Catalysis Communications 16 (2011) 194–197

Contents lists available at SciVerse ScienceDirect

Catalysis Communications

journal homepage: www.elsevier.com/locate/catcom

Short Communication

ZnO nanofluid as a structure base catalyst for chemoselective amidation of aliphatic carboxylic acids

Fatemeh Tamaddon *, Fatemeh Aboee, Alireza Nasiri

Department of Chemistry, Faculty of Science, Yazd University, Yazd 89195-741, Iran

ARTICLE INFO

Article history:
Received 13 July 2011
Received in revised form 19 September 2011
Accepted 19 September 2011
Available online 28 September 2011

Keywords:
Nanofluids
ZnO
Carboxylic acids
Acylation
Solvent-free
Direct amidation

ABSTRACT

ZnO nanofluids were synthesized and utilized as a new reaction media in the preparation of amides via direct amidation of aliphatic carboxylic acids with primary amines under solvent-free conditions. High yields and good selectivity are achieved with this psudo-homogeneous catalyst, while the recovered nanoZnO was reusable.

1. Introduction

Metal oxide promoted reactions at heterogeneous conditions is a proficient field of chemistry which is highlighted by the use of various nanosized catalysts [1–5]. Metal oxide surfaces exhibit both acid and base properties. These dualities make metal oxides as excellent adsorbent and activator of organic compounds. The promising factors which govern on the catalytic activity of metal oxides are the nature of metal cation, morphology, particle size, and surface area of them. Recent development on the nanoscience has provided great opportunity for the surface modification and chemical composition of nanosized metal oxides [5]. Metal oxide nanofluids are among the newer versions of nanocatalysts [6], which mimic the homogeneous catalysts make the maximum contact between starting materials and catalyst. They are colloidal suspension of nano-sized metal oxides in a base fluid and due to the better ability of dispersion they can be emerged as robust, active, and high surface area catalysts.

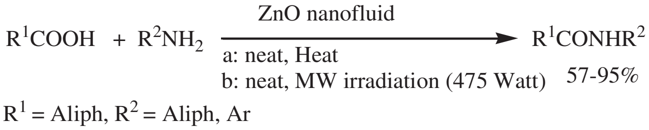
Zinc oxide is a low-priced versatile metal oxide which in both commercial and nano forms has been utilized as a professional environmentally benign catalyst in various organic transformations [7–11]. Its high heat capacity, high heat conductivity, low thermal expansion, and high melting point make it more attractive catalyst. Various nanopowder, nanoparticles, and nanofluids of ZnO have been artificially prepared by sol–gel processing and controlled hydrolysis of zinc halides, zinc alkoxides or zinc acetate [11–14]. The prepared nanoZnO by different processes vary in morphology, surface area, porosity, crystalinity, particle size, and hence catalytic properties. Recently, ZnO nanofluids have been prepared by dispersing of ZnO nanoparticles in glycerol as a base fluid and used as antibacterial agent [15].

Amides are among the most useful building blocks of natural products and biologically active compounds including drugs, peptides, lubricants, polymers, and agrochemicals [1,16–21]. Among the various developed synthetic methods, acylation of amines with acyldonors such as acid chlorides, anhydrides, esters, acyl azides and carboxylic acids have been widely used to produce amides [17–28]. Despite the less reactivity of acids, direct amidation is still the most favorite industrial process from both atom economy and environmental points of view. The low reactivity of carboxylic acid as acyldonor has been improved by the in situ activation of COOH group either in the presence of coupling agents, supports or catalysts [17–21]. Metal oxides are among the catalysts have been used as activating agents for carboxylic acids in acylation reactions [18–28]. We have recently used ZnO [29], nanoZnO [14], and other heterogeneous catalysts in a variety of organic transformations [30–32]. The drawbacks of amidation methodologies, high affinity of ZnO towards carboxyl group, and the similarity of nanofluids to homogeneous catalysts stimulated us to investigate the direct synthesis of amides using preparative ZnO nanofluids (Scheme 1).

---

* Corresponding author. Tel.: +98 3518122666; fax: +98 3518210644.
E-mail addresses: ftamaddon@yazduni.ac.ir (F. Tamaddon), ftamaddon@yazduni.ac.ir (F. Aboee), Nasiri_62@yahoo.com (A. Nasiri).

1566-7367/$ – see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.catcom.2011.09.023



$$R^1COOH + R^2NH_2 \xrightarrow[\text{a: neat, Heat; b: neat, MW irradiation (475 Watt)}]{\text{ZnO nanofluid}} R^1CONHR^2 \quad 57\text{-}95\%$$

R^1 = Aliph, R^2 = Aliph, Ar

Scheme 1. Amidation of carboxylic acids using ZnO nanofluid.

2. Experimental

Melting points were recorded on a Buchi 545 apparatus and compared with those reported in the literature. FT-IR spectra were recorded on a Brucker FT-IR. ^{1}H NMR and ^{13}C NMR were recorded on a Brucker 250, Avance in $CDCl_3$ at 250 and 62.9 MHz, respectively. All products showed the same melting points and spectroscopic data with those reported in the literature.

2.1. Preparation of ZnO nanofluids

ZnO nanoparticles were prepared according to the previously reported procedure [15]. Thus, zinc acetate dihydrate (5.5 g) was dissolved in 50 mL of deionized water and then solid NaOH (16 g) was added slowly into the solution under magnetic stirring at room temperature. A transparent $Zn(OH)_4$ solution was formed. Then 2 mL of ionic liquid 1-butyl-3-methylimidazolium bis (trifluoromethylsulfonyl) imide [bmim][NTf_2] was added to 3 mL of the above solution. The suspension was put into a domestic microwave oven (850 W) in air. 30% of the output power of the microwave was used to irradiate the mixture for 5 min (on for 10s, off for 5 s). The white precipitate was collected by centrifugation, washed with deionized water and ethanol several times, and dried in vacuum oven at 40 °C for 10 h. The mean particle size of these nanoparticles was between 37 and 47 nm [15].

ZnO nanofluids have been prepared by dispersing of ZnO nanoparticles in glycerol as a base fluid [15]. In this work, ZnO nanofluids were prepared as homogeny suspensions of ZnO nanoparticles in various amounts of glycerol. Thus, different weight ratios of optimized amount of ZnO nanoparticles (0.08 g, 1 mmol) to glycerol were magnetically stirred at room temperature to give ZnO nanofluids. No agglomeration and sedimentation of the particles in the samples was observed during their use.

2.2. General experimental procedure for ZnO nanofluid catalyzed preparation of amides

To a mixture of amine (10 mmol) and ZnO nanofluid (1.6 g, 1:1 weight ratio of nanoZno to glycerole) was added carboxylic acid (11 mmol) with stirring at 110 °C. For microwave-assisted reactions a well premixed mixture of reactants in a test tube, was subjected to MW irradiation at 475 W power in a domestic MW oven. After completion of the reaction (TLC monitoring), EtOAc was added. The mixture was centrifuged and filtered to remove the solid nanoZnO. Then, the organic layer was washed with 10% $NaHCO_3$, dried over Na_2SO_4, and evaporated in vacuum to produce amides in 50–95% yields.

Table 1
Recyclability of the ZnO nanofluid.

Run no.	Time (h)	Yield (%)
1	2	91
2	2	90
3	3	91

2.3. Representative analytical data for the selected products

2.3.1. N-benzyl propanamide (Table 1, entry 12)

Colorless needles (acetone: H_2O), mp 129 °C. IR (KBr); ν_{max} = 3280, 1630, 1550, 1430, 750 and 690 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.15 (t, J = 7.5 Hz, 3H, CH_3), 2.15 (q, J = 7.5 Hz, MeCH_2-C=O), 4.20 (d, J = 6H, NH-CH_2Ph), 7.20- 7.40 (m, 5H, H $_{arom.}$) ppm.

2.3.2. N-phenyl stearamide (Table 1, entry 17)

White needles, mp 90–94 °C; IR (KBr); ν_{max} = 3272, 1640, 1580, 1425, 750 and 690 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.90 (t, J = 6.9 Hz, 3H, CH_3), 1.20–1.40 (m, 28H, 14 × CH_2), 1.60–1.75 (m, 2H, CH_2), 2.25 (t, 2H, J = 7.5 Hz), 7.10 (m, 1H), 7.26 (brs, 1H, NH), 7.30 (m, 2H), 7.50–7.55 (m, 2H) ppm.

2.3.3. N-(4-chlorophenyl) stearamide (Table 1, entry 19)

Colorless (acetone:H_2O); mp 57–60 °C; IR (KBr); ν_{max} = 3300, 1645, 1585, 1438, 756 and 690 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.90 (t, J = 6.9 Hz, 3H, CH_3), 1.20-1.50 (m, 30H, 15 × CH_2), 2.22 (t, J = 7.5 Hz 2H, CH_2), 7.25 (brs, 1H, NH), 7.40 (d, J = 8.9 Hz, 2H), 7.60 (d, J = 8.89 Hz, 2H) ppm.

3. Results and discussion

Initially, the amidation of stearic acid with aniline as a model reaction was examined comparatively in the presence of 1 mmol of various pre-dried metal oxides include ZnO, prepared nanoZno, nanoTiO_2, TiO_2, SiO_2, Al_2O_3, CaO, MgO, and Fe_2O_3 at 110 °C for 4 h. Based on the isolated yield of N-phenyl stearamide (91–54%), the order of activities for examined mineral oxides were found to be nanoZnO > ZnO > nanoTiO_2 > TiO_2 > SiO_2 > MgO ≥ Al_2O_3 > Fe_2O_3 > CaO (Fig. 1).

The results indicate that, in the presence of basic metal oxides such as CaO or MgO stearate ion was formed before the reaction with aniline and hence the reactivity towards nucleophilic attack was reduced. ZnO catalysts were highly efficient and this efficiency is correlated to the oxophilicity of Zn, amphoteric nature of ZnO, and either Lewis acid or base properties of this metal oxide. This duality led to the activation of both coordinated COOH and NH groups to ZnO together with nearing of the activated reaction sites.

As Fig. 1 shows, 85% isolated yield of N-phenyl stearamide was obtained in the presence of ZnO nanoparticles, while too much higher

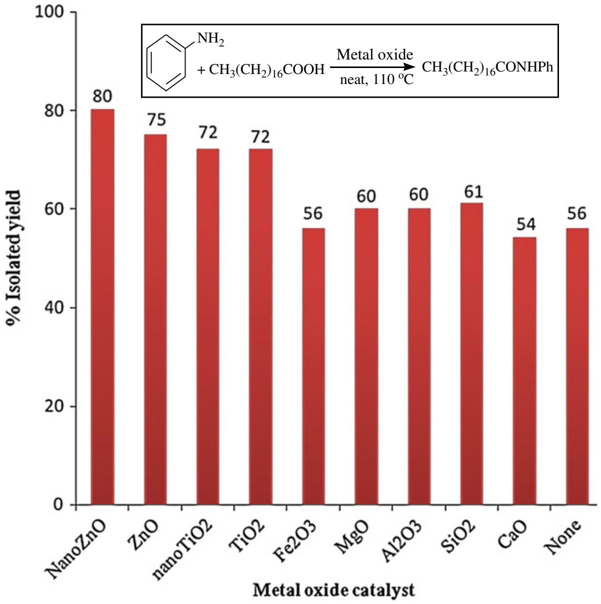


Fig. 1. Reaction of aniline with stearic acid in the presence of metal oxides.

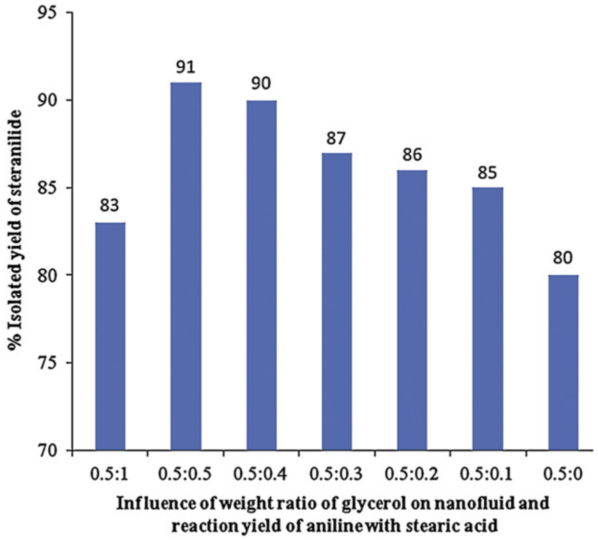


Fig. 2. Reaction of stearic acid and aniline in the presence of ZnO nanofluids (0.5 mmol scale).

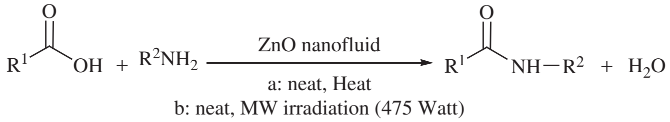
yield was expected than commercial ZnO. However, difference in yield is attributed to the better dispersion of ZnO nanoparticles in the reaction mixture and prompted us to increase the dispersion ability of catalyst by replacing ZnO nanofluids.

As a result, homogeny suspensions of different weight ratios of optimized amount of ZnO nanoparticles (0.08 g, 1 mmol) to glycerol were prepared as ZnO nanofluids. A study was made on the influence of glycerol amount in nanofluid on the condensation yield of aniline and stearic acid (Fig. 2).

Variation in the N-phenyl stearamide (stearanilide) yields in the presence of various types of ZnO can be attributed to the differences in the structure of catalysts, especially different diffusion and dispersion abilities of them in the reaction mixture. As the results show, higher yield of stearanilide was obtained with ZnO nanofluids prepared by dispersion of equal weight ratio of ZnO nanoparticles and base fluid. The advantage of ZnO nanofluids is due to providing homogeneity, high diffusion, and better dispersion of catalyst in the reaction mixture. In the absence of glycerol or its fewer amounts, lower yield of N-phenyl stearamide was obtained and shows that glycerol as a base fluid improves the dispersion of catalyst. Inferior yield was also obtained with nanofluid prepared by 1:2 weight ratio of nanoZnO to glycerol, probably due to the dilution of suspension and lower availability of catalyst (Fig. 2).

The reusability of ZnO nanofluid was also investigated, thus, EtOAc and water were added after first run of the model reaction. Then the mixture was centrifuged and filtered to remove the catalyst. The filtered ZnO nanoparticles was suspended and dispersed again in the same amount of glycerol by magnetically stirring of the mixture at room temperature. Using the recycled ZnO nanofluid for three consecutive times in the model reaction gave steranilide in nearly comparable yield with the freshly prepared catalyst (Table 1).

Table 2
ZnO nanofluid mediated direct preparation of amides from carboxylic acids.



Entry	R^1	R^2	Time Method a/Method b (h)/(s)	Yield[a,b] Method a/Method b (%)	Mp (°C) (Found) [ref]
1	CH_3	Ph	4/95	95/92	113–114 [33]
2	CH_3	Ph	4/90	93/90[c]	113–114 [33]
3	CH_3	$PhCH_2$	3/90	92/87	61–62 [33]
4	CH_3	CH_3–$(CH_2)_{11}$	4/90	90/85	95–98 [34]
5	CH_3	4-ClC_6H_4	3/90	88/88	177–179 [33]
6	CH_3	4-MeC_6H_4	2.5/80	91/85	153–155 [34]
7	CH_3	4-$NO_2C_6H_4$	10/180	60/50	208–210 [33]
8	H	Ph	3/60	92/90	45–47 [33]
9	CCl_3	Ph	–[d]	–[d]	–
10	CCl_3	$PhCH_2$	–[d]	–[d]	–
11	$PhCH_2$	Ph	2.5/90	85/76	118–120 [33]
12	CH_3 CH_2	$PhCH_2$	4/90	93/82	129–131 [33]
13	CH_3 CH_2	4-MeC_6H_4	3/90	91/85	122–124 [33]
14	CH_3 $(CH_2)_2$	Ph	4/90	90/80	94–95 [33]
15	CH_3–$(CH_2)_5$	Ph	3/90	89/82	70–72 [33]
16	CH_3 $(CH_2)_7$ C=C–$(CH_2)_7CH_2$	Ph	4/110	85/81	40–42 [33]
17	CH_3–$(CH_2)_{15}$–CH_2	Ph	4/120	91/88	90–94 [33]
18	CH_3–$(CH_2)_{15}$–CH_2	4-MeC_6H_4	4/100	91/90	69–72 [35]
19	CH_3–$(CH_2)_{15}$–CH_2	4-ClC_6H_4	5/120	86/83	57–60 [35]
20	CH_2COOH	Ph	5/90	88/83	222–225 [33]
21	COOH	Ph	6/90	90/82	256–258 [33]
22	Ph	Ph	10/120	60/65	160–162 [33]
23	Ph	$PhCH_2$	10/120	57/60	103–105 [33]
24	Ph and Me	Ph	8/120	90/90[e]	113–114 [33]
25	CH_3	Ph and PhNMe	8/120	90/87[e]	113–114 [33]

[a] Isolated yield.
[b] The reaction was carried out with prepared ZnO nanofluid [15].
[c] The reaction was run in 50 mol scale.
[d] When the reaction temperature rose to 80 °C, decarboxylation was immediately occurred.
[e] Only acetanilide was isolated.

The feasibility of scale up of the ZnO nanofluid-catalyzed reaction of aniline with stearic acid was demonstrated by running the reaction with 50 mmol of reactants at 110 °C and the yield was not changed significantly.

Based on these data, the most stable suspension of 1:1 nanoZnO to fluid can be used as the most suitable nanofluid catalyst in further studies. Therefore, the generality and versatility of direct amidation of carboxylic acids catalyzed by ZnO nanofluid was confirmed by converting various long and short chain aliphatic carboxylic acids and amines into their corresponding amides. Aliphatic carboxylic acids were reacted at 110 °C with aniline derivatives and aliphatic amines to give the corresponding amides. MW irradiation of a premixed mixture of reactants in an unmodified domestic oven produced the same products in good to excellent yields at very short times (Table 2).

Trichloroacetic acid was quickly decarboxylated under similar reaction conditions and suggested that, rapidly formed carboxylate salts of benzylamine or aniline were decomposed kinetically before condensation with amines (Table 2, entries 9 and 10).

Fatty acids were reacted with amines in the presence of ZnO nanofluid, to give the corresponding amides as emulsifiers, surfactants, lubricants, and coating materials (entries 16–19).

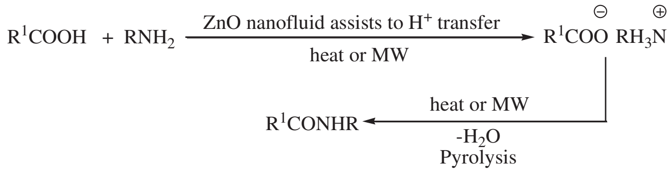
Diacids such as oxalic and malonic acid were also carried out the amidation with aniline under similar conditions and afforded the corresponding bisamides, oxanilide and malonanilide in high yields (entries 20 and 21).

However, the yields with aromatic carboxylic acids as lower active reactants were not so high. Thus, benzanilide and *N*-phenylbenzamide were obtained in 60 and 57% yields, respectively (entries 22 and 23).

Acylation of secondary hindered amines such as *N*-methylaniline or dipropylamine was not successfully and amines remained nearly unchanged in the reaction with benzoic acid (conversion by TLC monitoring <20%). Consequently, this simple procedure is highly chemoselctive for aliphatic carboxylic acids versus aromatic ones and primary amines versus secondary amines.

Furthermore, competitive reactions between aliphatic and aromatic substrates confirmed the chemoselectivity of ZnO nanofluid promoted amidation of carboxylic acids (entries 24 and 25). Halo-substituted acids such as 1- or 3-chloro-propionic acid were yielded a complex mixture of substituted amide products which were not isolated.

The mechanistic studies were not made, whereas according to the results it seems that carboxyl affinity of zinc oxide assisted to the proton exchange and improved the formation of carboxylic acid/amine salt as kinetic product. The advantage of ZnO nanofluids is enhanced formation of this salt due to the higher diffusion of catalyst in the reaction mixture. This fact can be supported by chemoselective reaction of aliphatic carboxylic acids which are able to contribute in a faster proton exchange process than aromatic ones. Subsequent thermal pyrolysis of the carboxylic acid/amine salt gives the corresponding amide as final thermodynamic product (Scheme 2).



Scheme 2. Proposed mechanism of the reaction.

4. Conclusion

In conclusion, ZnO nanofluid was used as a psudo-homogeneous and green media for the synthesis of amides from carboxylic acids. The method offers considerable advantages in terms of simplicity, feasibility of scale up, low environmental and economical impacts and high chemoselectivity.

Acknowledgments

We gratefully thank the Yazd University Research Council for financial support.

References

[1] G. Sartori, R. Maggi, Chemical Reviews 113 (2010) PR1–PR54.
[2] B.M. Choudary, K.V.S. Ranganath, J. Yadav, M.L. Kantam, Tetrahedron Letters 46 (2005) 1369–1371.
[3] G.A. Meshram, V.D. Patil, Tetrahedron Letters 50 (2009) 1117–1121.
[4] B. Karimi, J. Maleki, Journal of Organic Chemistry 68 (2003) 4951–4954.
[5] E. Comini, Analytica Chimica Acta 568 (2006) 28–40.
[6] S.K. Das, S.U.S. Choi, W. Yu, T. Pradeep, Nanofluids: Science and Technology, Wiley-Interscience, 2007, pp. 397–450.
[7] M. Hosseini Sarvari, H. Sharghi, Journal of Organic Chemistry 69 (2004) 2573–2576.
[8] Y.J. Kim, R.S. Varma, Tetrahedron Letters 45 (2004) 7205–7208.
[9] Z. Mirjafary, H. Saedian, A. Sadeghi, F. Matloubi Moghaddam, Catalysis Communications 9 (2008) 299–306.
[10] M. Hosseini Sarvari, H. Sharghi, Tetrahedron 61 (2005) 10903–11097.
[11] F. Matloubi Moghaddam, H. Saeidian, Materials Science and Engineering B 139 (2007) 265–269.
[12] E.K. Goharshadi, Y. Ding, P.J. Nancarrow, Physics and Chemistry of Solids 69 (2008) 2057–2060.
[13] A.L. Linsebigler, G.Q. Lu, J.T. Yates, Chemical Reviews 95 (1995) 735–758.
[14] F. Tamaddon, M.R. Sabeti, A.A. Jafari, F. Tirgir, E. Keshavarz, J. Mol. Catal. A: Chem. accepted.
[15] R. Jalal, E.K. Ghoharshadi, M. Abareshi, M. Moosavi, Materials Chemistry and Physics 121 (2010) 198–201.
[16] T.W. Greene, P.G.M. Wuts, Protecting Groups in Organic Synthesis, Third ed, Wiely, New York, 1999, pp. 76–86.
[17] C.A.G.N. Montalbetti, V. Falque, Tetrahedron 61 (2005) 10827–10852.
[18] J.R. Satam, R.V. Jayaram, Catalysis Communications 9 (2008) 2365–2370.
[19] R.D.C. Rodrigues, I.M.A. Barros, E.L.S. Lima, Tetrahedron Letters 46 (2005) 5945–5947.
[20] A. Khalafi-Nezhad, A. Parhami, M.N. SoltaniRad, A. Zarea, Tetrahedron Letters 46 (2005) 6879–6882.
[21] X. Wang, D.Z. Wang, Tetrahedron 67 (2011) 3406–3411.
[22] V. Theodorou, M. Gogou, M. Philippidou, V. Ragoussis, G. Paraskevopoulos, K. Skobridis, Tetrahedron 67 (2011) 5630–5634.
[23] K. Ahlford, H. Adolfsson, Catalysis Communications 12 (2001) 1118–1121.
[24] M. Sathishkumar, P. Shanmugavelan, S. Nagarajan, M. Maheswari, M. Dinesh, A. Ponnuswamy, Tetrahedron Letters 22 (2011) 2830–2833.
[25] P. Starkov, T.D. Sheppard, Organic and Biomolecular Chemistry 9 (2011) 1320–1323.
[26] X.D. Yang, X.H. Zeng, Y.H. Zhao, X.Q. Wang, Z.Q. Pan, L. Li, H.B. Zhang, Journal of Combinatorial Chemistry 12 (2010) 307–310.
[27] H. Firouzabadi, N. Iranpoor, K. Amani, Chemical Communications 6 (2003) 764–765.
[28] B. Das, M. Krishnaiah, P. Balasubramanyam, B. Veeranjaneyulu, D. Nandan Kumar, Tetrahedron Letters 49 (2008) 2225–2227.
[29] F. Tamaddon, M.A. Amrollahi, L. Sharafat, Tetrahedron Letters 46 (2005) 7841–7844.
[30] F. Tamaddon, M. Khoobi, E. Keshavarz, Tetrahedron Letters 48 (2007) 3643–3646.
[31] F. Tamaddon, F. Tavakoli, Journal of Molecular Catalysis A: Chemical 337 (2011) 52–55.
[32] F. Tamaddon, A. Nasiri, S. Farokhi, Catalysis Communications 12 (2011) 1477–1482.
[33] R.L. Shriner, R.C. Fuson, D.Y. Curtin, T.C. Morrill, The Systematic Identification of Organic Compounds, Sixth Ed, Wiley, New York, 1980, pp. 540–550.
[34] C. Ferroud, M. Godrast, S. Ung, H. Borderies, A. Guy, Tetrahedron Letters 49 (2008) 3004–3008.
[35] B. Narasimhan, ARKIVOC 15 (2007) 112–115.