5.5 mg) and HCl (3.7%, 0.02 mmol, 20 mg) in DCM (1 mL) were powerfully stirred at room temperature, aq. sodium bromate (0.35 mmol, 0.5 mL) was added once. The mixture was continuously and powerfully stirred for a certain period of time, the conversion and selectivity of the product were detected by GC. After completion of the reaction, H_2O (10 mL) and DCM (10 mL) were added, the organic layer was separated and the aqueous layer extracted with dichloromethane (10 mL×2). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified on silica gel column chromatography (petroleum/EtOAc＝10/1) to give the corresponding aldehydes or ketones.

4-Nitrobenzaldehyde ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.15 (s, 1H), 8.39 (d, J＝7.6 Hz, 2H), 8.07 (d, J＝8.4 Hz, 2H); ^{13}C NMR (100 Hz, $CDCl_3$) δ: 190.2, 151.1, 140.0, 130.4, 124.2.

2-Chlorobenzaldehyde ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.47 (s, 1H), 7.91 (d, J＝8 Hz, 1H), 7.51 (t, J＝8.4 Hz, 1H), 7.44 (d, J＝8 Hz, 1H), 7.37 (t, J＝8 Hz, 1H); ^{13}C NMR (100 Hz, $CDCl_3$) δ: 189.8, 137.9, 135.1, 132.4, 130.6, 129.3, 127.2.

Nicotinaldehyde ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.10 (s, 1H), 9.07 (s, 1H), 8.83 (d, J＝4.8 Hz, 1H), 8.16 (d, J＝8 Hz, 1H), 7.46－7.49 (dd, J_1＝J_2＝4.8 Hz, 1H).

Benzophenone ^{1}H NMR (400 MHz,$CDCl_3$) δ: 7.80 (d, J＝8 Hz, 4H), 7.58 (t, J＝8 Hz, 2H), 7.48 (t, J＝7.6 Hz, 4H).

1,7,7-Trimethylbicyclo[2.2.1]heptan-2-one ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.32 (d, J＝2.4 Hz, 1H), 2.28－2.27 (m, 1H), 2.10－2.00 (m, 1H), 1.91－1.88 (m, 1H), 1.82－1.77 (m, 1H), 1.67－1.60 (m, 1H), 1.36－1.32 (m, 2H), 0.91 (s, 3H), 0.86 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (100 Hz, $CDCl_3$) δ: 57.6, 46.7, 43.2, 43.0, 29.9, 27.0, 19.7, 19.1, 9.2.

(1*R*)-1,3,3-Trimethylbicyclo[2.2.1]heptan-2-one ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.10－2.08 (m, 1H), 1.78－1.63 (m, 3H), 1.54－1.47 (m, 2H), 1.37－1.30 (m, 1H), 1.09 (s, 3H), 0.98 (s, 6H).

4-Methoxycyclohexanone ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.61－3.55 (m, 1H), 3.37 (s, 3H), 2.56－2.48 (m, 2H), 2.25－2.19 (m, 2H), 2.09－2.01 (m, 2H), 1.94－1.85 (m, 2H).

1-Benzoylpyrrolidine-2-carbaldehyde ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.68 (s, 1H), 7.59－7.57 (m, 2H), 7.45－7.40 (m, 3H), 4.66 (t, J＝6.8 Hz, 1H), 3.66－3.53 (m, 2H), 2.24－2.16 (m, 1H), 2.07－2.00 (m, 1H), 1.96－1.89 (m, 2H); ^{13}C NMR (100 Hz, $CDCl_3$) δ: 199.3, 170.1, 135.6, 130.4, 128.2, 127.2, 65.0, 50.0, 26.2, 25.3.

2-Phenylacetaldehyde ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.75 (s, 1H), 7.39－7.21 (m, 5H), 3.68 (d, J＝2 Hz, 2H); ^{13}C NMR (100 Hz, $CDCl_3$) δ: 199.4, 131.8, 129.6, 129.0, 127.4, 50.5.

Octanal ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.75 (s, 1H), 2.42－2.41 (m, 2H), 1.63－1.61 (m, 2H), 1.29－1.27 (m, 8H), 0.87 (t, J＝7.2 Hz, 3H); ^{13}C NMR (100 Hz, $CDCl_3$) δ: 202.9, 43.8, 31.5, 29.0, 28.9, 22.5, 22.0, 14.0.

(2*S*,5*R*)-2-Isopropyl-5-methylcyclohexanone ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.30 (d, J＝12.8 Hz, 1H), 2.13－1.78 (m, 6H), 1.35－1.28 (m, 2H), 0.96 (d, J＝6.4 Hz, 3H), 0.89 (d, J＝6.8 Hz, 3H), 0.83 (d, J＝6.8 Hz, 3H); ^{13}C NMR (100 Hz, $CDCl_3$) δ: 212.2, 55.7, 50.7, 35.3, 33.8, 27.7, 25.8, 22.1, 21.1, 18.6.

Ethyl 2-oxopropanoate ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.32－4.26 (q, J＝7.2 Hz, 2H), 2.44 (d, J＝0.8 Hz, 3H), 1.34 (t, J＝7.2 Hz, 3H).

Acknowledgement

We are grateful to the financial support from the National Natural Science Foundation of China (No. 21072055) and the National High Technology Research and Development Program of China (863 Program) (No. 2008AA06Z306).

References

[1] Sheldon, R. A.; Kochi, J. K. *Metal-catalyzed Oxidation of Organic Compounds*, Academic Press, New York, **1981**; (b) Hudlicky, M. *Oxidations in Organic Chemistry*, ACS, Washington, DC, **1990**; (c) Backväll, J. E. *Modern Oxidation Methods*, Wiley-VCH, New York, **2004**; (d) Mallat, T.; Baiker, A. *Chem. Rev.* **2004**, *104*, 3037.

[2] (a) Skibida, I. P.; Sakharow, A. M. *Catal. Today* **1996**, *27*, 187; (b) Markó, I. E.; Giles, P. R.; Tsukazaki, M.; Brown, S. M.; Urch, C. J. *Science* **1996**, *274*, 2044; (c) Markó, I. E.; Giles, P. R.; Tsukazaki, M.; ChelléRegnaut, I.; Gautier, A.; Brown, S. M.; Urch, C. J. *J. Org. Chem.* **1999**, *64*, 2433; (d) Noyori, R.; Aoki, M.; Sato, K. *Chem. Commun.* **2003**, 1977; (e) Mallat, T.; Baiker, A. *Chem. Rev.* **2004**, *104*, 3037; (f) Jiang, N.; Ragauskas, A. J. *Tetrahedron Lett.* **2005**, *46*, 3323; (g) Velusamy, S.; Kumar, A. V.; Saini, R.; Punniyamurthy, T. *Tetrahedron Lett.* **2005**, *46*, 3819; (h) Miao, C.-X.; He, L.-N.; Wang, J.-Q.; Wang, J.-L. *Adv. Synth. Catal.* **2009**, *315*, 2209; (i) Hoover, J. M.; Stahl, S. S. *J. Am. Chem. Soc.* **2011**, *133*, 16901; (j) Wang, L.; Zhang, W.; Zeng, S.; Su, D.; Meng, X.; Xiao, F. *Chin. J. Chem.* **2012**, *30*, 2189; (k) Steves, J. E.; Stahl, S. S. *J. Am. Chem. Soc.* **2013**, *135*, 15742.

[3] Hayashi, M.; Shibuya, M.; Iwabuchi, Y. *J. Org. Chem.* **2012**, *77*, 3005.

[4] (a) Masuda, H.; Takase, K.; Nishio, M.; Hasegawa, A.; Nishiyama, Y.; Ishii, Y. *J. Org. Chem.* **1994**, *59*, 5550; (b) Agrawal, M. K.; Adimurthy, S.; Ganguly, B.; Ghosh, P. K. *Tetrahedron* **2009**, *65*, 2791.

[5] (a) Ali, M. H.; Mcdermott, M. *Tetrahedron Lett.* **2002**, *43*, 6271; (b) Shaabani, A.; Bazgir, A.; Soleimani, K.; Salehi, P. *Synth. Commun.* **2003**, *33*, 2935; (c) Joshi, G.; Bhadra, S.; Ghosh, S.; Agrawal, M. K.; Ganguly, B.; Adimurthy, S.; Ghosh, P. K.; Ranu, B. C. *Ind. Eng. Chem. Res.* **2010**, *49*, 1236.

[6] (a) Shaabani, A.; Ameri, M. *J. Chem. Res.* (*S*) **1998**, 100; (b) Kanemoto, S.; Tomioka, H.; Oshima, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 105; (c) Shirini, F.; Zolfigil, M. A.; Torabi, S. *Synth. Commun.* **2006**, *36*, 2833; (d) Shaabani, A.; Behnam, M.; Rezayan, A. H. *Catal. Commun.* **2009**, *10*, 1074; (e) Hu, Z.; Ma, L.; Xie, J.; Du, H.; Lam, W. W. Y.; Lau, T.-C. *New J. Chem.* **2013**, *37*, 1707.

[7] (a) Shaabani, A.; Bazgir, A.; Abdoli, M. *Synth. Commun.* **2002**, *32*, 675; (b) Shaabani, A.; Lee, D. G. *Synth. Commun.* **2003**, *33*, 1255; (c) Zhang, J.; Jiang, Z.; Zhao, D.; He, G.; Zhou, S.; Han, S. *Chin. J. Chem.* **2013**, *31*, 794.

[8] (a) Liu, R.; Liang, X.; Dong, C.; Hu, X. *J. Am. Chem. Soc.* **2004**, *126*, 4112; (b) Liu, R.; Dong, C.; Liang, X.; Wang, X.; Hu, X. *J. Org. Chem.* **2005**, *70*, 729; (c) Wang, X.; Liu, R.; Jin, Y.; Liang, X. *Chem. Eur. J.* **2008**, *14*, 2679; (d) Wang, N.; Liu, R.; Chen, J.; Liang, X. *Chem. Commun.* **2005**, 5322; (e) Yin, W.; Chu, C.; Lu, Q.; Tao, J.; Liang, X.; Liu, R. *Adv. Synth. Catal.* **2010**, *352*, 113; (f) Tao, J.; Lu, Q.; Chu, C.; Liu, R.; Liang, X. *Synthesis* **2010**, *23*, 3974; (g) Di, L.; Hua, Z. *Adv. Synth. Catal.* **2011**, *353*, 1253; (h) Karimi, B.; Badreh, E. *Org. Biomol. Chem.* **2011**, *9*, 4194; (i) Karimi, B.; Farhangi, E. *Chem. Eur. J.* **2011**, *17*, 6056; (j) 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; (k) Wang, X.; Wang, Z. *Tetrahedron* **2011**, *67*, 3406.

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