

An efficient synthesis of azidohydrin catalyzed by a novel polymeric ionic liquid

B. Mombeni Goodajdar*, F. Akbari

Department of Chemistry, Omidyeh Branch, Islamic Azad University, Omidyeh, Iran

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In the current study, PEG-supported dicationic ionic liquid was synthesized as a green catalyst and applied in the ring opening of epoxides under reflux conditions in water. The reactions occurred in water and furnished the corresponding β -azido alcohol in high yields. The method described herein is a very good, safe, clean, economical and environmentally friendly alternative to the classical procedures. The structural properties of the catalyst were investigated by FT-IR, UV-VIS, Raman spectra and TGA analysis.

Keywords; Epoxide, Azido alcohol, Magnetic ionic liquid, Regioselectivity, Ring opening

INTRODUCTION

The dicationic ionic liquids (DILs) have two head groups, linked *via* a flexible spacer or a rigid spacer. This type of ionic liquids (ILs) has revealed unique characteristics of critical micelle concentration (CMC), more efficient behavior as lubricants, properties of electrolytes, surface tension, and greater thermal stabilities than monocationic ILs and other traditional solvents. Dicationic ionic liquids are an attractive new group of ionic liquids that acquire higher melting point, wider liquid range and better thermal stability. In addition to a combination of anion and cation, simple changes in the length of the spacer or in the aliphatic chains on the cations allow to tailor ILs' physical properties for certain applications [1-3].

PEG-DILs are new salts making the link between two distinct but very similar fluids: ionic liquids and poly (ethylene glycol). They exhibit excellent properties of ionic liquids in relation to green chemistry including low volatility, non-flammability, high thermal and chemical stability, negligible vapour pressure, and high solubility for both organic and inorganic materials [4].

The use of environmentally benign solvents instead of traditional organic solvents is an important and efficient strategy in green chemistry. Water is a promising green solvent for use in chemistry because it is cheap, readily available, and nontoxic. There is increasing recognition that organic reactions carried out in water may offer advantages over those in organic solvents. However, the poor solubility of reactants in water is the main obstacle to the use of water as a reaction solvent [5, 6].

Multiphase reactions are always difficult to take place owing to their immiscibility with each other

(basically aqueous and organic phases). However, with the help of an amphiphilic agent that is soluble both in aqueous and organic phases such reactions are now possible. These agents are phase transfer catalysts that along with helping the transfer of ion-pairs across the interfaces also help in enhancing the reaction rate. This process is called phase transfer catalysis (PTC). It's a green route to synthesize fine chemicals because of the advantages it has over other methods. In PTC, mild operating conditions are required, the yield of desired product is very high, unwanted side reactions are eliminated, and there is no generation of hazardous waste after the reaction completion. [7, 8].

Vicinal azido alcohols are an important class of organic compounds and they serve as precursors in the synthesis of vicinal aminoalcohols, carbohydrates, nucleosides, lactams, and oxazolines. They are usually prepared through ring opening of epoxides by using different kinds of azides in suitable solvents. The reactions are often carried out under either alkaline or acidic conditions and several different methods have been devised in order to obtain the direct azidolysis of epoxides in the presence of sodium azide. Under these conditions, azidolysis is usually carried out over a long reaction time and obtaining of azidohydrin is often accompanied by isomerization, epimerization, and rearrangement of products. In order to overcome some of these limitations, a number of alternative procedures have been reported over the past few years using a variety of catalysts [9–17].

As a part of our program aiming at developing selective and environmentally friendly methodologies for the preparation of fine chemicals and in continuation of our interest in magnetic ionic liquid-promoted organic reactions, in this work, H₂O-PEG-MDIL was designed and applied for the

* To whom all correspondence should be sent:

E-mail: bmombeni@gmail.com, mombeni.b@iauo.ac.ir

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regioselective ring opening of epoxide under mild reaction conditions.

EXPERIMENTAL

Material and Methods

Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance DPX 400 MHz spectrometer using TMS as the internal standard in CDCl_3 . IR spectra were recorded on a BOMEM MB-Series 1988 FT-IR spectrometer. Raman spectra were recorded on a Bruker RFS 100/s Raman spectrometer. Thermogravimetric analysis was performed under nitrogen by means of a Perkin Elmer instrument. Epoxides and PEG-400 were purchased from Merck Company in high purity. Products were characterized by comparison of their physical and spectroscopic data with those of known samples. Checking of products purity and reaction monitoring was accomplished by TLC on silica gel Poly Gram SILG/UV 254 plates.

The synthesis of dichloro substituted (Cl-PEG-Cl)

PEG-400 (15 g, 0.025 mol) and pyridine (5 mL, 0.0625 mol) were dissolved in toluene (20 mL), stirred at 87°C , thionyl chloride (5 mL, 0.0625 mol) was added slowly, and the resultant reaction mixture was stirred at 87°C for 15 h. Then the resulting solid was removed by filtration. After removal of the solvent under reduced pressure a viscous liquid residual was collected as dichloro substituted PEG-400 (91.6%).

Procedure for preparation of poly(ethylene glycol) bis(methylimidazolium chloride) (PEG-DIL). 1-Methylimidazole (2 mmol), and polyethylene glycol dichloride (1 mmol) were placed in a Pyrex glass tube, sealed and heated at 80°C for 16 h or at 110°C for 20 h. The organic solvent was removed and the residue was extracted with ethyl acetate (3×20 mL) and then washed with water (2×20 mL) and ether (2×10 mL), and dried over anhydrous magnesium sulfate. The solvent was removed under vacuum at 65°C overnight to give a colorless product.

Procedure for preparation of PEG-DIL based $\text{MnCl}_4 \cdot 2\text{H}_2\text{O}$. A solution of (0.2 g, 1 mmol) of $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$ in ethanol (10 mL) was added to a solution (1.0 mmol) of PEG-DIL [18] in ethanol (10 mL). After heating under reflux for 4 h, to give a pale yellow solution, preconcentration under reduced pressure led to a viscous liquid (90%).

General procedure for preparation of 1,2-azido alcohols. In a round-bottomed flask (25 mL) equipped with a condenser and a magnetic stirrer

bar, epoxide (1 mmol), nucleophilic reagent (NaN_3) (2 mmol), and Mn-DIL-MnCl_4 (0.2 g) in water (5 ml) were added, and heated under reflux conditions for an appropriate time (Table 2). The progress of the reaction was monitored by TLC (eluent: n-hexane/ethyl acetate 80:20). After completion of the reaction, the mixture was extracted with ether (2×10 ml). The extract was dried over anhydrous calcium chloride, and concentrated under vacuum to obtain 1,2-azido alcohols in 82-90% isolated yields.

1-Azido-3-phenoxypropan-2-ol (3a): FT-IR (neat): ν_{max} N_3 (2100 cm^{-1}); ^1H NMR (400 MHz, CDCl_3): 3.51 (d, 2H), 3.88–3.98 (m, 1H), 4.00 (d, 2H), 4.16 (s, 1H), 6.93–7.00 (m, 2H), 7.01–7.06 (m, 1H), 7.26–7.36 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3): 53.50, 69.23, 69.20, 114.29, 121.15, 129.43, 158.37.

2-Azido-2-phenyl-1-ethanol (3b): FT-IR (neat): ν_{max} N_3 (2103 cm^{-1}); ^1H NMR (400 MHz, CDCl_3): 3.36 (s, 1H), 3.73 (m, 2H), 4.65 (m, 1H), 7.33–7.44 (m, 5H). ^{13}C NMR (100 MHz, CDCl_3): 66.27, 68.03, 127.47, 128.40, 128.51, 136.27 ppm.

2-Azidocyclohexan-1-ol (3c): FT-IR (neat): ν_{max} N_3 (2097 cm^{-1}); ^1H -NMR (400 MHz, CDCl_3): 1.20–1.36 (m, 4H), 1.71–1.78 (m, 2H), 2.00–2.08 (m, 2H), 2.52 (s, 1H), 3.10–3.22 (m, 1H), 3.28–3.42 (m, 1H). ^{13}C -NMR (100 MHz, CDCl_3): 24.36, 24.47, 24.52, 33.14, 62.15, 73.78.

1-Azido-3-propoxypropan-2-ol (3d): FT-IR (neat): ν_{max} N_3 (2102 cm^{-1}); ^1H NMR (400 MHz, CDCl_3): δ : 1.07 (t, 3H), 1.70–1.78 (m, 2H), 3.82 (s, 1H), 3.30 (m, 2H), 3.38 (t, 2H), 3.42 (d, 2H), 3.86 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ : 19.15, 31.74, 53.50, 69.73, 70.59, 71.71 ppm.

1-Azido-3-allyloxy propan-2-ol (3e): FT-IR (neat): ν_{max} N_3 (2098 cm^{-1}), OH (3398 cm^{-1}); ^1H NMR (400 MHz, CDCl_3): δ : 5.85 (m, 1H), 5.2 (dd, 2H), 3.9 (q, 2H), 3.8 (s, 1H), 3.6 (q, 3H), 3.3 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ : 53.37, 69.52, 71.33, 72.17, 117.57, 134.46 ppm.

1-Azido-3-isopropoxypropan-2-ol (3f) liquid; FT-IR (neat): ν_{max} N_3 (2103 cm^{-1}); ^1H NMR (CDCl_3 , 400 MHz): δ : 1.40 (d, $J = 6.5$ Hz, 6H), 3.01 (m, 1H), 3.20 (dd, $J = 7.0, 11.5$ Hz, 1H), 3.25 (dd, $J = 4.0, 11.5$ Hz, 1H), 3.30–3.50 (m, 2H), 3.96 (brs, 1H, OH), 3.97–4.0 (m, 1H). ^{13}C NMR (CDCl_3 , 100 MHz) δ : 25.7, 53.4, 70.3, 71.12, 72.33 ppm.

1-Azidobutan-2-ol (3g): FT-IR (neat): ν_{max} N_3 (2098 cm^{-1}); ^1H NMR (400 MHz, CDCl_3): δ : 0.96 (t, 3H), 1.47 (m, 2H), 3.2 (m, 1H), 3.4 (d, 2H), 3.96 (br, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ : 8.2, 27.6, 53, 71.2 ppm.

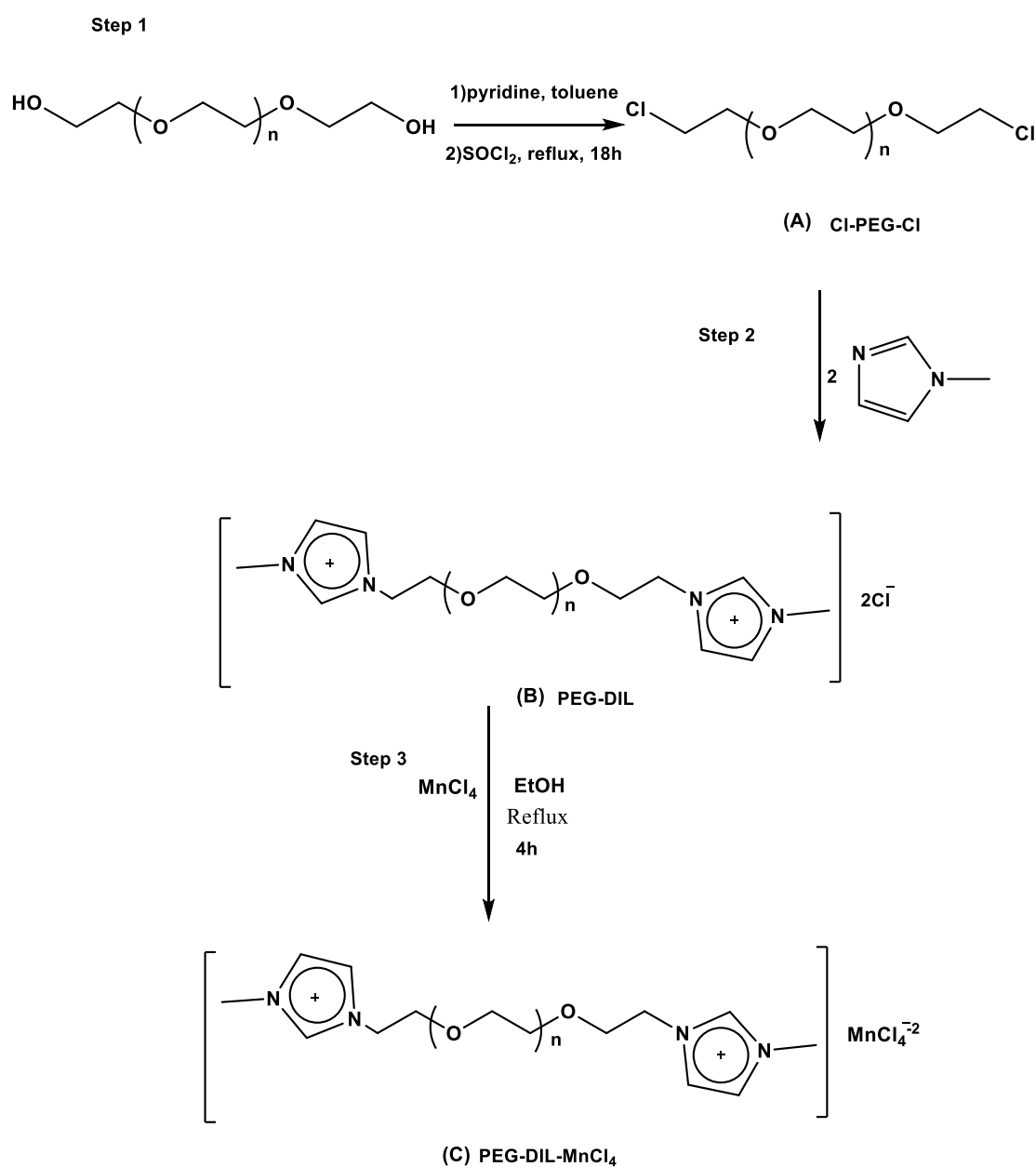
RESULTS AND DISCUSSION

In recent years, ionic liquids have been considered as catalysts or solvents in organic reactions and separation approaches. Herein, we desire to report the synthesis and application of a polymeric dicationic ionic liquid due to numerous benefits along with eco-friendliness, ease of separation of products, energy saving, and availability. The preparation route of PEG-DIL based MnCl_4^{2-} is shown in scheme 1.

The novel catalyst was characterized by FT-IR, UV-VIS, Raman, and TGA analysis. The FT-IR spectra of the native Cl-PEG-Cl and of the PEG-DIL- MnCl_4 sample are shown in Fig. 1. The lack of

OH peak in the poly (ethylene glycol) dichloride spectrum and appeared absorption frequency of C-Cl at 663 cm^{-1} suggests that the reaction between PEG and SOCl_2 has successfully occurred (Fig. 1a). There are peaks at about 1145 cm^{-1} , which were assigned to the characteristic absorption of N- CH_2 in the functionalized PEG-MDIL.

The absorption bands at 3152 and 3013 cm^{-1} (imidazolium CH stretching modes), presented in the inset of Figure 3 demonstrate modification of the PEG. The absorption at 2911 cm^{-1} is usually assigned to CH_2 stretching of the polyether linkage chains. The absorption observed at 1571 cm^{-1} is also characteristic of the imidazolium ring and is assigned to imidazolium ring stretching (Fig. 1b).



Scheme 1. Synthesis of PEG-MDIL- MnCl_4 .

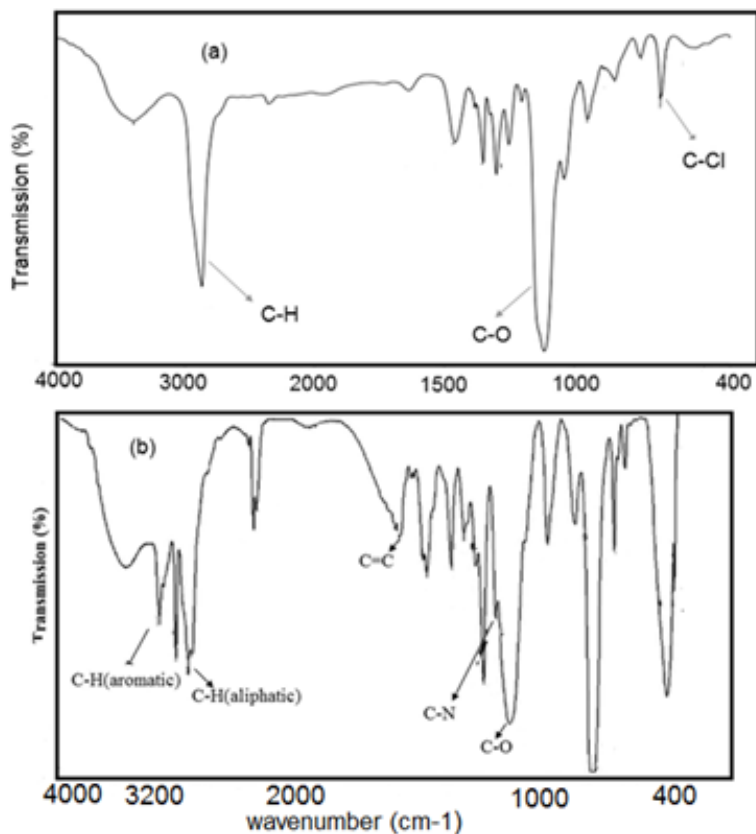


Fig. 1. FT-IR spectra of Cl-PEG-Cl(1a) and of PEG-DIL-MnCl₄(1b)

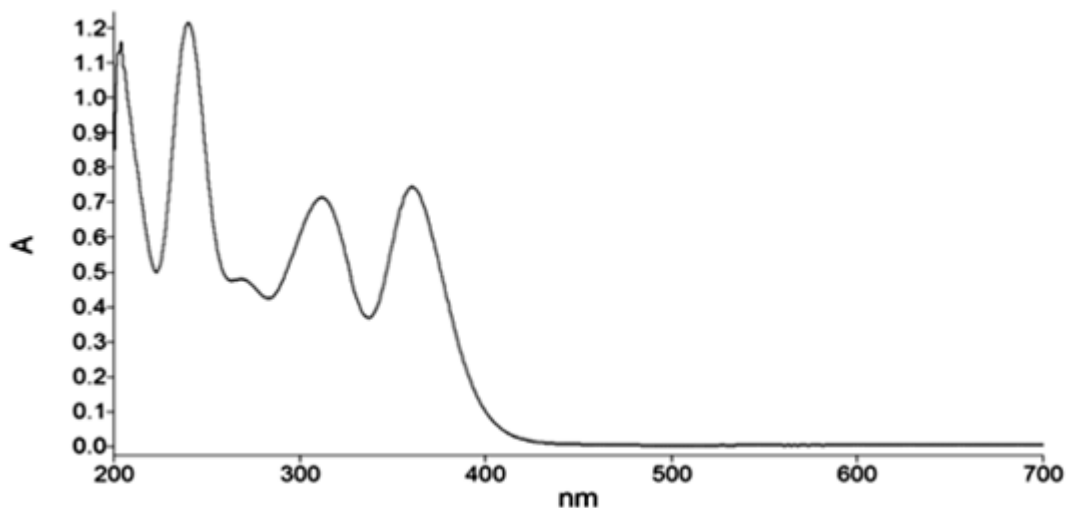


Fig. 2. Visible spectrum of PEG-DIL-MnCl₄

The UV/Vis spectrum of PEG-DIL-MnCl₄ is quite similar showing a strong band at 230-270 nm which corresponds to the π - π^* transition at the imidazolium cation and a band at 305-350 nm which is associated with ligand-to-metal charge transfer transition (Fig. 2). The thermal stability of PEG-DIL-MnCl₄ was studied by the use of TGA under N₂ atmosphere. From the TGA curve, it can be concluded that PEG-DIL based MnCl₄²⁻ is thermally

stable up to the temperature of about 250 °C under N₂ atmosphere. Weight loss of up to 200 °C is related to absorbed water evaporation. The significant weight loss occurs at 250 -400 °C, which is related to the degradation of imidazole rings and polyethylene glycol chains (Fig. 3).

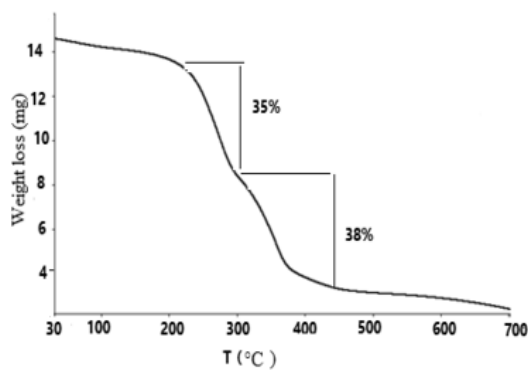


Fig. 3. TGA of PEG-DIL-MnCl₄

The Raman spectrum was used to prove the presence of the MnCl₄²⁻ anion in the structure of the ionic liquid. As shown in Fig. 4, strong and sharp peaks at 1296 and 1590 cm⁻¹ are related to imidazole rings, while the relatively weak peaks at 164.9 and 431.85 cm⁻¹ can be attributed to the presence of MnCl₄²⁻ anion in the structure of ionic liquid.

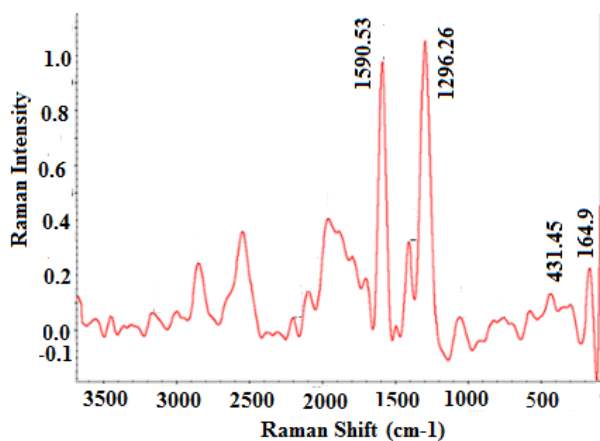


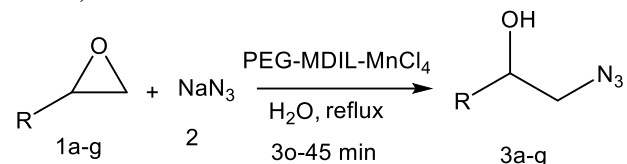
Fig. 4. Raman spectrum of PEG-DIL-MnCl₄

Table 1. Effect of the amount of PEG-DIL-MnCl₄, temperature and solvent in the synthesis of β-azidoalcohol

Entry	Catalyst (g)	T (°C)	Solvent	Time(min)	Yield
1	-	100	H ₂ O	180	-
2	0.05	100	H ₂ O	90	40
3	0.1	100	H ₂ O	90	70
4	0.2	100	H ₂ O	30	92
5	0.3	100	H ₂ O	30	92
6	0.2	100	CH ₃ CN	60	87
7	0.2	100	DMSO	30	88
8	0.2	100	CH ₂ Cl ₂	120	-
9	0.2	25	H ₂ O	180	Trace

After characterization, the possible catalytic properties of PEG-DIL-MnCl₄ in the azidolysis reaction of epoxides with azide anion in water were studied (scheme 2).

To optimize the reaction conditions, the mixture of phenyl glycidyl ether (1 mmol) and NaN₃ (2 mmol) in water were chosen for the model reaction.

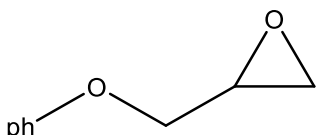
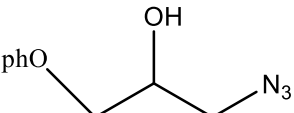
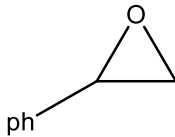
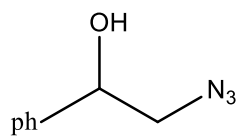
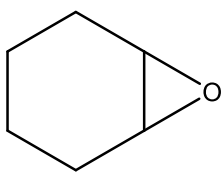
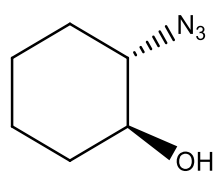
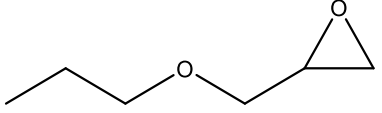
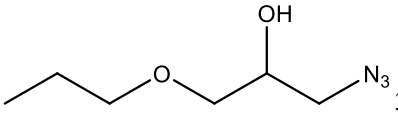
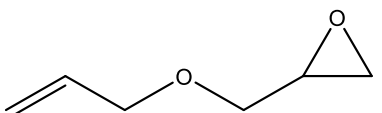
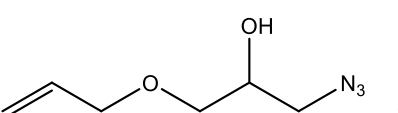
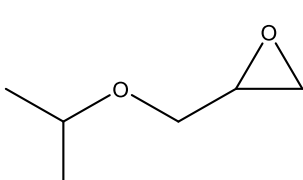
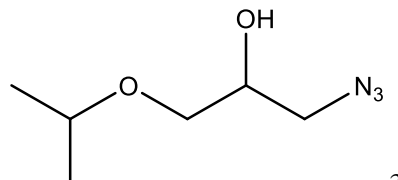
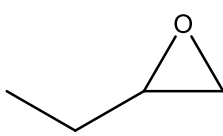
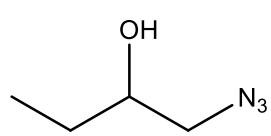


Scheme 2. Synthesis of β-azido alcohols in the presence of PEG-MDIL-MnCl₄.

The reaction was conducted with different amounts of catalyst and solvent in the temperature range from room temperature up to 100 °C. It was observed that the reaction model did not carry out at room temperature with different amounts of the catalyst. The best yield (92%) and reaction time (30 min) for preparation of azidoalcohol were obtained in the presence of 0.2 g of PEG-DIL-MnCl₄ in water as a green solvent at 100 °C. It is worth noting that in the absence of catalyst, the reaction was sluggish and, even after long reaction times, a considerable amount of starting material remained (Table 1).

Thus, water is an excellent solvent in terms of cost, availability, environmental impact and shorter reaction times. Epoxides bearing activated and deactivated groups were quickly and efficiently converted to the virtually pure β-azidoalcohol in high isolated yields (Table 2).

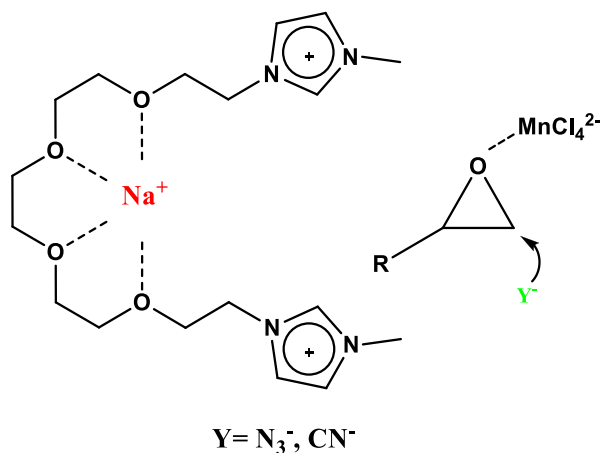
Table 2. Ring opening of various epoxides in the presence of PEG-DIL-MnCl₄

Substrate	Product	No.	N ₃ ⁻	
			Time (min)	Yield (%)
		3a	30	92
		3b	40	87
		3c	30	84
		3d	30	86
		3e	30	85
		3f	35	83
		3g	30	79

No evidence for the formation of diols or by-products of the reactions was observed and the products were obtained in pure form without further purification. All the products were characterized and identified by comparison of their spectral data (IR, ¹H NMR and ¹³CNMR) with those of authentic samples [19].

After completion of the reaction, the mixture was cooled and the organic phase was extracted with diethyl ether.

The PEG-DIL-MnCl₄ showed remarkable reactivity as a Lewis acid reagent and considerably accelerated the reactions. It seems that the counter cation (PEG-DIL) encapsulates alkali metal cations, much like crown ethers, and these complexes cause the anion to be activated. Also, Mn²⁺ in the MnCl₄²⁻ groups can act as a Lewis acid, catalyzing the ring opening of epoxides (Scheme 3).



Scheme 3. Possible mechanism for promotion of the reaction by PEG-DIL- $MnCl_4$

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