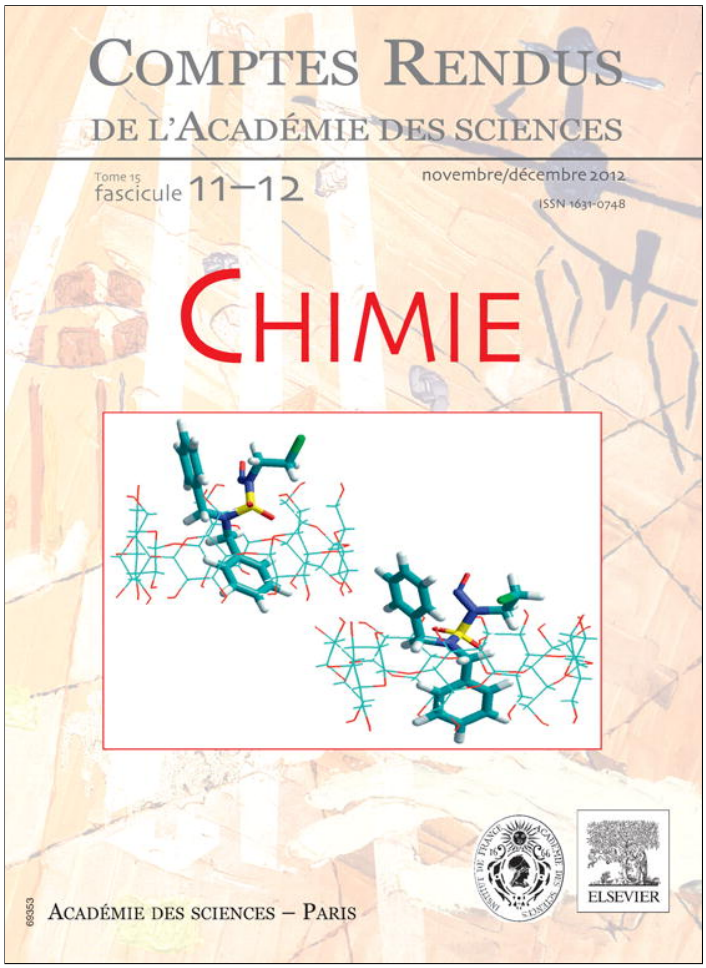


C. R. Chimie 15 (2012) 1072–1076

Contents lists available at SciVerse ScienceDirect

Comptes Rendus Chimie

www.sciencedirect.com

Full paper/Mémoire

A rapid, convenient and chemoselective synthesis of acylals from aldehydes catalyzed by reusable nano-ordered MCM-41-SO_3H

Hesam Tourani, Mohammad Reza Naimi-Jamal *, Mohammad Ghorban Dekamin, Meysam Amirnejad

Research Laboratory of Green Organic Synthesis, Department of Chemistry, Iran University of Science and Technology, 16846 Tehran, Iran

ARTICLE INFO

Article history:
Received 26 April 2012
Accepted after revision 28 June 2012
Available online 11 August 2012

Keywords:
Aldehydes
Acylation
MCM-41-SO_3H
Carbonyl protection
Solvent-free conditions
Heterogeneous catalysis

ABSTRACT

Acylals were prepared by direct condensation of aldehydes with acetic anhydride using nano-ordered MCM-41-SO_3H as a heterogeneous catalyst under solvent-free conditions at room temperature in a very short reaction time and excellent yields. The catalyst is recyclable, non-toxic, neither air nor moisture sensitive, and easy to handle. High chemoselectivity toward aldehydes in the presence of ketones is another advantage of the present method which provides selective protection of aldehydes in their mixtures with ketones.

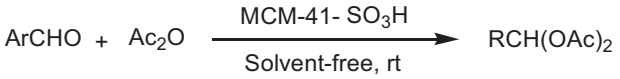
1. Introduction

During the synthesis of many molecules, especially in drug synthesis, protection of a carbonyl group is often necessary [1]. Different reagents have been employed for this purpose such as alcohols [2], ethane dithiol [3], trialkyl orthoformates [4], 2-mercaptoethanol [5], acetic anhydride [6], etc. Among these protecting agents, acetic anhydride is of special interest and has been widely used for protection of carbonyl compounds, due to the stability of gem-diacetates (acylals) in neutral and mild basic conditions, as well as acidic medium [7]. Furthermore, the diacetates serve as valuable precursors for the preparation of 1-acetoxydienes [8], vinyl acetates [9], and arylnitriles [10], and cyanohydrin esters [11]. Usually diacetates are prepared by condensation of aldehydes and acetic anhydride in the presence of a protonic acid such as 1-H-3-methyl-imidazolium hydrogen sulfate [12], silica phosphoric acid [13], $HClO_4$–SiO_2 [14], sulfamic acid [15] or a Lewis acid such as $LiClO_4$ [16], Ti (IV) halides [17], $NbCl_5$ [18], iron(III) fluoride [19], NBS [20], $RuCl_3 \bullet xH_2O$ [21], P_2O_5/Al_2O_3 [22], $SnCl_4/SiO_2$ [23], etc. Furthermore, many inorganic heterogeneous catalysts such as montmorillonite clay [24], Amberlyst-15 [25], and $AlPW_{12}O_{40}$ [26] have been also used. Although in many cases the gem-diacetates are obtained in good yields most of these methods suffer from some disadvantages such as long reaction time, tedious work-up procedure, the use of homogenous catalysts or harmful solvents, and high reaction temperature. Consequently, the development of mild catalytic methods for the preparation of acylals is still desirable.

In recent years, the use of heterogeneous catalysts has been widely studied [27] because they are easily removable from the reaction media by simple filtration after completion of the reaction and in many cases they are reusable. In order to overcome the lower reaction rate of heterogeneous catalysts compared to homogeneous ones, the use of high surface area materials such as MCMs, SBA, and zeolites have been widely investigated [28].

* Corresponding author.
E-mail address: naimi@iust.ac.ir (M.R. Naimi-Jamal).

1631-0748/$ – see front matter © 2012 Académie des sciences. Published by Elsevier Masson SAS. All rights reserved.
http://dx.doi.org/10.1016/j.crci.2012.06.014

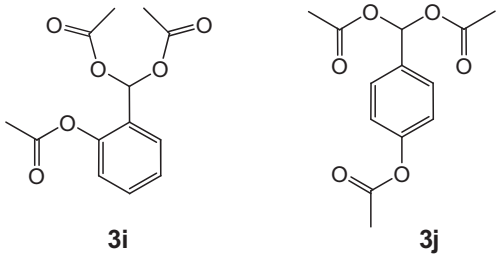


Scheme 1. Solvent-free synthesis of acylals from aldehydes and acetic anhydride catalyzed by nanoporous MCM-41-SO_3H.

We herein wish to report an efficient procedure for the rapid synthesis of acylals from various aldehydes with acetic anhydride using MCM-41-SO_3H as a heterogonous catalyst under solvent-free conditions (Scheme 1).

2. Results and discussion

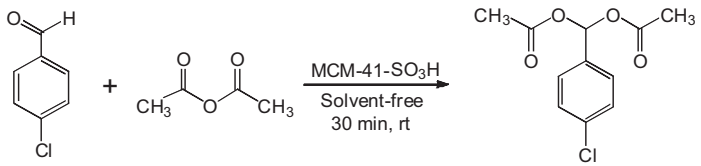
In order to optimize the amount of acetic anhydride and the catalyst loading, the reaction of 4-chlorobenzaldehyde (**1c**) was studied as the model reaction at room temperature. Different amounts of acetic anhydride (**2**) (1.0, 3.0, and 5.0 mmol) and MCM-41-SO_3H catalyst (0, 5, 10 and 20 mg) were investigated in the presence of 1.0 mmol 4-chlorobenzaldehyde. The reaction progress was monitored by GC. The mixture was then diluted with 5.0 mL CH_2Cl_2 and filtered. The organic layer was subsequently washed with saturated 10% aqueous $NaHCO_3$ solution and water, and then dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and the solid crude product was recrystallized from n-hexane:EtOH to afford pure acylal **3c**. The structure of the product was determined on the basis of its spectral data. The ^1H NMR spectra of the product showed a characteristic signal at about 7.67 ppm for benzylic H. The results have been summarized in Table 1. As it is shown, in the absence of the catalyst no product was obtained, even in excess amount of acetic anhydride. When MCM-41-SO_3H was added, different yields of the desired product were obtained, depending on the amount of the catalyst used. As it is obvious from the Table 1, the best result was obtained when 5.0 mmol of **2** and 10 mg of the catalyst were used. It is notable that when 20 mg of catalyst was used, the yield of the desired product decreased dramatically. This is presumably due to the considerable protonation of acetic anhydride oxygen atoms by acidic protons on the catalyst surface which decreases their nucleophilic activity towards the carbonyl group of aldehyde. Further experiments using optimized conditions revealed that only 3 min is enough to complete the model reaction affording 99% of the product **3c**.



Scheme 2. Acetylated products of salicylaldehyde (**1i**) and 4-hydroxybenzaldehyde (**1j**).

Encouraged by these results, the scope of the method was investigated with different aldehydes. The results have been summarized in Table 2. As it is shown, different aromatic aldehydes bearing both electron withdrawing (Entries 2–8) and electron releasing groups (Entries 9–12) afforded the corresponding acylals in high to excellent yields. The nature and position of the substituents on the aromatic ring strongly affected both reaction yield and required time for the completion of the reaction. Therefore, electron donating groups increased the required reaction time and afforded lower yields compared to electron withdrawing groups. As a consequence, 4-dimethylamino benzaldehyde (**1m**) was not converted to the corresponding acylal, due to the strong

Table 1
Optimization of the amount of acetic anhydride and the catalyst loading in the model reaction.



1c (mmol)	**2** (mmol)	Catalyst (mg)	Yield (%)
1.0	1.0	–	–
		5	43
		10	52
		20	35
1.0	3.0	–	–
		5	75
		10	82
		20	60
1.0	5.0	–	–
		5	88
		10	99
		20	75

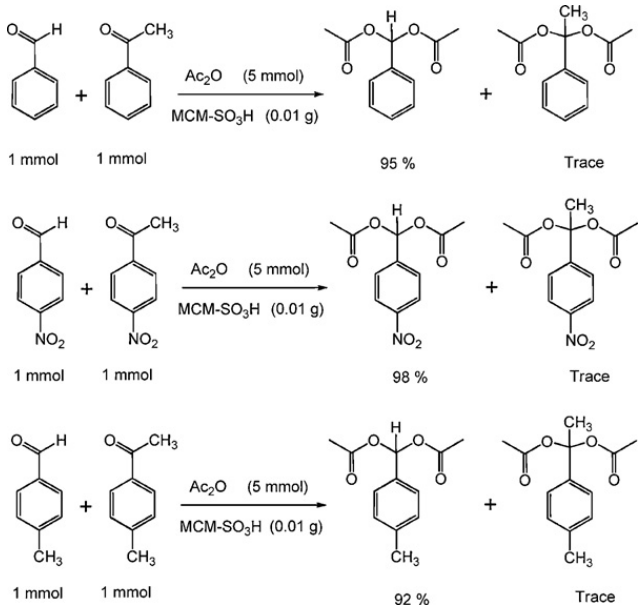
Table 2
MCM-41-SO_3H catalyzed acetylation of aldehydes with acetic anhydride[a].

Entry	Substrate		Product	Time (min)	Yield[b] (%)	Mp (°C) (ref)
1	Benzaldehyde	**1a**	**3a**	3	95	43–45 (44–45) [15]
2	2-Chlorobenzaldehyde	**1b**	**3b**	5	90	56–58 (55–56) [29]
3	4-Chlorobenzaldehyde	**1c**	**3c**	3	99	80–82 (80) [31]
4	2-Nitrobenzaldehyde	**1d**	**3d**	3	93	89–90 (90–91) [15]
5	3-Nitrobenzaldehyde	**1e**	**3e**	5	95	65–67 (65–66) [15]
6	4-Nitrobenzaldehyde	**1f**	**3f**	3	98	124–126 (125–127) [15]
7	4-Cyanobenzaldehyde	**1g**	**3g**	6	99	100–101 (100–101) [12]
8	4-Bromobenzaldehyde	**1h**	**3h**	5	90	94–95 (93–95) [12]
9	Salicylaldehyde	**1i**	**3i**	4	95	101–103 (101–103) [29]
10	4-Hydroxybenzaldehyde	**1j**	**3j**	6	93	93–94 (90–92) [12]
11	4-Methoxybenzaldehyde	**1k**	**3k**	5	85	63–65 (63–64) [29]
12	4-Methylbenzaldehyde	**1l**	**3l**	5	92	80–82 (80–82) [12]
13	4-Dimethylaminobenzaldehyde	**1m**	**3m**	180	–	–
14	Cinnamaldehyde	**1n**	**3n**	10	85	83–84 (83–85) [29]

[a] Reaction conditions: aldehyde (1 mmol), acetic anhydride (5 mmol), catalyst (0.01 g), solvent-free, and at room temperature.
[b] Isolated yield.

electron donating nature of the amino group in accordance with literature data [6,29] (Entry 13). Furthermore, steric hindrance in 2-isomers may be the reason that theses substrates required longer reaction time compared to their 4-isomer (e.g. Entries 2 and 3).

This protocol also tolerated acid-sensitive α,β-unsaturated substrates such as cinnamaldehyde (**1n**, Entry 14) which can polymerize under homogeneous acidic conditions. Furthermore, when aldehydes bearing hydroxyl group on aromatic ring (e.g. **1i** and **1j**) were used, acetylation of the hydroxyl group was also observed (Scheme 2). The structure of these products was secured by spectroscopic data. However some works have mistakenly reported the same melting points for the acylals with free hydroxyl group [30].



Scheme 3. Competition reaction between equimolar mixtures of some aldehydes and similar ketones with acetic anhydride.

The reusability of the catalyst was also investigated in further runs of the model reaction. The filtered catalyst after each run was washed several times with acetone and ethanol and dried in an oven at 80 °C for 5 h. The results of catalyst recyclability have been summarized in Fig. 1.

To investigate the chemoselectivity of this method, a competition reaction between equimolar mixtures of some aldehydes and similar ketones with acetic anhydride was studied (Scheme 3). As it is shown, whereas aldehydes were quantitatively converted to the corresponding acylals, ketones remained practically intact.

According to the obtained results, the following mechanism can be proposed for protection of aldehydes with acetic anhydride in the presence of MCM-41-SO_3H (Scheme 4).

In order to show the merit of the present work, comparison of the catalytic activity of some homogeneous and heterogeneous catalysts in the acylation reaction of 4-nitrobenzaldehyde (**1f**) has been presented in Table 3. The results clearly show the advantages of this method in terms of the obtained yield of the desired product, reaction time and catalyst loading. Whereas most of the reported methods require reaction times in order of some hours to be completed, the present method needs only 3 min to afford the product **3f** quantitatively.

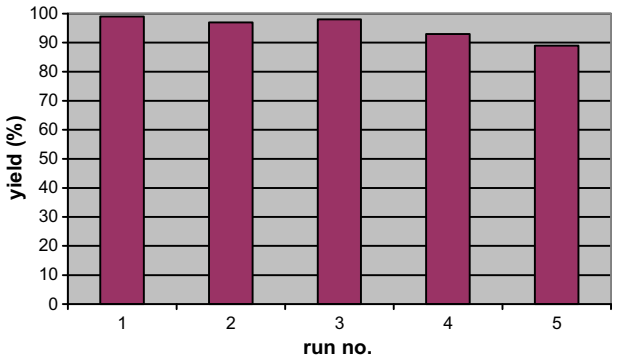
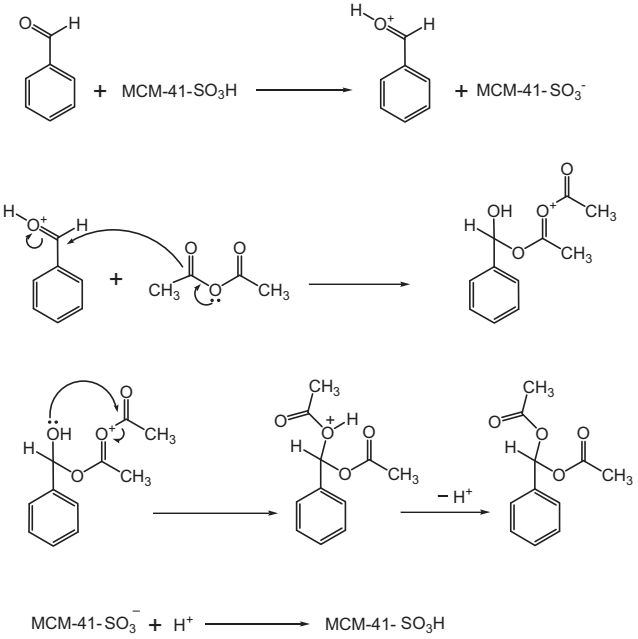


Fig. 1. Reusability study of the catalyst in the model reaction.

Table 3
Comparison of the present method with some reported methods in the acylation reaction of 1.0 mmol of 4-nitrobenzaldehyde.

Catalyst	Temp.	Time	Catalyst Loading	Yield (%)
LiOTf [32]	rt	15 h	20 mol%	94
$Ph_3P^+CH_2COMeBr^-$ [31]	rt	11 h	10 mol%	75
SPDTSA[a] [33]	rt	4 min	10 mg	94
NBS [20]	rt	8 h	10 mol%	98
$H_3PW_{12}O_{40}$/MCM-41 [34]	60 °C	2 h	20 mg	61
$TiCl_4$ [17]	rt	2.66 h	10 mol%	53
$SnCl_4/SiO_2$ [23]	rt	15 min	100 mg	92
$Mg(CH_3SO_3)_2$-HOAc [29]	rt	12 h	1.5 mol%	55
Montmorillonite Clay in CCl_4 [24]	rt	1 h	20 mg	96
Amberlyst-15 in CH_2Cl_2 [25]	rt	1 h	500 mg	95
This work	rt	3 min	10 mg	98

[a] Silica-bonded propyl-diethylene-triamine-*N*-sulfamic acid.



Scheme 4. Proposed mechanism for acetalyzation of benzaldehyde catalyzed by MCM-41-SO_3H.

3. Conclusion

In conclusion, a mild, efficient and recoverable heterogeneous catalyst has been developed for the preparation of gem-diacetates from aldehydes and acetic anhydride under solvent-free conditions at room temperature. We found that various aldehydes were converted to acylals chemoselectively in high to quantitative yields and the required reaction time was considerably shorter than many of the previously described methods.

4. Experimental

4.1. Materials and methods

FT-IR spectra were recorded as KBr pellets on a Shimadzu FT-IR- 8400S spectrometer. ^1H NMR (500 MHz) Spectra were obtained using a Bruker DRX-500 AVANCE spectrometer. All NMR spectra were determined in $CDCl_3$ at ambient temperature. Gas chromatograph was a Perkin Elmer GC 8400. Melting points were determined using an electrothermal apparatus and are uncorrected. All chemicals were purchased from Merck or Aldrich and have been used as received, except for liquid aldehydes which have been freshly distilled prior to use.

4.2. Typical procedure for synthesis of acylals

Aldehyde (1.0 mmol), Ac_2O (5.0 mmol) and MCM-41-SO_3H (10 mg) were poured in a 20 mL round bottom flask and stirred magnetically at ambient temperature for an appropriate time (Table 2). The reaction progress was monitored by TLC (Hexane: EtOAc; 5:1) or GC. After completion of the reaction, the mixture was diluted with CH_2Cl_2 and filtered. The organic layer was washed with saturated 10% aq. $NaHCO_3$ solution and water, and then dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and the solid crude was recrystallized from n-hexane:EtOH to afford the pure solid products. The structures of all products were determined on the basis of their analytical and/or spectral data comparing with the literature data (Table 2).

4.3. General procedure for preparation of MCM-41

To 42 mL deionized water in a 500 mL beaker, 2.7 g diethylamine was added at ambient temperature and stirred. Then, 1.47 g cetyltributylammonium bromide (CTAB) was gradually added to the above mixture until a clear solution was obtained. Tetraethyl orthosilicate (2.1 g) was added drop-wise to the solution and the pH was fixed at 8.5 by addition of 1 M HCl solution. After 2 h, the resulting solid product was filtered and washed several times with deionized water, and dried at 45 °C for 12 h. The obtained MCM-41 was calcined at 550 °C for 5 h to remove all the surfactant [35].

4.4. General procedure for preparation of MCM-41-SO_3H

MCM-41 (1 g) was suspended in CH_2Cl_2 (5 mL) in a 100 mL round bottom flask equipped with a gas outlet tube and a dropping funnel containing a solution of chlorosulfonic acid (2 mL) in dichloromethane (15 mL). The chlorosulfonic acid solution was added drop-wise to the

obtained suspension over a period of 30 min at room temperature. HCl gas evolved from the reaction mixture was conducted via the gas outlet tube into a NaOH solution. After the completion of the reaction, the solvent was evaporated under reduced pressure and the MCM-41-SO_3H was collected as a white solid [35].

4.5. Physical and spectral data of selected products:

4.5.1. Compound 3c

White solid; mp 80–82 °C (Lit. [31] 80 °C); IR (KBr): 3092, 1757, 1742, 1246, 1202, 1011 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.67 (s, 1 H), 7.48–7.50 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.40–7.42 (dd, *J* = 8.0, 1.5 Hz, 1 H), 2.17 (s, 6 H).

4.5.2. Compound 3i

White solid; mp 101–103 °C (Lit. [29] 101–103 °C); IR (KBr): 3040, 1747, 1495, 1373, 1250, 1211, 1192 cm^{-1};^1H NMR (500 MHz, $CDCl_3$): δ = 7.93 (s, 1 H), 7.66–7.67 (dd, *J* = 8.0, 1.0 Hz, 1 H), 7.44–7.47 (m, 1 H), 7.30–7.34 (m, 1 H), 7.14–7.16 (d, *J* = 8.0 Hz, 1 H), 2.37 (s, 3 H), 2.13 (s, 6 H).

Acknowledgment

We acknowledge Iran University of Science and Technology (IUST) for partial financial support of this work, and Professor Gerd Kaupp from University of Oldenburg, Germany for his kind donation of some chemicals.

References

[1] P.G.M. Wuts, T.W. Greene, Greene's protective groups in organic synthesis, 4th ed, Wiley, New Jersey, 2007.
[2] S. Madabhushi, K.K.R. Mallu, N. Chinthala, C.R. Beeram, V.S. Vangipuram, Tetrahedron Lett. 53 (2011) 697.
[3] G. Perin, L.G. Mello, C.S. Radatz, L. Savegnago, D. Alves, R.G. Jacob, E.J. Lenardão, Tetrahedron Lett. 51 (2010) 4354.
[4] A. Roy, M. Rahman, S. Das, D. Kundu, S.K. Kundu, A. Majee, A. Hajra, Synth. Commun. 39 (2009) 590.
[5] F. Shirini, P. Sadeghzadeh, M. Abedini, Chin. Chem. Lett. 20 (2009) 1457.
[6] N.G. Khaligh, F.J. Shirini, Catal. A: Chem. 20 (2011) 348.
[7] K.S. Kochhar, B.S. Bal, R.P. Deshpande, S.N. Rajadhyaksha, H.W. Pinnick, J. Org. Chem. 48 (1983) 1765.
[8] M.J. Gregory, J. Chem. Soc. B. (1970) 1201 http://pubs.rsc.org/en/content/articlelanding/1970/j2/j29700001201.
[9] G.M. Whitesides, J.S. Filippo Jr., J. Am. Chem. Soc. 92 (1970) 6611.
[10] M. Sandberg, L.K. Sydnes, Tetrahedron Lett. 39 (1998) 6361.
[11] M. Sandberg, L.K. Sydnes, Org. Lett. 2 (2000) 687.
[12] A.R. Hajipour, L. Khazdooz, A.E. Ruoho, Catal. Commun. 9 (2008) 89.
[13] F. Zhang, H. Liu, Q.J. Zhang, Y.F. Zhao, F.L. Yang, Synth. Commun. 40 (2010) 3240.
[14] V.T. Kamble, V.S. Jamode, N.S. Joshi, A.V. Biradar, R.Y. Deshmukh, Tetrahedron Lett. 47 (2006) 5573.
[15] T.S. Jin, G. Sun, Y.W. Li, T.S. Li, Green Chem. 4 (2002) 255.
[16] A. Ziyaei, N. Azizi, M.R. Saidi, J. Mol. Catal. A: Chem. 238 (2005) 138.
[17] M. Jung, J. Yoon, H.S. Kim, J.S. Ryu, Synthesis 16 (2010) 2713.
[18] S.T. Gao, Y. Zhao, C. Li, J.J. Ma, C. Wang, Synth. Commun. 39 (2009) 2221.
[19] V.T. Kamble, R.A. Tayade, B.S. Davane, K.R. Kadam, Aust. J. Chem. 60 (2007) 590.
[20] B. Karimi, H. Seradj, G.R. Ebrahimian, Synlett. 5 (2000) 623.
[21] A. Saini, S. Kumar, J.S. Sandhu, Synth. Commun. 38 (2008) 106.
[22] A.R. Hajipour, A. Zarei, A.E. Ruoho, Tetrahedron Lett. 48 (2007) 2881.
[23] Y.Q. Li, L.H. Cheng, Chin. Chem. Lett. 12 (2001) 565.
[24] Z.H. Zhang, T.S. Li, C.G. Fu, J. Chem. Res. (S). 5 (1997) 174.
[25] A.V. Reddy, K. Ravinder, V.L.N. Reddy, V. Ravinkanth, Y. Yenkateswarlu, Synth. Commun. 33 (2003) 1531.
[26] H. Firouzabadi, N. Iranpoor, F. Nowrouzi, K. Amani, Tetrahedron Lett. 44 (2003) 3951.
[27] G.V. Smith, F. Notheisz, Heterogeneous Catalysis in Organic Chemistry, first ed., Academic Press, NY, 1999.
[28] (a) J.Y. Ying, C.P. Mehnert, M.S. Wong, Angew. Chem. Int. Ed. 38 (1999) 56;
(b) R.J. Kalbasi, A.R. Massah, A.J. Shafiei, Mol. Catal. A: Chem. 335 (2011) 51;
(c) A.R. Massah, R.J. Kalbasi, A. Shafiei, Monatsh. Chem. 143 (2012) 643.
[29] Q. Liu, H.M. Ai, S. Feng, Synth. Commun. 42 (2012) 122.
[30] M. Moosavifar, S. Tangestaninejad, M. Moghadam, V. Mirkhani, I. Mohammadpoor-Baltork, C. R. Chimie 14 (2011) 953.
[31] A.T. Khan, L.H. Choudhury, S. Ghosh, Eur. J. Org. Chem. 13 (2005) 2782.
[32] B. Karimi, J. Maleki, J. Org. Chem. 68 (2003) 4951.
[33] M. Nouri Sefat, A. Deris, K. Niknam, Chin. J. Chem. 29 (2011) 2361.
[34] B. Rabindran Jermy, A. Pandurangan, Catal. Commun. 9 (2008) 577.
[35] M.G. Dekamin, Z. Mokhtari, Tetrahedron 68 (2012) 922.