Journal of
NANOSTRUCTURES
JNS
NANOSTRUCTURES
JNS.kashanu.ac.ir

Application of Sulfonic Acid Functionalized SBA-15 as a Nanoporous Acid Catalyst in Microwave Assisted Synthesis of 2-Aryl Benzoxazoles

M. Shakiba Nahad,[a] G. Mohammadi Ziarani,[a*] A. Badiei,[b] A. Banan[c]

[a] *Department of Chemistry, Alzahra University, Vanak Square, Tehran, Iran, P. O. Box 19938939973, Iran.*

[b] *School of Chemistry. College of Science, University of Tehran, Tehran, Iran*

[c] *Department of Chemistry Imam Hossein University, Tehran, Iran*

**Corresponding author: Tel: 0098-88041344. Fax: 0098-88041344. E-mail: gmziarani@hotmail.com*

Article history:
Received 3/10/2013
Accepted 9/12/2013
Published online 1/3/2014

Keywords:
Nanoporous
2-aryl benzoxazoles
Microwave assisted,
SBA-Pr-SO_3H

**Corresponding author:*
gmziarani@hotmail.com

Phone: +98 21 *88041344*
Fax: +98 21 *88041344*

Abstract

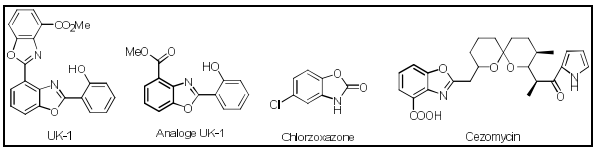
Sulfonic acid functionalized SBA-15 as a nanoporous acid catalyst was used in the synthesis of 2-Aryl benzoxazoles **4** by the condensation of 2-aminophenol **1** and benzoyl chlorides **2** under microwave irradiation in solvent free reaction conditions. The advantages of this methodology are good product yields (60-98%), being environmentally benign, short reaction times and easy work up.

1. Introduction

Since the discovery of M41S in 1992, mesoporous silicas have attracted much attention because of their innovative synthesis mechanisms, characteristic mesoscale pore structure and broad applications in the fields of adsorption, separation, biotechnology, drug delivery, catalyst support and particularly heterogeneous catalysis [1-3]. SBA-15 is new mesoporous silica, have received increasing scientific interest because of their narrow pore size distribution, high surface area and pore volume. The size of pores can be varied in a relatively long range between 5-20 nm depending on the synthesis conditions [4]. Integration of acidic functional groups (*e.g.*, -SO_3H) into SBA-15 has been investigated to make promising solid acids [5]. Applications of these nanocatalysts in organic synthesis and one-pot reactions have great importance.

Benzoxazoles have shown different pharmacological activities such as antibiotic [6], anthelmintic [7], anti inflammatory [8, 9, 10], anti

stress, anti ulcer [11, 12], anti cancer [13], antimicrobial, antiviral agents. These compounds also have antihistaminic, anti fungal, anti tumor, anticonvulsant, hypoglycemic and antitubercular activity [14, 15, 16, 17, 18]. They can act as Topoisomerase I and II [19] and Cyclooxygenase inhibitors. Substituted benzoxazole were used as elastase inhibitors and H_2 antagonists [20]. Benzoxazole derivatives exhibit considerable activity against some viruses such as RNA [21]. The benzoxazole structure can be found in the some drugs such as UK-1 and their analoges [22], Chlorzoxazone [23] and Cezomycin [24] (Scheme 1).



Scheme 1. Structure of some benzoxazole drugs.

There are several reports for the synthesis of benzoxazoles, but the most popular methods for the synthesis of these compounds involve the reaction between 2-aminophenol with carboxylic acid derivatives (acid chlorides, aldehydes, nitriles, amides, aldehydes, esters [25] and ortho esters [26]) and the copper-catalyzed intramolecular *ortho* arylation of *o*-haloanilides or intermolecular domino annulations of *o*-aryl halides with acylamides [27] using strong acids at high temperature [28] or in the presence of microwave conditions [20] and the oxidative cyclization of phenolic schiff bases derived from the condensation of 2-aminophenols and aldehydes or carboxylic acids using barium manganate, lead tetra-acetate, nickel oxide, thianthrene cation radical, diacetoxyiodobenzene, manganese (III) acetate, MnO_2/silica, pyridinium chlorochromate, and copper-catalyzed approaches followed by oxidation [28].

Various catalysts such as $In(OTf)_3$ [27], MCM-41 [29], *p*-toluene sulfunic acid [30-32], pyridinium *p*-toluenesulfonic acid [32], silica sulfuric acid as heterogeneous catalyst [25], BINAM–Copper (II) [33], $Cu(OTf)_3$ [34], imidazolium based ionic liquids [35] and KAl $(SO_4)_2.12H_2O$ (Alum) under microwave irradiation [26] were used in this synthesis. Therefore, in this article we used SBA-Pr-SO_3H as heterogeneous nano catalyst in the one pot synthesis of benzoxazoles. The heterogeneous catalysts can conveniently be removed from the reaction mixture, making the experimental procedure simple and eco-friendly [36]. SBA-Pr-SO_3H has mesoporous silica structure with pore size of 6 nm which can act as reactive nanoreactor in organic synthesis [37].

Here in we want to report the development of a one-pot and green microwave-assisted protocol for the synthesis of benzoxazole derivatives.

2. Experimental procedure

2.1. Materials and methods

The chemicals employed in this work were obtained from Merck Company and were used with no purification. GC-Mass analysis was performed on a GC-Mass model: 5973 network mass selective detector, GC 6890 egilent. IR spectra were obtained with a brucker 500 scientific spectrometer. Products were recorded on a FT-NMR Bruker 250 MHz. Melting points were measured by using the capillary tube method with an electro thermal 9200 apparatus. Microwave-assisted reactions were carried out using a MicroSYNTH Microwave Labstation. SEM analysis was performed on a Philips XL-30 field-emission scanning electron microscope operated at 16 kV, while TEM was carried out on a Tecnai G^2 F30 at 300 kV.

2.2. Preparation of catalyst

The nanoporous compound SBA-15 was synthesized and functionalizaed according to our previous report and the modified SBA-15-Pr-SO_3H was used as nanoporous solid acid catalyst in the following reaction [38].

2.3. General procedure for the preparation of 2-aryl benzoxazoles 4

2-Aminophenol (3mmol, 0.32 g) and appropriate benzoyl chloride (3mmol) were mixed in a glass tube and irradiated in the microwave oven for about 5 min at maximum microwave power level (700 watts). After completion of reaction which was indicated by TLC (n-hexane/EtOAc, 2/1), hot EtOH (Table 1, entry 1-4, 8) or mixture of hot EtOH/THF (Table 1, entry 5-7) were added to dissolve the crude products, and after evaporation of solvent the pure crystals of products were obtained.

2.4. Spectral Data of Products

2-(2-Chlorophenyl)benzoxazole **(4a):** IR (KBr, cm^{-1}): υ_{max}= 3052, 1686, 1647, 1534, 1280. ^{1}H NMR (250 MHz, DMSO-d_6) δ= 7.38-7.47 (m, 4H), 7.63-7.59 (m, 2H), 7.86-7.84 (m, 1H), 8.14 (d, 1H). MS (m/z): 229, 201, 167, 111.

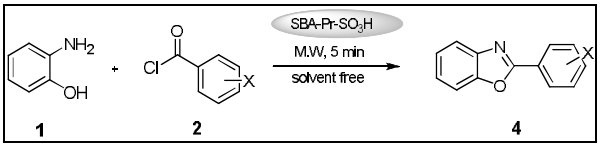
2-(3-Chlorophenyl)benzoxazole **(4b):** IR (KBr, cm^{-1}): υ_{max}= 3074, 1696, 1649, 1569, 1288. ^{1}H NMR (250 MHz, DMSO-d_6): 7.29-7.50 (m, 4H), 7.52-7.59 (m, 1H), 7.72-7.81 (m, 1H), 8.06-8.14 (m, 1 H), 8.19-8.25 (m, 1H) ppm. MS (m/z): 229, 63.

2-(4-Chlorophenyl)benzoxazole **(4c):** IR (KBr, cm^{-1}): υ_{max}= 3085, 1677, 1538, 1273. ^{1}H NMR (250 MHz, DMSO-d_6): 7.37-7.35 (m, 2 H), 7.52-7.47 (m, 2H), 7.60-7.55 (m, 1H), 7.79-7.75 (m, 1H), 8.20-8.17 (m, 2H) ppm. MS (m/z): 229, 201, 63.

2-(2-methylphenyl)benzoxazole **(4h):** IR (KBr) (Cm^{-1}): 1610 , 1510, 1230. MS (m/z): 209, 180, 133, 91, 63, 39. IR (KBr) (Cm^{-1}): 1610 , 1510, 1230. ^{1}H NMR (250 MHz) δ=2.84 (S, 3H), 7.35 (m, 5H), 7.58 (m, 1H), 7.78 (m, 1H), 8.19 (d, 1H)[25]. MS (m/z): 209, 180, 133, 91,63, 39.

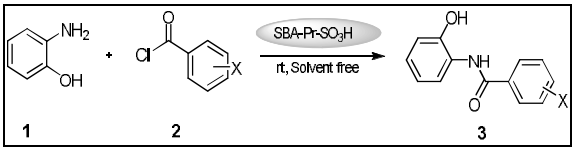
3. Results and discussion

In this paper, some 2-aryl benzoxazoles **4** were prepared by the condensation of 2-aminophenol **1** with benzoyl chlorides **2** under microwave irradiation in solvent free condition in the presence of SBA-Pr-SO_3H (Scheme 2).



Scheme 2. Synthesis of benzoxazole derivatives **4**

The reaction goes to completion in microwave oven for about 5 minutes at the maximum power level (700 watts). The crude products were obtained from convenient crystallization from solvent (Table 1). When this reaction was taken place in rt, the products were hydroxy benzanilide derivatives **3** (Scheme 3).



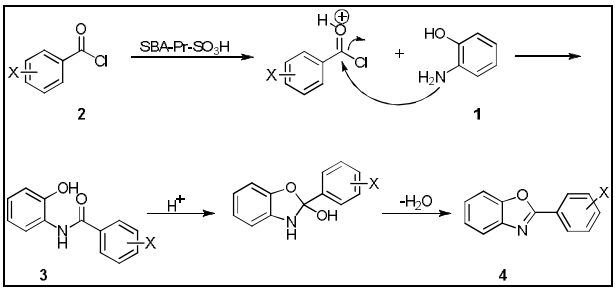
Scheme 3. The reaction of 2-aminophenol **1** with benzoyl chlorides **2.**

As shown in Table 1, in the most cases, 2-aminophenol reacted with a wide variety of substituted benzoyl chlorides completely and afforded the corresponding benzoxazoles in good to excellent yields. As results shown in Table 1, the benzoyls with electron-withdrawing groups which were predicted to be more reactive toward compound **1** led to benzoxazole derivatives **4** in higher yields. Electron-donating substituent on the

aromatic ring of benzoyl chloride decreased the yield of reaction (entry 8, Table 1). When NO_2 group is present in the molecule, it will deactivate *para* position in benzoyl compound, for this reason in entry 6, the yield of reaction will be decreased.

The reaction may tentatively be visualized to occur via a sequence of reactions depicted in Scheme 4. At first, SBA-Pr-SO_3H as a bronsted nano-catalyst protonates the carbonyl group of benzoyl chloride. then carbonyl group of **2** which undergoes condensation with **1**, produces hydroxyl benzanilide **3** as intermediate. The nucleophilic attack of OH to carbonyl group of compound **3**, gave the cyclization product. Then dehydration followed by ring closure lead to benzoxazole **4**.

The synthesis of 2-aryl benzoxazoles have been studied with several catalysts and solvents in literature as shown in Table 2. In entry 3, carboxylic acid was utilized and in entry 6 orthoesters were used as starting material for the synthesis of benzoxazoles. It demonstrates that the use of benzoyl chlorides in MW condition is better than the other methods. In contrast with other existing methods, the present methodology offers an efficient, experimentally simple, and economically attractive intramolecular cyclization. SBA-Pr-SO_3H with its distinct features such as the pore size of 6 nm, acts as an efficient nano-reactor in this reaction (Figure 1).



Scheme 4. The proposed mechanism for the synthesis of benzoxazole derivatives

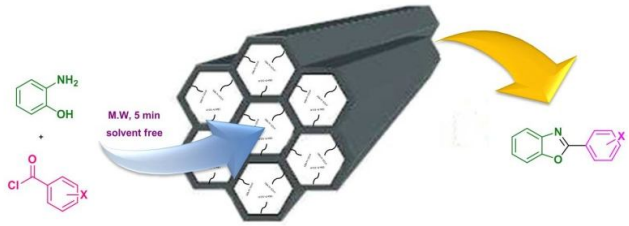


Fig. 1. SBA-Pr-SO_3H acts as a nano-reactor.

The SEM and TEM images of SBA-Pr-SO_3H illustrates in Figure 2. SEM image (Fig. 2, a) shows uniform particles about 1μm. The same morphology was observed for SBA-15. It can be concluded that morphology of solid was saved without change during the surface modifications. On the other hand, the TEM image (Fig. 2, b) reveals the parallel channels, which resemble the pores configuration of SBA-15. This indicates that the pore of SBA-Pr-SO_3H was not collapsed during two-steps reactions.

For the preparation of the catalyst, at first, the surface of SBA-15 was functionalized and grafted with (3-mercaptopropyl) trimethoxysilane (MPTS), the thiol groups have been incorporated to surface of SBA-15 under reflux condition in dry toluene. Then the thiol groups were oxidized into sulfonic acid groups by hydrogen peroxide (Figure 3) [39, 40].

Table 1. Synthesis of benzoxazole derivatives by M.W.

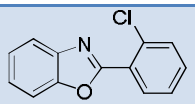
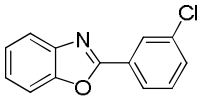
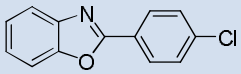
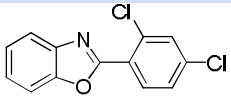
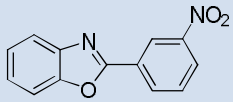
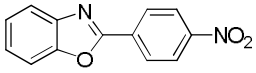
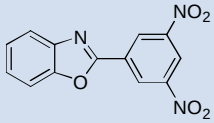
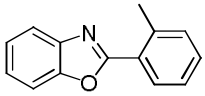
Entry	Product	Crystallization solvent	Yield (%)	mp (°C)	mp (Ref.)
1	 **4a**	EtOH	90	126-128	125-125.5 [41]
2	 **4b**	EtOH	98	123-125	124-125 [42]
3	 **4c**	EtOH	98	141-143	140-142 [33]
4	 **4d**	EtOH	98	119 -120	118-119 [27]
5	 **4e**	EtOH/THF	98	205-207	207 [42]
6	 **4f**	EtOH/THF	64	269-270	269-270 [43]
7	 **4g**	EtOH/THF	98	205-207	205-206 [44]
8	 **4h**	EtOH	65	63-64	63-65 [45]

Table 2. Efficiency comparison of various conditions in the synthesis of benzoxazole derivatives.

Entry	Catalyst	Solvent	Conditions	Yield (%)	Time (min)	Ref.
1	-	[Hbim]BF_4	28 °C	79-96	10-25	[35]
2	-	[bbim]BF4	28 °C	79-94	40-120	[35]
3	Ps-PPh_3/ CCl_3CN	MeCN	M.W.	77-97	15	[46]
4	Silica sulfuric acid	-	85 °C	85-97	1.5-10	[25]
5	MCM-41	-	heating	88-94	25-35	[29]
6	Alum	-	M.W.	70-90	1.5-4	[26]
7	In $(OTf)_3$	-	70-110 °C	55-96	9-18 h	[27]
8	SBA-Pr-SO_3H	-	M.W.	60-98	5	**This work**

[Hbim]BF_4: 1-butylimidazolium tetra flouroborate

[bbim]BF4: 1,3-di-*n*-butylimidazolium tetrafluoroborate

Alum: $KAl(SO_4)_2.12H_2O$

4. Conclusion

In summary, a novel and highly efficient method for the synthesis of benzoxazoles **4** has been achieved by the reaction of aromatic benzoyl chlorides **2** with 2-aminophenol **1** under solvent free condition in the presence of microwave irradiation

and SBA-Pr-SO_3H as catalyst. In comparison to other methods, the use of benzoyl derivatives will increase the yield of reaction. The attractive features of this protocol are simple procedure, short reaction time, high yields, simple workup and non-chromatographic purification of products.

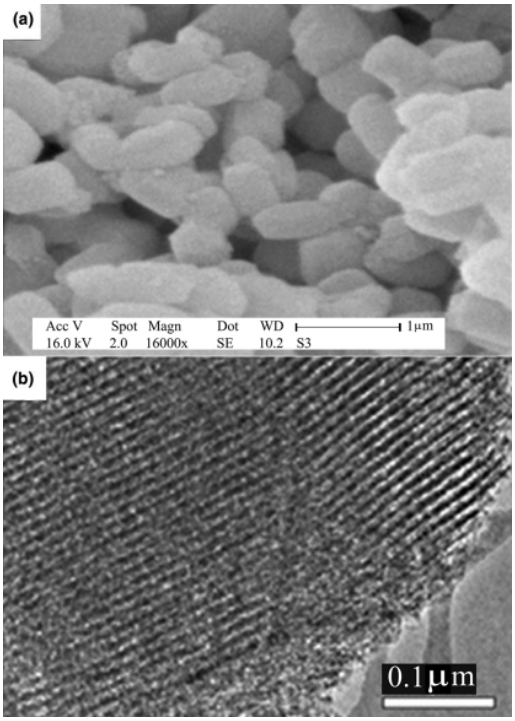


Fig. 2. SEM (a) and TEM (b) images of SBA-Pr-SO_3H.

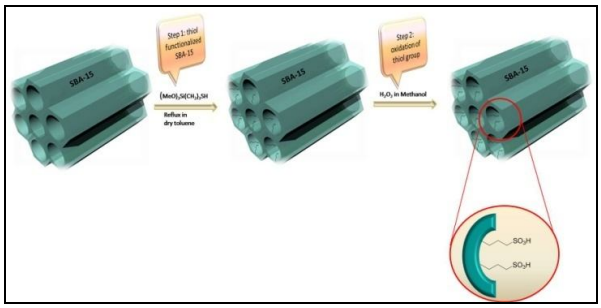


Fig. 3. Preparation of SBA-Pr-SO_3H.

Acknowledgment

We gratefully acknowledge the financial support from the Research Council of Alzahra University and the University of Tehran.

References

[1] G. Zhu, Q. Yang, D. Jiang, J. Yang, L. Zhang, Y. Li,C. Li, J. Chromatogr. A. 1103 (2006) 257-264.

[2] X. M. Tai, H. X. Wang,X. Q. Shi, Chin. Chem. Lett. 16 (2005) 843-845.

[3] J. Tang, J. Liu, P. Wang, H. Zhong,Q. Yang, Microporous Mesoporous Mater. 127 (2010) 119-125.

[4] D. Procha´zkova´, M. Bejblova´, J. Vlk,J. C. ejka, Top Catal. 52 (2009) 618-626.

[5] D. Margolese, J. A. Melero, S. C. Christiansen, B. F. Chmelka,G. D. Stucky, Chem. Mater. 12 (2000) 2448-2459.

[6] J. W. Westly, C. M. Liu, J. F. Blount, L. H. Sello, N. Troupe,P. A. Miller, J. Antibiot. 36 (1983) 1275-1278.

[7] R. D. Haugwitz, B. V. Maurer, G. A. Jacobs, V. L. Narayanan, L. Cruthers,J. Szanto, J. Med. Chem. 22 (1979) 1113-1118.

[8] D. W. Dunwell, D. Evans, T. A. Hicks, C. H. Cashin,A. Kitchen, J. Med. Chem. 18 (1975) 53-58.

[9] D. W. Dunwell, D. Evans, J. Med. Chem. 20 (1977) 797-801.

[10] G. Balaswamy, K. S rinivas, P. Predeep, M. Sarangapani, Int. J. Chem. Sci. 10 (2012) 619-626.

[11] Y. Katsura, S. Nishino, Y. Inoue, M. Tomoi, H. Itoh, H. Takasugi, Chem. Pharm. Bull. 40 (1992) 371-380.

[12] R. R. Jadhava, G. Srikanth, P. Harathic, P. G. Shinde, Journal of Pharmacy Research, 4 (2011) 3562-3565.

[13] M. L. McKee,S. M. Kerwin, Bioorg. Med. Chem. 16 (2008) 1775-1783.

[14] S. T. Patil,P. A. Bhatt, Der Pharmacia Sinica. 1 (2010) 105-112.

[15] S. T. Patil, P. A. Bhatt, Der Pharmacia Sinica. 1 (2010) 105-112.

[16] P. C. R. Stella, S. Rajam, B. R. Venkatraman, J. Chem. Pharm. Res. 4 (2012) 2988-2993

[17] M. M. Kandeel, E. K. A. Abdelall, M. K. A. Hamida, M. A. Abdelgawad, J. N. Philoppes, J. Chem. Pharm. Res. 5 (2013) 16-21.
[18] P. Xiang, T. Zhou, L. Wang, C. Y. Sun, J. Hu, Y. L. Zhao, L. Yang, Molecules. 17 (2012) 873-883.
[19] Ö. Temiz-Arpacı, İ. Yıldız, S. Özkan, F. Kaynak, E. Akı-Şener,İ. Yalçın, Eur. J. Med. Chem. 43 (2008) 1423-1431.
[20] R. S. Pottorf, N. K. Chadha, M. Katkevics, V. Ozola, E. Suna, H. Ghane, T. Regberg, M. R. Player, Tetrahedron Lett. 44 (2003) 175-178.
[21] I. Tamm, P. B. Sehgal, Adv. Virus. Res. 22 (1978) 187-258.
[22] M. L. McKee, S. M. Kerwin, Bioorg. Med. Chem. 16 (2008) 1775–1783.
[23] M. S. R. Murty, K. R. Ram, R. V. Rao, J. S. Yadav, J. V. Rao, V. T. Cheriyan, R. J. Anto, Med. Chem. Res. 20 (2011) 576-586.
[24] L. David, A. Kergomard, J Antibiot (Tokyo). 35 (1982) 1409-1411.
[25] I. Mohammadpoor-Baltork, M. Moghadam, S. Tangestaninejad, V. Mirkhani, M. A. Zolfigol, S. F. Hojati, J. Iran. Chem. Soc. 5 (2008) S65-S70.
[26] A. A. Mohammadi, J. Appl. Chem. Res. 11 (2009) 34-39.
[27] B. Wang, Y. Zhang, P. Li, L. Wang, Chin. J. Chem. 28 (2010) 1697-1703.
[28] S. S. Patil, V. D. Bobade, Synth. Commun. 40 (2010) 206-212.
[29] R. H. Shoar, M. Heidary, M. Farzaneh, R. Malakouti, Synth. Commun. 39 (2009) 1742-1751.
[30] G. Raspanti,G. Zanchi, US 0085981 (2002)
[31] G. Raspanti,G. Zanchi, US 5639446 (1997)
[32] C. J. Smith, A. Ali, L. Chen, M. L. Hammond, M. S. Anderson, Y. Chen, S. S. Eveland, Q. Guo, S. A. Hyland, D. P. Milot, C. P. Sparrow, S. D. Wright,P. J. Sinclair, Bioorg. Med. Chem. Lett. 20 (2010) 346-349.
[33] A. B. Naidu,G. Sekar, Synthesis (2010) 579-586.
[34] S. Ueda, H. Nagasawa, J. Org. Chem. 74 (2009) 4272-4277.
[35] R. N. Nadaf, S. A. Siddiqui, T. Daniel, R. J. Lahoti,K. V. Srinivasan, J. Mol. Catal. A: Chem. 214 (2004) 155-160.
[36] G. Mohammadi Ziarani, A. Badiei, Z. Aslani, N. Lashgari, Arab. J. Chem. (2012), In press, DOI: 10.1016/j.arabjc.2011.06.20.
[37] K. Bahrami, M. M. Khodaei,P. Fattahpour, Catal. Sci. Technol. 1 (2011) 389-393.
[38] G. Mohammadi Ziarani, A. R. Badiei, Y. Khaniania, M. Haddadpour, Iran. J. Chem. Chem. Eng. 29 (2010) 1-10.
[39] W. M. V. Rhijn, D. E. D. Vos, B. F. Sels, W. D. Bossaert, P. A. Jacobs, Chem. Commun. (1998) 317-318.
[40] M. H. Lim, C. F. Blanford, A. Stein, Chem. Mater. 10 (1998) 467-470.
[41] H. Schwartz, NL 6607039 (1966)
[42] L. Keurulainen, O. Salin, A. Siiskonen, J. M. Kern, J. Alvesalo, P. Kiuru, M. Maass, J. Yli-Kauhaluoma,P. Vuorela, J. Med. Chem. 53 (2010) 7664-7674.
[43] Y. Kawashita, M. Hayashi, Y. Juichi, T. Fujii, Bull. Chem. Soc. Jpn. 82 (2009) 482 - 488
[44] A. B. Berezina, V. V. Korshak, G. M. Tseitlin, A. I. Pavlov, B. B. Brezin,N. A. Plaksina, Tr. Mosk. Khim-Tekhnol. Inst. 86 (1975) 152-154.
[45] S. Ueda, H. Nagasawa, Angew. Chem. Int. Ed. 47 (2008) 6411-6413.
[46] Y. Wang, K. Sarris, D. R. Sauer, S. W. Djuric, Tetrahedron Lett. 47 (2006) 4823-4826.