

Regioselective conversion of epoxides to vicinal nitrohydrins catalyzed by silica-bound 3-{2-[poly(ethylene glycol)]ethyl}-substituted 1-methyl-1H-imidazol-3-ium bromide as a green and reusable catalyst under aqueous thermal conditions

Neda Ayashi^a, Mehdi Fallah-Mehrjardi^{b,c}, Ali Reza Kiasat^{a,*}

^aDepartment of Chemistry, College of Science, Shahid Chamran University of Ahvaz, P.O. Box 61357-4-3169, Ahvaz, Iran.

^bDepartment of Chemistry, Payame Noor University, P.O. Box 19395-3697, Tehran, Iran.

^cResearch Center of Environmental Chemistry, Payame Noor University, Ardakan, Yazd, Iran.

Received 21 December 2017; received in revised form 19 March 2018; accepted 13 April 2018

ABSTRACT

An environmentally benign procedure for the synthesis of vicinal nitrohydrins *via* the regioselective ring opening reaction of epoxides with nitrite anion using silica-bound 3-{2-[poly(ethylene glycol)]ethyl}-substituted 1-methyl-1H-imidazol-3-ium bromide as an effective heterogeneous phase transfer catalyst was described. Short reaction time, high yield of products, simple work-up procedure, and recyclability of the catalyst were some of the striking features of the present protocol. The recovered catalyst could be reused five times without any loss in its catalytic activity and selectivity.

Keywords: 2-Nitroalcohols, Phase transfer catalyst, Ring opening of epoxides, Regioselective, Green chemistry.

1. Introduction

Nitrohydrins are important precursors for the synthesis of β -aminoalcohols [1]. Some of them are significant as β -adrenergic blocking agents and highly effective antagonists for the treatment of cardiovascular diseases. They are also useful as chiral auxiliaries in asymmetric synthesis [2]. In addition, this class of compounds is also useful intermediates for the synthesis of amino sugars [3], carbocyclic nucleosides [4] and β -aminoalcohols derivatives such as ephedrine and norephedrine [5].

Although the nucleophilic addition of nitrite anion to epoxides is the classic procedure for the preparation of 2-nitroalcohols, the cleavage of epoxides by nitrite anion is difficult because of its low nucleophilicity. Systematic literature survey reveals that so far very few reports are available in the successful regioselective ring opening of epoxides with nitrite ion. Some of the catalysts used for this transformation are $MgSO_4$ [6], Amberlite/IRA-400 [7], $Ce(OTf)_4/SDS$ [8], poly[N-(2-aminoethyl) acrylamido]trimethyl ammonium chloride [9], $LaCl_3 \cdot 7H_2O$ [10] and Poly (N-bromoacrylamide) [11].

Although these catalytic methods have their own advantages, many of them suffer from one or more drawbacks such as prolonged reaction times, poor regioselectivity, expensive catalysts in stoichiometric quantities, difficulty in work-up and lack of reusability of the catalyst. Therefore, the development of mild, effective and environmentally friendly processes which are suitable for the ring opening of epoxides to 2-nitroalcohols is highly desirable.

One of the most promising approaches that is less hazardous to human and environment uses water as the reaction medium in organic syntheses. Advantages of catalytic reactions in aqueous systems include low cost, inflammability, non-toxicity, availability, and safety [12]. However, unfortunately, water does not dissolve most of the organic reactants and this problem can stop the reaction performance. The addition of a phase transfer agent enables the reaction to improve between two substances located in different immiscible phases [13]. Immobilization of the phase transfer catalyst on an insoluble matrix can provide reusability of catalyst and simple isolation of product [14, 15].

In continuation of our interest in the applications of silica-bound 3-{2-[poly(ethylene glycol)]ethyl}-substituted 1-methyl-1H-imidazol-3-ium bromide

*Corresponding author email: akiasat@scu.ac.ir
Tel.: +98 61 1333 1746; Fax: +98 61 1333 1746

2-Nitrocyclohexanol (6):

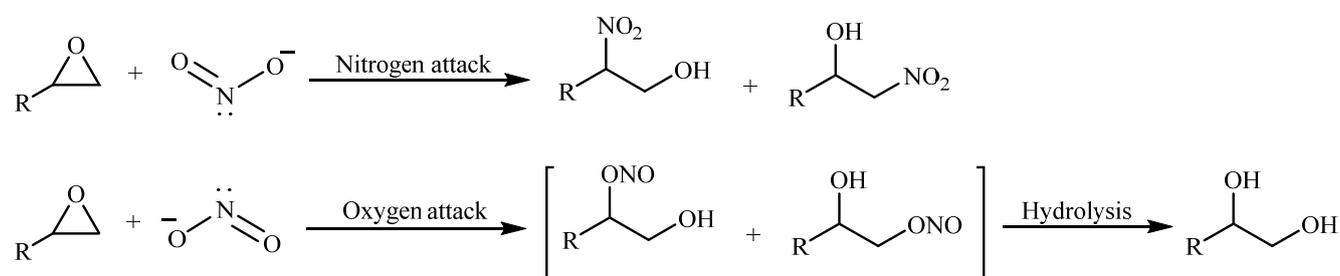
IR (neat): $\bar{\nu} = 1378$ and 1555 (NO_2) cm^{-1} . ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 89.4$ (CHNO_2), 72.1 (CHOH), 32.5 (CH_2), 28.3 (CH_2), 25.1 (CH_2), 24.4 (CH_2) ppm.

3. Results and Discussion

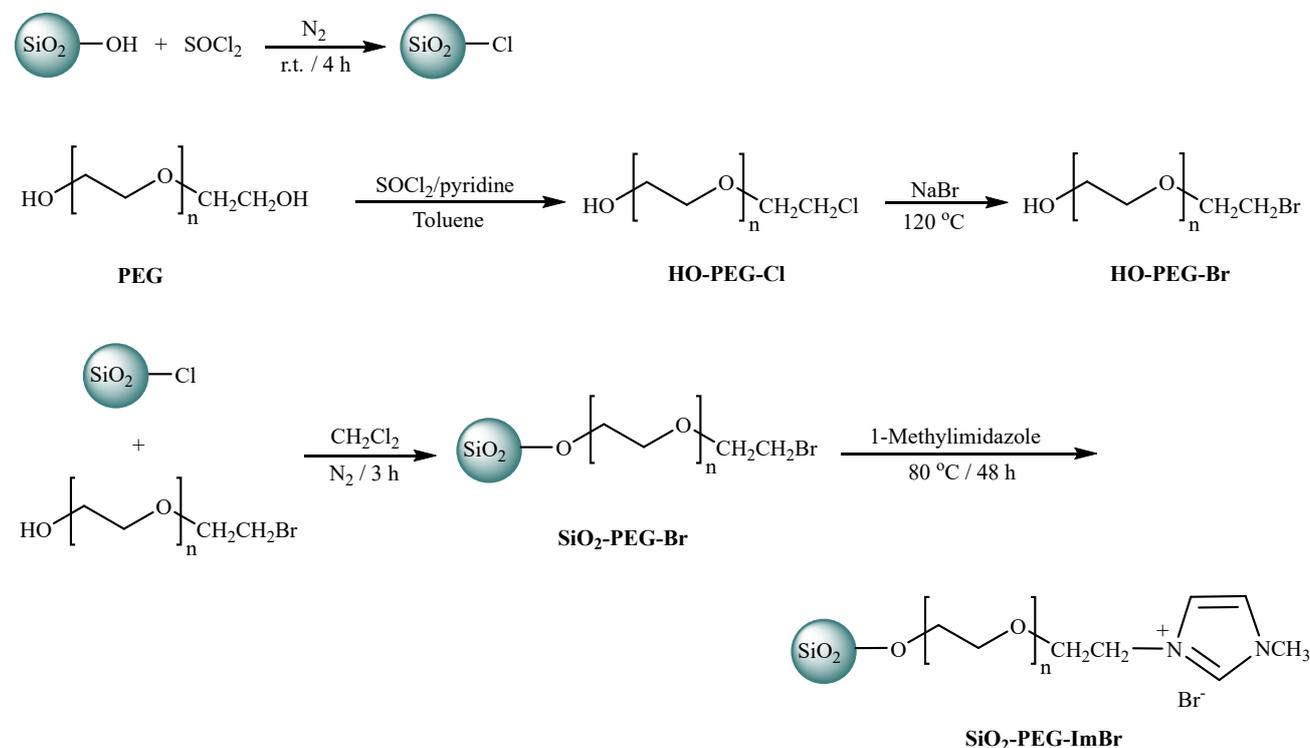
Nitrite anion is an ambident nucleophile and it can attack epoxides through its nitrogen or oxygen. Theoretically it can be expected four types of adducts as shown in Scheme 2. The formation of products depends on two types of regioselectivity: nitrogen or oxygen attack, and α - or β -selectivity of the attack on the epoxide ring. Attack to the nitrogen can lead to the formation of 2-nitroalcohols, which are stable and can be

isolated as final products, while attack to the oxygen causes unstable nitrite esters, which can be spontaneously hydrolyzed to their corresponding diols [25].

Because of the low nucleophilicity of nitrite anion, the ring opening of epoxides with this anion has not proceeded as desired, when only NaNO_2 was used. These reactions can be sped up by the addition of a catalyst. We now wish to report the catalytic application of silica-bound 3-{2-[poly(ethylene glycol)]ethyl}-substituted 1-methyl-1H-imidazol-3-ium bromide, SiO_2 -PEG-ImBr, as an efficient phase transfer catalyst in the regioselective preparation of nitrohydrins in aqueous media. A general synthetic route for the preparation of SiO_2 -PEG-ImBr is presented in Scheme 3.



Scheme 2. Possible ring opening reactions of an epoxide with nitrite ion, depending on α/β and N/O selectivity of the nucleophilic attack.



Scheme 3. Preparation of SiO_2 -PEG-ImBr.

In the FT-IR spectrum of SiO₂-PEG-ImBr (Fig. 1), the C–H stretching and bending bands can be observed at 2800–2950 cm⁻¹ and 1400–1500 cm⁻¹, respectively. In addition, the presence of imidazolium unit was confirmed by the bands at 1619 cm⁻¹ (imidazole C=N bending) and 1567 cm⁻¹ (imidazole ring stretching). Therefore, the successful introduction of PEG-ImBr onto silica surface was verified through the FT-IR spectra.

The thermogravimetric analysis (TGA) curve of the SiO₂-PEG-ImBr showed the mass loss of the organic materials as they decompose upon heating (Fig. 2). The initial weight loss up to 126 °C is due to the removal of physically adsorbed water and surface hydroxyl groups. The weight loss of about 18 % between 150 and 420 °C may be associated to the thermal decomposition of PEG-ImBr. On the basis of this observation, the good grafting of PEG-ImBr on the SiO₂ surface was also verified.

To determine the amount of imidazolium bromide in SiO₂-PEG-ImBr, 0.01 g of the catalyst was immersed in 20 mL of 0.1 mol L⁻¹ aqueous HNO₃ solution. The bromide ions were determined by the Volhard's method. The amount of bromide equaled by imidazolium units was 2.85 mmol g⁻¹. The amount of imidazolium units was also determined by the CHN analysis method (2.667 mmol g⁻¹) (Fig. 3); this value is in good agreement with the obtained result from the Volhard's titration method.

In order to find the best experimental conditions, the catalytic activity of SiO₂-PEG-ImBr in the ring opening of 3-phenyloxy-1,2-epoxypropane with NaNO₂ in water was tested. After a series of preliminary experiments, the best conversion was observed when 5 mmol NaNO₂ and 0.2 g PTC were added to the 1.0 mmol epoxide in 5 mL water and the mixture was stirred at 90 °C. In this condition, after 1.5 h the corresponding 2-nitroalcohol was obtained in 85% yield (Table 1, entry 3).

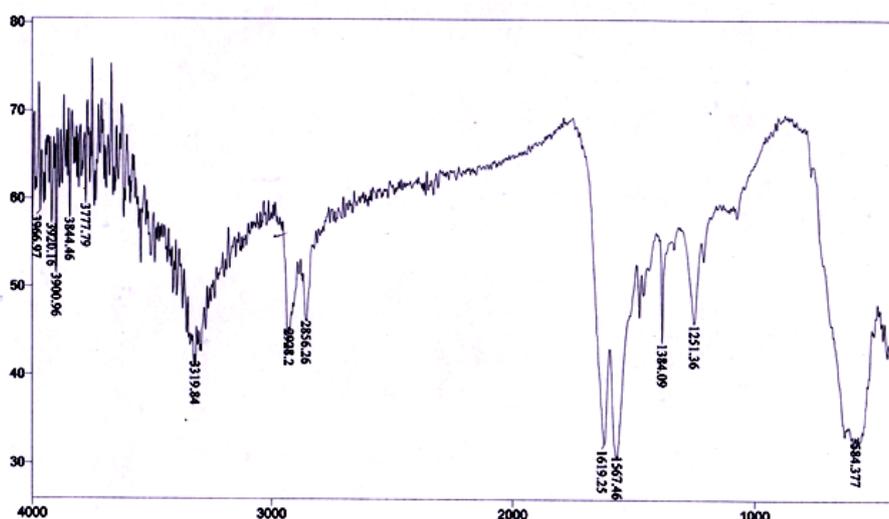


Fig. 1. The FT-IR spectrum of SiO₂-PEG-ImBr.

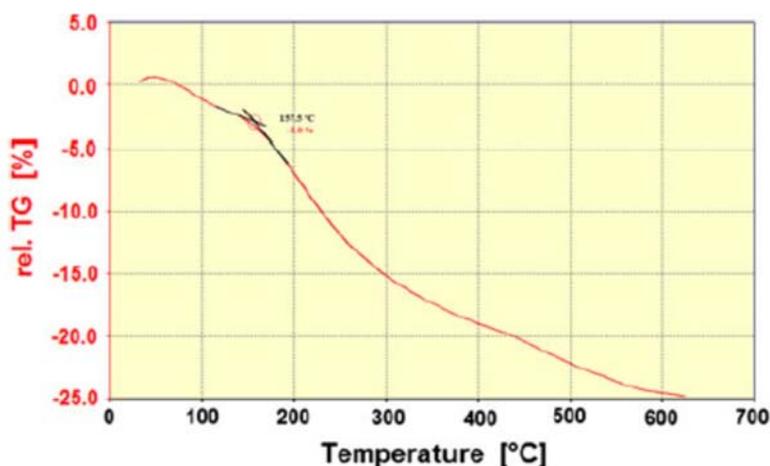


Fig. 2. TGA curve of SiO₂-PEG-ImBr.

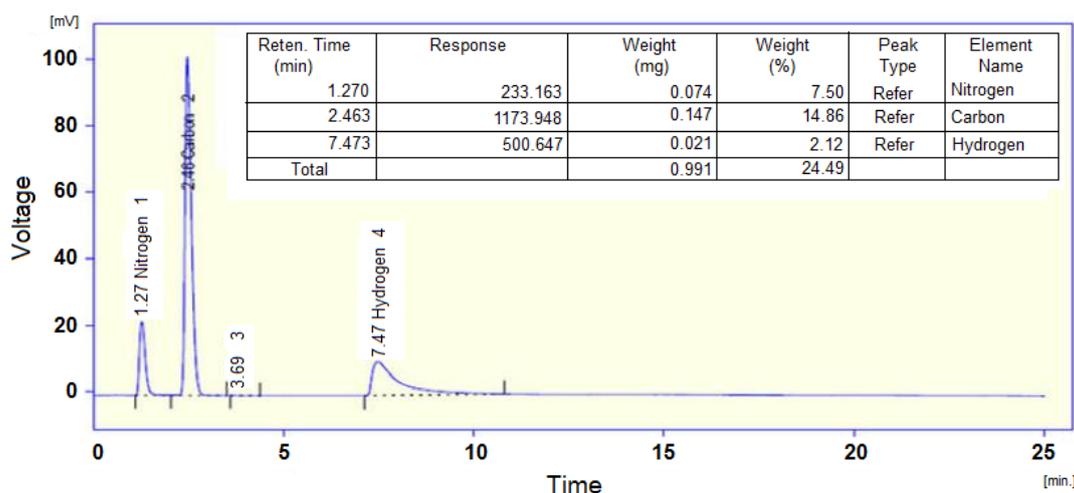


Fig. 3. CHN analysis of SiO₂-PEG-ImBr.

After optimizing the reaction conditions, the generality and synthetic scope of this method for synthesizing a series of 2-nitroalcohols were demonstrated by the reaction of various epoxides with NaNO₂ under optimal conditions (Table 2). As shown in Table 2, yields of products are good to excellent for epoxides bearing both electron-donating and electron-withdrawing groups.

The direction of ring opening is characteristically observed for terminal epoxides under S_N2 conditions and probably dictated by steric and electronic factors. Styrene oxide underwent cleavage with sodium nitrite in the presence of catalytic amount of SiO₂-PEG-ImBr with the preferential attack at the benzylic position to give the corresponding 2-nitroalcohol in 80% yield (Table 2, entry 1). Except the reaction of styrene oxide, the reactions of other epoxides bears carrying electron withdrawing groups, it is the steric factor which predominates and the nucleophilic attack of nitrite anion

is strongly favored on the less substituted carbon atom of epoxides (Table 2, entries 2-5). Furthermore, the reactions with epoxides derived from cyclic olefins afforded exclusively *trans* isomers (Scheme 4 and Table 2, entries 6-8).

In the absence of the catalyst, the reactions were very slow in the water. The addition of SiO₂-PEG-ImBr significantly improved the reaction rates and yields. This is probably due to the activation of the epoxide by the hydrogen bonding between silanol hydroxy groups on the silica gel surface and the oxygen of epoxide. In addition, polyethylene glycol units in PTC can encapsulate sodium cation, much like crown ethers, and this complex causes the nitrite anion to be activated. The 1-methylimidazol-3-ium units introduced ionic liquid property to the catalyst and the bromide to nitrite anion exchange can facilitate the rate of reaction (Scheme 5).

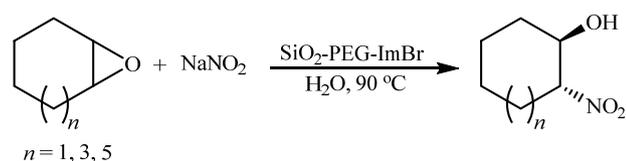
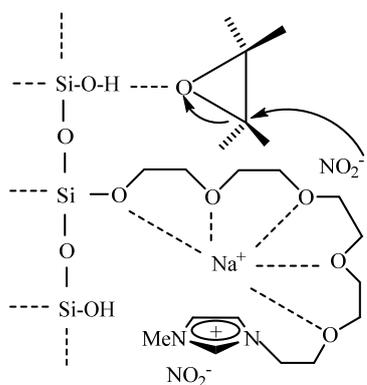
Table 1. Optimization of the reaction conditions for the ring opening of 3-phenyloxy-1,2-epoxypropane by NaNO₂.

Entry	NaNO ₂ (mmol)	Catalyst (g)	Conditions	Time (h)	Yields (%) ^a
1	5	-	H ₂ O, 90 °C	3	trace
2	5	0.1	H ₂ O, 90 °C	2.5	82
3	5	0.2	H ₂ O, 90 °C	1.5	85
4	5	0.2	H ₂ O, r.t.	3	35
5	5	0.2	H ₂ O, 50 °C	3	58
6	5	0.3	H ₂ O, 90 °C	1.25	83
7	4	0.2	H ₂ O, 90 °C	2.5	85
8	5	0.2	MeCN, reflux	3	70
9	5	0.2	EtOAc, reflux	3	65
10	5	0.2	EtOH, 90 °C	3	69

^aIsolated yields.

Table 2. Synthesis of 2-nitroalcohols from epoxides in the presence of SiO₂-PEG-ImBr in water at 90 °C.

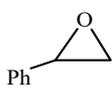
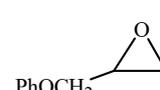
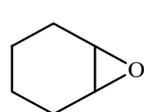
Entry	Substrate	Product	Time (h)	Yields (%) ^a
1			1	80
2			1.5	85
3			0.5	81
4			0.5	75
5			1.5	75
6			1	75
7			2.5	83
8			1.5	82

^aIsolated yields.**Scheme 4.** Stereospecificity in ring opening of cycloalkyl epoxide.**Scheme 5.** The catalytic activity of SiO₂-PEG-ImBr.

Because of the importance of the catalyst reusability in the large-scale operation and industrial point of view, the recovery and reusability of SiO₂-PEG-ImBr were examined. After performing the reaction of styrene oxide under the reaction conditions, the catalyst was recovered by filtration, washed with water and methanol and dried at 70 °C, and then reused for a consecutive run under the same reaction conditions. Thus, after the first run, which gave the corresponding 2-nitroalcohol in 100% conversion and 80% isolated yield, after recovery, the catalyst was subjected four times to the same reaction from which it also gave the corresponding product in 78%, 79%, 80% and 78% yield, respectively.

The superiority of using SiO₂-PEG-ImBr as the catalyst for the synthesis of 2-nitroalcohols by the ring opening of epoxides with nitrite anion is shown by comparing with those of the previously reported methods in the literature (Table 3).

Table 3. Comparison of the ring opening of epoxides with nitrite ion in the presence of different catalysts.

Entry	Epoxides	Reagent systems	Solvent	Temp. (°C)	Time (min)	Yield (%)	Ref.
1 ^a		NaNO ₂ , MgSO ₄	MeOH	65	270	0:75	[6]
		Amberlit IRA-400, NO ₂ ⁻	EtOH	50	120	32:48	[7]
		NaNO ₂ , SDS ^b , Ce(OTf) ₄	H ₂ O	25	5	90:0	[8]
		NaNO ₂ , QPA ^c	MeCN	25	60	85:8	[9]
		NaNO ₂ , LaCl ₃ .7H ₂ O, Bu ₄ NBr	Et ₂ O-H ₂ O	25	480	79:10	[10]
		NaNO ₂ , PNBA ^d	H ₂ O	25	90	80:10	[11]
2		NaNO ₂ , MgSO ₄	MeOH	65	180	86	[6]
		Amberlit IRA-400, NO ₂ ⁻	EtOH	50	120	80	[7]
		NaNO ₂ , QPA	MeCN	25	66	94	[9]
		NaNO ₂ , PNBA	H ₂ O	25	60	85	[11]
		NaNO ₂ , SiO ₂ -PEG-ImBr	H ₂ O	90	90	85	-
		3		NaNO ₂ , MgSO ₄	MeOH	65	420
Amberlit IRA-400, NO ₂ ⁻	EtOH			50	120	80	[7]
NaNO ₂ , SDS, Ce(OTf) ₄	H ₂ O			25	10	78	[8]
NaNO ₂ , QPA	MeCN			25	60	91	[9]
NaNO ₂ , SiO ₂ -PEG-ImBr	H ₂ O			90	60	75	-

^aThe yield percentage for this epoxide has been shown as the percentage of PhCH(NO₂)CH₂OH and PhCH(OH)CH₂NO₂, respectively.

^bSDS: Sodium dodecyl sulfate.

^cQPA: Poly[N-(2-aminoethyl)acrylamido]trimethyl ammonium chloride resin.

^dPNBA: Poly (N-bromoacrylamide).

^ePresent procedure.

4. Conclusions

In conclusion, in this study, we have introduced a simple and efficient procedure for the regioselective synthesis of 2-nitroalcohols using catalytic amounts of SiO₂-PEG-ImBr as an effective and recyclable phase transfer catalyst. The advantages of the present procedure, such as relatively short reaction times, simplicity in operation, high yield of products, excellent regioselectivity, and recyclability of the catalyst make this new process an attractive alternative to current methodologies.

Acknowledgments

We are grateful to the Research Council of Shahid Chamran University for financial support.

References

- [1] N. Ono, *The nitro group in organic synthesis*, Wiley-VCH, New York, 2001.
- [2] D.J. Ager, I. Prakash, D. Schaad, *Chem. Rev.* 96 (1996) 835–876.
- [3] Y. Bleriot, N. Auberger, Y. Jagadeesh, C. Gauthier, G. Prencipe, A.T. Tran, J. Marrot, J. Desire, A. Yamamoto, A. Kato, M. Sollogoub, *Org. Lett.* 16 (2014) 5512–5515.
- [4] D.M. Coe, P.L. Myers, D.M. Parry, S.M. Roberts, R. Storerb, *J. Chem. Soc. Chem. Commun.* (1990) 151–154.
- [5] T. Suami, K.I. Tadano, A. Suga, Y. Ueno, *J. Carbohydr. Chem.* 3 (1984) 429–441.
- [6] B. Kalita, N.C. Barua, M. Bezbarua, G. Bez, *Synlett* (2001) 1411–1414.
- [7] B. Tamami, N. Iranpoor, R. Rezaie, *Iran. Polym. J.* 13 (2004) 495–501.
- [8] N. Iranpoor, H. Firouzabadi, M. Shekarize, *Org. Biomol. Chem.* 1 (2003) 724–727.
- [9] H. Mahdavi, B. Tamami, *React. Funct. Polym.* 64 (2005) 179–185.
- [10] J.C. Borah, S. Gogoi, J. Boruwa, N.C. Barua, *Synth. Commun.* 35 (2005) 873–878.
- [11] F. Ebrahimzadeh, R. Rooydell, *Chem. Sin.* 3 (2012) 1146–1152.
- [12] M. Doble, A.K. Kruthiventi, *Green chemistry and engineering*, Academic Press, 2007.
- [13] E. Murugan, G. Tamizharasu, P. Shanmugam, *React. Kinet. Mech. Cat.* 113 (2014) 39–59.

- [14] D. Xin, J. Yuan, K.Y. Wong, K. Burgess, *J. Org. Chem.* 81 (2016) 8071-8081.
- [15] S. Sayyahi, S. Heidari, *Iran. J. Catal.* 6 (2016) 167-172.
- [16] A.R. Kiasat, N. Ayashi, M. Fallah-Mehrjardi, *Helv. Chim. Acta* 96 (2013) 275-279.
- [17] A.R. Kiasat, N. Ayashi, M. Fallah-Mehrjardi, *J. Iran. Chem. Soc.* 10 (2013) 1175-1181.
- [18] A.R. Kiasat, M. Fallah-Mehrjardi, *Catal. Commun.* 9 (2008) 1497-1500.
- [19] A.R. Kiasat, R. Mirzajani, H. Shalhaf, T. Tabatabaei, M. Fallah-Mehrjardi, *J. Chin. Chem. Soc.* 56 (2009) 594-599.
- [20] A.R. Kiasat, F. Ataieian, M. Fallah-Mehrjardi, *Iran. J. Catal.* 2 (2012) 1-5.
- [21] A.R. Kiasat, F. Chadorian, S.J. Saghanezhad, *C.R. Chim.* 18 (2015) 1297-1306.
- [22] F. Moheiseni, A.R. Kiasat, *Iran. J. Catal.* 7 (2017) 153-159.
- [23] H. Firouzabadi, N. Iranpoor, B. Karimi, H. Hazarkhami, *Synlett* (2000) 263-265.
- [24] S. Grinberg, E. Shaubi, *Tetrahedron* 47 (1991) 2895-2902.
- [25] G. Hasnaoui, J.H.L. Spelberg, E. Vries, L. Tang, B. Hauer, D.B. Janssen, *Tetrahedron: Asymmetry* 16 (2005) 1685-1692.