



Poly (*N*-bromoacrylamide) as highly efficient, regioselective and recyclable catalyst for preparation of β -azidoalcohols, β -cyanoalcohols, β -nitroalcohols and β -nitratolcohols from epoxides under aqueous conditions

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ABSTRACT

*Poly (*N*-bromoacrylamide) with electrophilic bromine are introduced as polymeric catalyst for efficient and regioselective conversion of epoxides to azidoalcohols, cyanoalcohols, nitroalcohols and nitratolcohols in good to excellent yields under mild reaction conditions. The advantages of these reagents over some of those reported in the literature are easy work-up procedure, reusability of the catalyst, clean and neutral reaction conditions.*

Keywords: functionalized polymer; epoxide, β -azido alcohols, β -cyanoalcohols, β -nitro alcohols and β -nitratolcohols.

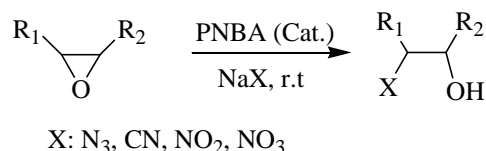
INTRODUCTION

Epoxides are important and versatile synthetic intermediates in organic synthesis and their reactions with variety of reagents such as nucleophiles, electrophiles, reducing agents, acids, bases, and some oxidizing agents are widely studied.[1] These compound can be opened under a variety of conditions, although the most practical and widely employed strategy for the synthesis of 1,2- bifunctional compounds is via nucleophilic ring-opening using a strong base or a Lewis acid.[2] Under the reported conditions, these reactions have restricted applicability and suffer from weakness such as high acidity, the non-catalytic nature of the reagents, long reaction times, and use of anhydrous organic solvents, moisture sensitive and hazardous reagents, inconvenient handling procedures and low yields.[3] Also In most of the epoxide ring opening reactions under acidic conditions, the formation of a mixture of regioisomers and polymerization is observed. [4]In view of these limitations, the introductions of new methods for the nucleophilic ring-opening of epoxides, which work under mild conditions, are still in request and are significant in synthetic of organic chemistry.

Functional polymers are macromolecules have the potential advantages of small molecules with the same functional groups. The most important advantage in using a these polymer as a reagent or a catalyst is the simplification of product work-up, separation, and isolation. Insolubility, physical stability, compatibility with a wide range of solvents including water, is the most advantages of this kind of material [5]. Among polymer supported reagents, polymers incorporated with reactive electrophilic halogen such as Poly (*N*-bromo benzene- 1,3- sulfonamide) ,[6] poly (*N*-bromomaleimide),[7] poly (*N*-bromoacrylamide)[8] poly(4-vinylpyridine) supported iodine [9] have been extensive growth in the application of as reagents or catalyst in organic synthesis.

Poly (*N*-bromoacrylamide) (PNBA) as heterogeneous polymer is a stable solid compound with high activity. This polymer supported counterparts are highly air stable and can be kept for months without any loss in its activity and can be handled easily and also it can be prepared quantitatively by the reaction of polyacrylamide with KBr and Oxone as oxidizing agent in water.[8]

It would seem, there has been no report in the literature on the use of polymeric catalyst with supported electrophilic bromine for the ring opening of epoxides. Here, we report a very simple and efficient method for the regioselective ring opening of epoxides with PNBA in high yields under aqueous condition. Small negatively charged ions like azide, cyanide, nitrite and nitrate are accepted in the ring opening reaction by this polymeric catalyst in water. In this way some β -Azidoalcohols, β -Cyanoalcohols, β -Nitroalcohols and β -Nitratolcohols were prepared in good to excellent yield in mild reaction condition. (Scheme 1)



Scheme 1

MATERIALS AND METHODS

All chemicals were supplied by either Merck or Fluka. The progress of the reactions was followed with TLC, using silica gel SILG-UV 254 plates. Silica gel 60 was used for column chromatography. The identities of products were determined by comparison of their physical and spectral data with those reported in the literature. FT-IR spectra were recorded on a Shimadzu DR-8001 spectrometer. NMR spectra were recorded on a BrukerAvance DPX 250MHz instrument.

General procedure for nucleophilic addition to epoxide

To a stirred suspension of PNBA (0.1 gr, 0.5 mmol) and oxirane (1 mmol) in H₂O (5 ml) was added nucleophile (NaN₃, NaCN, NaNO₂, NaNO₃) (2 mmol) in H₂O (3 ml) slowly at room temperature. The reaction mixture was stirred for the appropriate times (Tables 2-4). After completion of reaction, the mixture was filtrated to remove the catalyst. CH₂Cl₂ was added and the organic phase was washed with brine (10 mL) and water (2 ×10 mL) and the filtrate was dried over anhydrous Na₂SO₄. After evaporation of the solvent on a rotary evaporator, the pure product was collected. The characterization of products was performed by comparison of their IR, ¹H-NMR, ¹³C-NMR, and physical data with those of authentic samples.

Some spectra data

Azido-3-phenoxy-propan-2-ol :IR (CCl₄), ν_{\max} (cm⁻¹): 3400 (br), 2960 (s), 2950 (s), 2150 (s), 1630 (s), 1520 (s), 1500 (s), 1480 (m), 1320 (m), 1260 (s), 1120 (m), 1050 (m), 780 (s), 720 (m). ¹H-NMR (CDCl₃), δ (ppm): 7.3-7.4 (2H, m), 6.9-7.0 (3H, m), 4.2 (1H, m), 4.0 (2H, m), 3.5 (2H, m), 2.9 (1H, d). ¹³C-NMR (CCl₄), δ (ppm): 159.1, 130.1, 122.1, 115.1, 69.8, 69.7, 54.0.

3-Hydroxy-4-phenoxybutyronitrile :IR (CCl₄), ν_{\max} (cm⁻¹): 3400 (br), 3000 (s), 2960 (s), 2950 (m), 2400 (m), 1680 (s), 1600 (s), 1500 (s), 1430 (m), 1210 (s), 1070 (s), 950 (m), 680 (s). ¹H-NMR (CCl₄), δ (ppm): 7.4-7.5 (2H, m), 7.0-7.2 (3H, m), 4.5 (1H, m), 4.2 (2H, m), 3.4 (1H, d), 2.9 (2H, m). ¹³C-NMR (CDCl₃), δ (ppm): 158.2, 130.0, 122.1, 114.9, 70.1, 66.7, 22.9.

1-Nitro-3-phenoxy-propan-2-olIR (CCl₄), ν_{\max} (cm⁻¹): 3370 (br), 2950 (m), 2900 (w), 2380 (w), 1600 (s), 1570 (s), 1500 (s), 1475 (m), 1250 (s), 1120 (m), 1060 (m), 720 (m).

¹H-NMR (CDCl₃), δ (ppm): 7.2-7.3 (2H, m), 6.9-7.0 (3H, m), 4.1 (3H, m), 3.8 (2H, m), 2.7 (1H, br). ¹³C-NMR (CCl₄), δ (ppm): 130.0, 121.7, 115.1, 70.9, 69.6, 64.2.

1-Nitrooxy-3-phenoxy-propan-2-olNO₃= IR (CCl₄), ν_{\max} (cm⁻¹): 3370 (br), 2950 (m), 2900 (w), 2380 (w), 1600 (s), 1570 (s), 1500 (s), 1475 (m), 1250 (s), 1120 (m), 1060 (m), 720 (m). ¹H-NMR (CDCl₃), δ (ppm): 7.2-7.3 (2H, m), 6.9-7.0 (3H, m), 4.1 (3H, m), 3.8 (2H, m), 2.7 (1H, br). ¹³C-NMR (CCl₄), δ (ppm): 130.0, 121.7, 115.1, 70.9, 69.6, 64.2.

RESULTS AND DISCUSSION

Preparation of β -Azidoalcohols by PNBA as catalyst in water

Since the β -amino alcohols are very important in both organic and medical chemistry[10], and they serve as precursors in the synthesis of β -aminoalcohols, amino sugars and carbocyclic nucleosides.[11] The ring cleavage of epoxides with azide[12] and nitro compounds [13] presents usual synthetic routes of β -amino alcohols. The ring cleavage reaction of epoxides with azide compounds 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[14]. Preparations of these compounds usually need high temperatures and/or long reaction times, and as side reactions, isomerizations, epimerization, and rearrangements may be induced by alkaline conditions of the reactions with alkali azides in these systems.

Due to the importance of the direct synthesis of β -azido alcohol from epoxides the ring-opening reaction of various epoxides with sodium azide and PNBA was studied.

Figure 1 showed IR spectrum of PNBA. Reactions of different aliphatic and cyclic epoxides including those electron-withdrawing substituents were performed in water at room temperature.

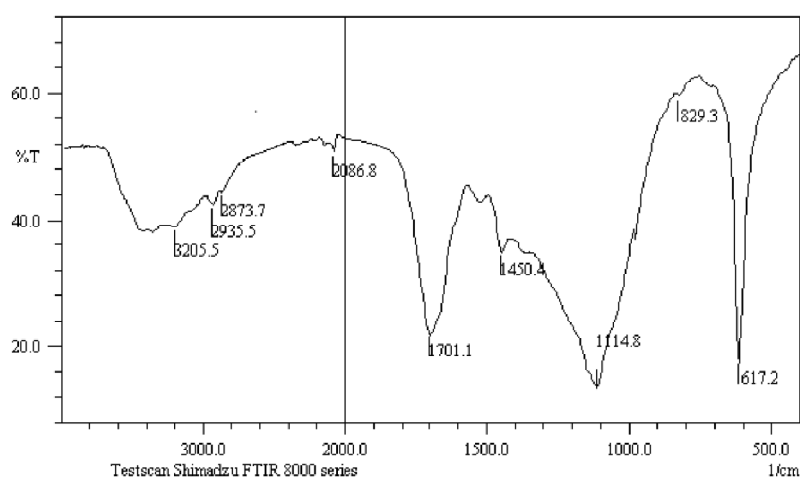


Figure 1: IR spectrum of cross-linked poly (*N*-bromoacrylamide)

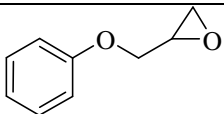
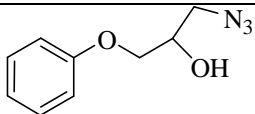
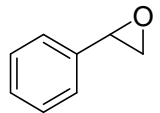
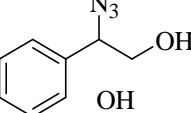
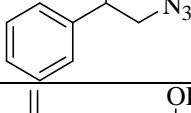
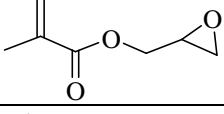
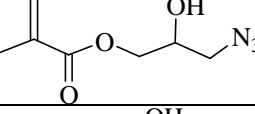
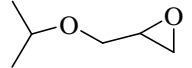
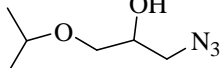
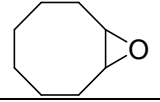
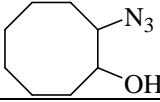
The effects of solvent and molar ratio of the polymer on the ring opening reaction of epoxides were investigated. As a typical example, the reaction of phenyl glycidyl ether (1 mmol) was tested with a mixture of PNBA (0.5 mmol) and NaN_3 (1 mmol) in different solvent.(Table 1). The experimental results showed that acetonitrile can also be used as a solvent in this reaction; however, because of its toxicity, cost and environmental problems, water was preferred as the most suitable solvent. After 2 h the complete conversion was achieved at water in room temperature to afford 1-azido-3-phenoxy-2-propanol in 100% conversion.

Table 1: The effect of the solvent on the reaction of phenyl glycidyl ether with NaN_3 using PNBA as catalyst (The molar ratio of the polymeric catalyst to styrene oxide was 0.5:1mmol)

Entry	Solvent	Time (h)	Conversion (%)
1	THF	5h	20
2	CHCl_3	5h	10
3	CH_2Cl_2	5h	5
4	EtOAc	5h	80
5	CH_3CN	3h	100
6	H_2O	2h	100

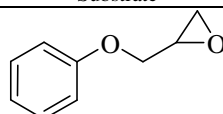
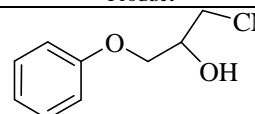
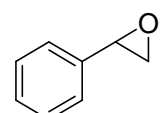
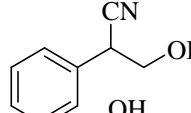
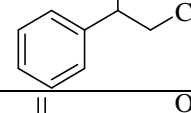
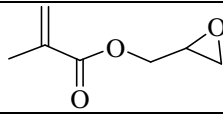
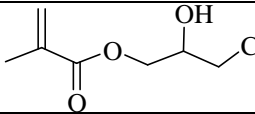
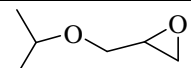
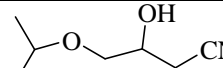
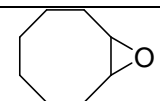
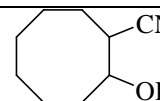
Because of the predominant attack of azide ion on the less hindered carbon of the epoxide, all the terminal epoxides gave highly regioselective azidoalcohols in quantitative yields. The results obtained for the ring opening of different substituted epoxides with PNBA are shown in Tables 2.

Table 2: Reaction of epoxides with NaN₃ in water catalyzed by PNBA

Entry	Substrate	Product	Time	Yield (%) ^a
1			1h	92
2		  minor	50 min	90(10)
3			1h	90
4			1h	95
5			2h	100 ^b

(a) All reaction was carried out at room temperature. the molar ratio of PNBA to epoxide was 0.5:1 (b) GC Yield

Table 3: Reaction of Epoxides with NaCN in the Presence of PNBA

Entry	Substrate	Product	Time	Yield (%) ^{a,b,c}
1			1.5h	92
2		  minor	30 min	90(10)
3			1h	85(10)
4			1h	70(25)
5			2h	100 ^d

(a) Reactions were carried out at room temperature. (b) Products were identified by comparison of their IR and NMR spectra and/or physical data with the authentic samples. (c) Yield refers to isolated product.

Functional groups such as simple esters (Table 2, Entry 1) are stable under the reaction conditions, because this reaction is essentially allowed to be completed without any transesterification reaction.

As an advantage, the spent polymeric catalyst can be regenerated and reused several times without appreciable loss in its capacity and efficiency.

Obviously, in these reactions, the attack appears to be largely at the primary carbon atom of the epoxide ring and this is probably dictated by steric and electronic factors. Except for the reaction of styrene oxide, which produced

some of the other regioisomer (Table 2, entry 2) as a side product, the reaction of other epoxides was found to be highly regioselective and only one isomer was obtained.

Preparation of β -cyano alcohol

In continuation of our work, we decided to study the ring opening reaction of epoxides with the NaCN in water with PNBA as catalyst. Among these nucleophiles cyanide is particularly interesting because of its synthetic versatility. Since a nitrile group can be transformed into an amino, amide, carboxy, or carbonyl group.

The effects of solvent and molar ratio of the polymer on the ring opening reaction of epoxides were investigated. The experimental results showed that water was the most suitable solvent. The optimum molar ratio of PNBA to substrate was found to be 0.5:1 mmol.

The reaction of different epoxides with sodium cyanide was performed effectively and in high yields in water (Table 3).

Table 4: Reaction of epoxides with NaNO₂ and NaNO₃ in the presence of PNBA

Entry	Substrate	Major Product	Time	Yield (%) ^{a,b,c}
1			1h	85
2			1h	70
3			1.5h	80(10)
4			1.5h	82(5)
5			2h	80
6			2h	85
7			2h	92
8			2h	91
9			100min	90
10			100min	92
11			1.5h	100 ^d
12			1.5h	100 ^d

(a) Reactions were carried out at room temperature. (b) Products were identified by comparison of their IR and NMR spectra and/or physical data with the authentic samples. (c) Yield refers to isolated product. (d) GC yield

Preparation of β - nitroalcohols and β -nitratoalcohols by PNBA:

Nitrate containing organic compounds have useful applications in organic synthesis. They are useful reagents for the preparation of important class of nitrate compounds [15] through their reaction with carbanions. In continue of above research, the ring opening of various epoxides was achieved under mild conditions using PNBA. β -nitro alcohols and β -nitrate alcohol, were efficiently obtained from the corresponding epoxide (1 mmol) using NaNO_3 or NaNO_2 (2 mmol) nucleophile in present of PNBA (0.5 mmol) as catalyst in water at room temperature. The results are shown in Table 4.

Reactions in water often proceed faster than in organic solvents even if one or more reagents and products seem to be insoluble.

Except for the reaction of styrene oxide (entry 1) and which produce a small percentage of the other regioisomer, the reaction of other epoxides were found to be highly regioselective and only one isomer was obtained. Obviously, in these reactions, the attack appears to be largely, if not entirely, at the primary carbon atom of the epoxide ring. The direction of ring opening is that characteristically observed for reactions of monoalkyl-substituted epoxides under $\text{S}_\text{N}2$ conditions and is probably dictated by steric and electronic factors. In the reaction with styrene oxide, the anion ion attacks exclusively at the secondary carbon atom of the epoxide ring, a fact, this is reasonably well established. Electrophilic bromine in PNBA can act sensitive epoxide to ring opening by nucleophile. In all of case the used polymeric catalyst can be recycle and reused several times without any decrease in their reactivity.

CONCLUSION

In conclusion, the use of PNBA as catalyst in aqueous solutions provides excellent conditions for the ring opening of epoxides with different anionic nucleophiles. The absence of organic solvent, simplicity in operation, increase of the yields of the products, acceleration of the reactions rates and high regioselectivity of the reactions are strong points of performing these reactions in water.

Another convenient aspect of the present procedure is the use of easily available and very cheap sodium salts of nucleophiles instead of costly and usually hygroscopic quaternary ammonium salts.

The polymeric catalysts were very stable at room temperature and could be recycled and reused for several times and also this polymeric catalyst could be stored as a bench top catalyst for months without appropriate change in their reactivity.

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