

B-podands as efficient catalysts for the ring opening of epoxides in water: A versatile and atom economical method for the synthesis of vicinal azidoalcohols

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ABSTRACT

For the first time B-podands have been studied as an efficient and powerful catalysts in the ring opening of epoxides with azide anion in water. The reaction afforded the corresponding 1,2-azidoalcohols with high regioselectivity under mild reaction conditions and in a highly atom economic fashion.

Keywords: Phase transfer catalyst, B-podands, 1,2-Azidoalcohol, Epoxide, Atom economic, Ring opening.

1. Introduction

Nowadays, chemical processes employ large amounts of hazardous and toxic solvents. One of the challenges for the chemists is to come up with new approaches that are less hazardous to human and environment. The choice of pursuing a low waste route and reusable reaction media, and minimize the economic cost and environmental impact of a chemical process, are becoming ever more urgent for the future. One of the most promising approaches uses water as reaction medium. Water is an abundant, cheap, nontoxic, and nondangerous solvent. Obviously, it does not dissolve most of the organic reactants, but that fact has been recognized as a benefit on rates and selectivity of several transformations [1, 2]. Moreover, the addition of a phase transfer agent enables to improve an intimate contact with an organic layer [3-7].

Polyodands, acyclic ligands in which several polyether chains are linked to the same binding centre being either an atom (N, B, P, Si), or a multi- branched structural arrangement, have attracted increasing interest as anion activators in homogeneous and heterogeneous systems. These compounds represent a high effectiveness, relative non-toxicity and low cost, and therefore, they can be used alternatively to cyclic crown ethers and cryptands. In addition, the possibility of regulating their complex-forming properties by altering their structure makes them particularly

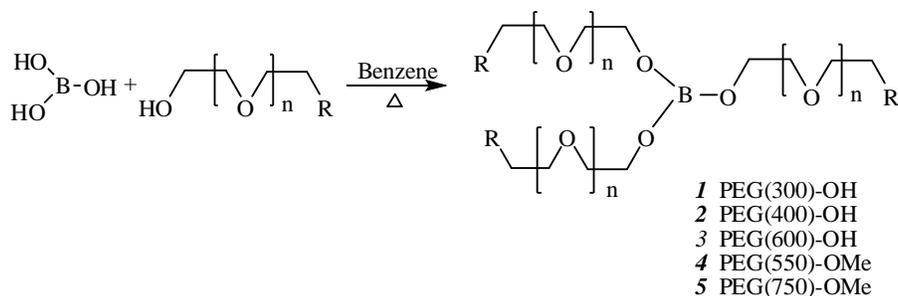
suitable ligands for phase-transfer catalyzed (PTC) processes [8, 9]. The first application of podands in PTC was reported by Lehmkuhl et al. [10] who studied a variety of nucleophilic substitution of benzyl bromide with different potassium salts. Very recently, the application of a series of boron podands as strong complexing agents of alkali metal cations and catalysts in typical anion promoted reactions in organic solvent and under solid-liquid conditions were reported [9].

From the fundamental point of view, azidolysis of epoxides is a well-established route to vicinal azidoalcohols that has been applied for the preparation of amino sugars [11], carboxylic nucleosides [12], lactames [13], and oxazolines [14] and of important intermediates for the synthesis of aminoalcohols and compounds of biological and pharmacological interest [15]. Generally, azidoalcohols are prepared through the ring opening of epoxides by using different azides in suitable solvents. Even though the classical protocol uses sodium azide and ammonium chloride, the azidolysis reaction requires a long reaction time (12-48 h) and the azidoalcohol 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 [16-19].

However, many of these methods involve the use of expensive and stoichiometric amounts of reagents or catalysts, suffer from poor regioselectivity, strongly acidic conditions and also require extended reaction times. Consequently, the development of novel and efficient protocol for this transformation under mild and more

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Scheme 1. Preparation of B-podands.

convenient conditions has attracted sustained interest in organic synthesis.

Systematic literature survey reveals that so far very few reports are available in the successful regioselective azidolysis of epoxides in water [20, 21]. As a part of our efforts to introduce novel catalysts for organic transformations [22, 23], we have described a simple effective approach to vicinal azidoalcohols by using B-podands as the catalyst in water. As described here, a variety of azidoalcohols can be synthesized in atom economical manner with high regioselectivity under mild and non-toxic conditions.

2. Experimental

Some 1,2-epoxyethanes and other chemical materials were purchased from Fluka and Merck in high purity. Boron podands were prepared according to the previously reported procedure [23]. All of the azidohydrine compounds were prepared by our procedure, and their spectroscopic and physical data were compared with those of the authentic samples [24]. NMR spectra were recorded in CDCl₃ on a Bruker Advanced DPX 400 MHz instrument spectrometer using TMS as internal standard. IR spectra were recorded on a BOMEM MB-Series 1998 FT-IR spectrometer. The purity determination of the products and reaction monitoring were accomplished by TLC on silica gel polygram SILG/UV 254 plates.

2.1. General procedure for the preparation of 1,2-azidoalcohols catalyzed by B[PEG(300)-OH]₃

B[PEG(300)-OH]₃ (0.25mmol, 0.228 g) was dissolved in water (5 mL) followed by the addition of NaN₃ (2 mmol) and epoxide (1 mmol) and the whole was stirred in reflux condition for the lengths of time shown in Table 2. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was extracted with ether (2×10 mL). The combined organic extracts (dried over CaCl₂) were evaporated under reduced pressure. The desired azidohydrin was obtained in good to excellent isolated yields (79-90%). For styrene oxide, further purification was achieved by preparative TLC or by silica gel column chromatography. The aqueous layer containing B[PEG(300)-OH]₃ and excess sodium azide was utilized in further runs by an addition of epoxide (1 mmol) and NaN₃ (1 mmol).

3. Results and Discussion

Star polymer, boron podands, with a different number of polyether chains, can be efficiently prepared in high yields in the reaction presented in Scheme 1 between boric acid and an appropriate polyethylene glycol according to the procedure described previously [10].

Initially, the ring opening of 2,3-epoxypropyl phenyl ether with azide anion and in the presence of B[PEG(300)-OH]₃ was chosen as a model and the role of various solvents on the reaction system was investigated. TLC analysis of the reaction mixture did not show completion of the reaction in water, toluene, tetrahydrofuran, and methylene dichloride after 5 h, but by increasing the temperature to reflux condition in water, the reaction was completed within 30 min and produced 1-azido-3-phenoxy-2-propanol in quantitative yield. Although, it is believed that B-podands react with water, the catalytic activity of star polymers 1–5 was evaluated in the nucleophilic ring opening of 2,3-epoxypropyl phenyl ether by NaN₃ in water. The reactions were performed under reflux condition and in the presence of catalytic amounts of polymeric catalysts (0.25 mmol/mmol of substrate) and with a 2/1 molar ratio of NaN₃:2,3-epoxypropyl phenyl ether. The obtained results are summarized in Table 1 and clearly shown that the best results were obtained by polypodands (1-3) that have hydroxyl group in their ends.

According to the obtained results, we tried to use B[PEG(300)-OH]₃ as an efficient and recoverable promoter of ring opening of different types of epoxides by azide ion in

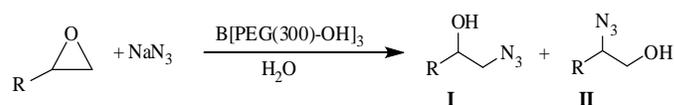
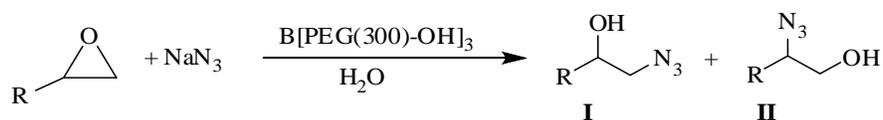


Table 1. Investigation of catalytic activity of star polymers.

No	Catalyst	Time (min)	Conversion (%)
1	B[PEG(300)-OH] ₃	30	100
2	B[PEG(400)-OH] ₃	30	100
3	B[PEG(600)-OH] ₃	35	100
4	B[PEG(550)-OMe] ₃	60	100
5	B[PEG(750)-OMe] ₃	70	100

**Table 2.** Reaction of different epoxides with NaN_3 catalyzed by B[PEG(300)-OH]_3 in water.

Entry	Substrate	Product(s) ^a	Time (min)	Yields (%) ^b
1			30	85
2		+	20	85 (91/9) ^c
3			20	79
4			25	82
5			30	79
6			30	81
7			60	90
8			30	88

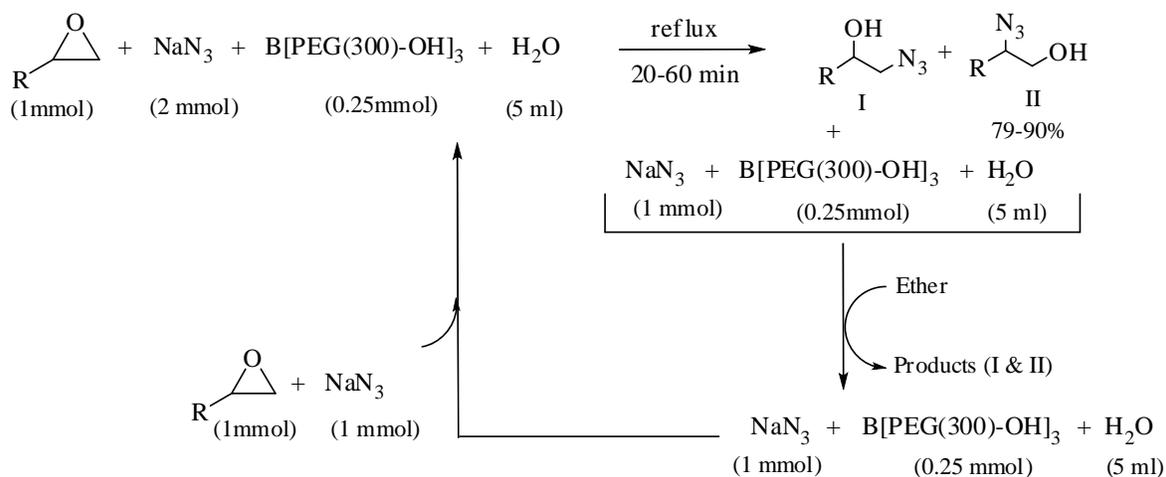
^aProducts were identified by comparison of their physical and spectral data with those of authentic samples.^bIsolated yields.^cAccording to GC analysis.

H_2O . To determine the optimum conditions, the conversion of styrene oxide to the corresponding azidoalcohol in the presence of polymeric catalyst as a phase-transfer catalyst in water was investigated. The optimum molar ratio of the catalyst to epoxide was found to be 0.25mmol/1 mmol of epoxide.

In order to show the general applicability of the method, we extended it to a variety of epoxides (Table 2) and in all cases a very clean reaction was observed. The structure of all the products were settled from their analytical and spectral (IR, ^1H NMR) data and by direct comparison with authentic samples. The regioselectivity of the ring opening of epoxides is thoroughly dependent on the mechanism of the reaction and particularly on steric and electronic factors. The reaction of styrene oxide with NaN_3 in water was completed after 20 min and produced 2-azido-1-phenylethanol (**II**) and 2-azido-2-phenylethanol (**I**) with the ratio of 91/9 in 85% total yield. As shown in Table 2, aliphatic epoxides reacted under similar reaction conditions and their corresponding azidoalcohol were produced in

excellent yields and regioselectivity. In these cases, with the attack of the azide ion on the less substituted oxirane carbon, the regioselectivity is reversed and the azidoalcohol (**I**) is obtained. The probable reason may be that in styrene oxide the positive charge on oxygen appears to be localized on the more highly substituted benzylic carbon leading to the major product. Whereas in case of aliphatic epoxides steric factors predominate over electronic factors thereby facilitating the attack at the less hindered carbon atom of the epoxide ring. Furthermore cyclohexene oxide as a cycloalkyl epoxide reacted smoothly in a $\text{S}_{\text{N}}2$ fashion with NaN_3 and in the presence of catalytic amount of B[PEG(300)-OH]_3 to afford the corresponding azidoalcohol in excellent yield. The stereochemistry of the ring opening product was found to be trans from the coupling constants of the ring protons in ^1H NMR spectrum.

The most ideal synthetic methodology could be defined as a system wherein 100% atom economy is preserved, the solvent is recycled to the fullest extent and the catalyst or excess of reagent remains throughout in the solvent medium



Scheme 2. Facile nucleophilic ring opening of epoxides in the atom economical method.

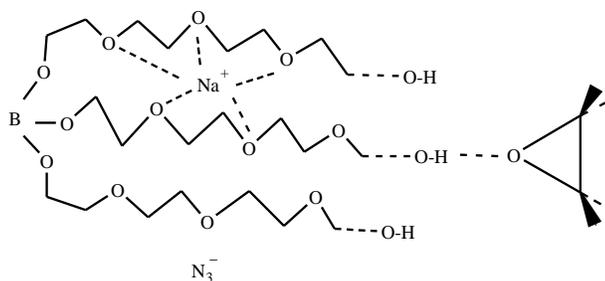
Table 3. Comparison of azidolysis of some epoxides with different catalysts.

No	Epoxide	Catalyst/Reagent/Solvent [19,21,25,26]	Time(h)	Yield (%) (II/I)
1		Zn(OTf) ₂ / NaN ₃ / CH ₃ CN ^a	2	88
		Polymeric PTC / NaN ₃ / H ₂ O ^b	12	94
		LiClO ₄ / NaN ₃ / CH ₃ CN	5	97
		CeCl ₃ / NaN ₃ / CH ₃ CN	3	99
		Mg(ClO ₄) ₂ / NaN ₃ / CH ₃ CN	2	96
		NH ₄ Cl / NaN ₃ / MeOH-H ₂ O	12	95
		LiOTf / NaN ₃ / CH ₃ CN	5	92
		Bu ₃ SnCl / NaN ₃ / Solvent Free	6	95(6/94)
		B(PEG-OH) ₃ / NaN ₃ / H ₂ O ^c	0.5	85
		2		Zr(OTf) ₂ / TMGA / CH ₃ CN ^a
Polymeric PTC / NaN ₃ / H ₂ O ^b	6			95(91/9)
LiClO ₄ / NaN ₃ / CH ₃ CN	5			92(82/18)
CeCl ₃ / NaN ₃ / CH ₃ CN	3			89(89/11)
R ₄ NCl / Me ₃ SiN ₃ / Solvent Free	24			67(74/26)
Mg(ClO ₄) ₂ / NaN ₃ / CH ₃ CN	2			78(83/17)
NH ₄ Cl / NaN ₃ / MeOH-H ₂ O	20			94(79/21)
Bu ₃ SnCl / NaN ₃ / Solvent Free	14			86(93/7)
B(PEG-OH) ₃ / NaN ₃ / H ₂ O ^c	0.3			85(91/9)
3				Zr(OTf) ₂ / TMGA / CH ₃ CN ^a
		Polymeric PTC / NaN ₃ / H ₂ O ^b	8	89
		LiClO ₄ / NaN ₃ / CH ₃ CN	36	95
		CeCl ₃ / NaN ₃ / CH ₃ CN	3	98
		R ₄ NCl / Me ₃ SiN ₃ / Solvent Free	24	89
		Mg(ClO ₄) ₂ / NaN ₃ / CH ₃ CN	24	94
		NH ₄ Cl / NaN ₃ / MeOH-H ₂ O	36	92
		Bu ₃ SnCl / NaN ₃ / Solvent Free	0.4	89
B(PEG-OH) ₃ / NaN ₃ / H ₂ O ^c	0.5	88		

^a TMGA: 1,1,3,3-tetramethylguanidinium azide.

^b Polymeric PTC: poly[N-(2-aminoethyl)acrylamido]- trimethyl ammonium iodide.

^c Present method.



Scheme 3. Postulated roles of B[PEG(300)-OH]₃ in the azidolysis of epoxides.

and without losing activity for several runs. In general, the methodology worked well independently on the nature of the epoxide, furnishing the corresponding azidoalcohols in high yields. The B[PEG(300)-OH]₃ and the additional sodium azide (1mmol) were conveniently separated from the reaction mixture by simple extraction of product in ether phase. The aqueous phase reused for five consecutive times with only slight variation in the yields of the corresponding products. Scheme 2 describes the facile nucleophilic ring-opening of epoxides with sodium azide in the atom economical method. In order to show the merit of the presented protocol for the ring opening of epoxides with azide anion, we have compared the results obtained catalyzed by B[PEG(300)-OH]₃ with some of those previously reported in the literature (Table 3). In the present conversion, the role of B[PEG(300)-OH]₃ is possibly to form complexes with cation, much like crown ethers, and these complexes cause the anion to be activated. In addition polymeric catalyst, probably, can be facilitated the ring opening of the epoxide by hydrogen bonding as shown in Scheme 3.

4. Conclusion

In conclusion, boron podands can be easily prepared from inexpensive and non-toxic materials and serves as excellent catalysts in the conversion of variety of epoxides carrying activated and deactivated groups into their corresponding 1,2-azidoalcohols in water. The advantages of present protocol, such as environmentally friendly alternative, short reaction times, simplicity in operation, the low cost of reagents, highly regioselectivity, and high yields of products, make this new process an attractive alternative to current methodologies.

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