

Efficient synthesis of β -azidoalcohols from epoxides and sodium azide using 1,4-bis(triphenylphosphonium)-2-butene dichloride as a new catalyst

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Abstract. 1,4-bis(triphenylphosphonium)-2-butene dichloride was developed as a new phase transfer catalyst. This quaternized phosphonium salt catalyzed the regioselective ring opening of epoxides by azide ion to give azido alcohols in high yields under mild conditions.

Keywords: 1,4-bis(triphenylphosphonium)-2-butene dichloride, phase transfer catalyst, azidoalcohols, epoxides.

1. Introduction

Organic reactions in water have recently attracted great interests [1]. The substitution of organic solvent as reaction media by water minimizes the environmental impact, besides lowering the cost and decreasing operational danger. In addition to the economic and human aspects, water presents many physico-chemical properties that can be useful in the reactions, such as high polarity, ion solvating capacity, and the ability to form hydrogen bonds to form a structured liquid, and to aggregate apolar molecules dissolved in the water. Therefore, performing organic reactions in water may profit by these beneficial aspects. Most often the reaction medium for the ring opening reactions are organic or organic/water binary systems. So, the concept of water mediated displacement reactions, as a green protocol, needs more attention.

Phase transfer catalysis is a widely accepted method in industry and organic synthesis as an effective synthetic tool by which liquid-liquid or liquid-solid phase-separated reactions are accelerated [2]. Extensive reviews both on chemistry and engineering viewpoints of phase transfer catalysts (PTC)s have been published in the last few decades [3]. PTCs are also widely used in manufacturing specialty chemicals. Onium salts (ammonium, phosphonium and sulfonium salts), crown ethers and cryptands, and solvents and co-solvents have been widely used as PTCs.

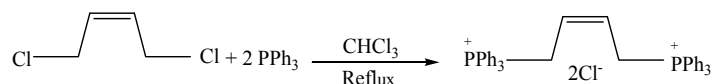
2-Azidoalcohols are important precursors for the synthesis of β -aminoalcohols [4], some of which are of significance as β -adrenergic blocking agents, as highly effective antagonists for the treatment of cardiovascular diseases, cardiac failure and asthma, and are also useful as chiral auxiliaries in asymmetric synthesis. [5] They are also useful intermediates for the synthesis of amino sugars and carbocyclic nucleosides [6]. The simple and the most straight forward synthetic method for the preparation of 2-azidoalcohols involves the regioselective ring opening of oxiranes with sodium azide under various reaction conditions [7]. These epoxide opening reactions are, however, generally carried out under either acidic or basic conditions [4-6,7] and they usually require high temperatures and/or long reaction times, and side reactions, such as isomerization, epimerization and rearrangements may be induced by the alkaline conditions. Furthermore, high temperatures are not only detrimental to certain functional groups, but also to the control of

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regioselectivity. A variety of activators or promoters have been reported to assist epoxide ring-opening reactions with sodium azide under mild conditions [8-10].

In continuation of our studies on the use of phosphonium salts in organic synthesis [11], we describe our successful results that led to an extremely convenient method for preparation of β -aminoalcohols from epoxides using sodium azide and in the presence 1,4-bis(triphenylphosphonium)-2-butene dichloride as an efficient homogeneous PTC in aqueous media in high isolated yields.

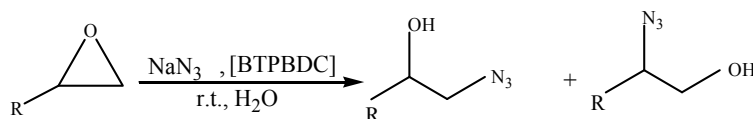
1,4-bis(triphenylphosphonium)-2-butene dichloride [BTPBDC] was easily prepared by reacting 1,4-dichlorobutene with triphenylphosphine in chloroform under reflux condition (Scheme 1). The reaction is very clean and phase transfer catalyst can be easily precipitated in acetone. This reagent is stable and can be stored for months at room temperature without losing its activity.



Scheme 1: Preparation of 1,4-Bis(triphenylphosphonium)-2-Butene Dichloride

In this article, we report the use of phase transfer catalysts as novel and recyclable reaction media for the synthesis of 2-azido alcohols from oxiranes and sodium azide under mild and neutral conditions (Scheme 2).

The effects of the solvent and molar ratio of the BTPBDC to substrate on the ring opening of oxiranes were investigated. The reaction was carried out in different solvents such as Et₂O, CH₂Cl₂, CHCl₃, EtOAc, CH₃CN, and H₂O. The results were clearly shown that although acetonitrile was the best among organic solvents tested, the best result was obtained in water. This can be largely attributed to the polar nature of the catalyst and its compatibility with both organic and aqueous phases. Molar ratio of the catalyst to epoxide was also optimized in water at room temperature. Therefore, phenyl glycidyl ether (1.0 mmol) was reacted with sodium azide (1.5 mmol) in the presence of BTPBDC. TLC analysis was showed at room temperature, conversion was completed after 4 hours and corresponding product was produced in 88% isolated yield. According to obtained results, this catalyst acted very efficiently and it was observed that only 0.4 mmol of the catalyst is enough to convert different epoxides to their corresponding 2-Azidoalcohols in high isolated yields (Scheme 2).



Scheme 2: Synthesis of 2-azidoalcohols from oxiranes, sodium azide and 1,4-bis(triphenylphosphonium)-2-butene dichloride as a new catalyst.

In the present conversion, the ring cleavage of epoxides occurred with high regio and stereoselectivity. styrene oxide, formed the product by opening at the benzylic position and 2-alkyl epoxides formed the products by cleavage at the terminal position. The ring-opening of bicyclic epoxides with sodium azide furnished the azo-compounds with trans-configuration indicating the conversion to be anti- stereoselective. In the ¹H NMR spectra, the ring protons of 6 appeared at d 3.21 (1H, ddd, J =9.6, 9.1, 4.0 Hz) [CH (OH)] and 3.01 (1H, ddd, J =9.4, 9.1, 4.0Hz) [CH N₃].

In conclusion, we have developed a mild and simple method for the preparation of 1,2-azidoalcohols by ring-opening of epoxides with NaN₃ using [BTPBDC] as a catalyst. The high yields and excellent regio- and stereoselectivity are advantages of the present protocol.

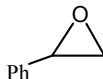
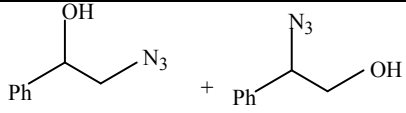
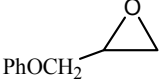
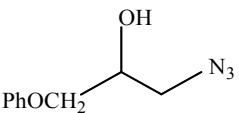
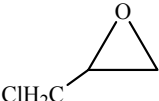
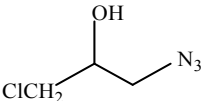

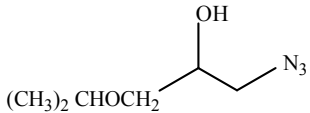
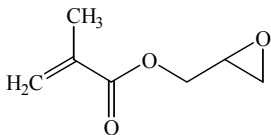
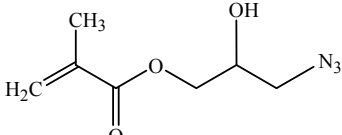
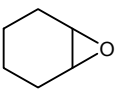
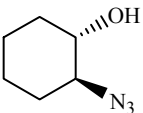
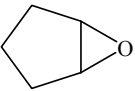
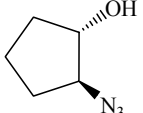

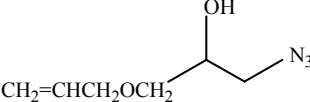
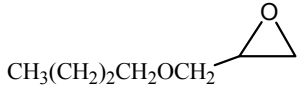
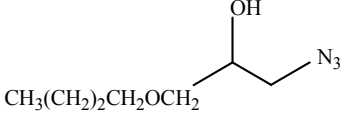
2. Experimental

1,4-Bis(triphenylphosphonium)-2-butene dichloride was prepared and other chemicals were purchased from Merck chemical company Darmstadt, Germany. The purity determination of the products and reaction

monitoring were accomplished by TLC on polygram SILG/UV 254 plates. IR spectra were recorded on Bomem MB-Series 1998 FT-IR spectrometer. ¹H NMR and ¹³C NMR spectra were taken on a 400 MHz Broucker spectrometer. Melting points were measured on a mettler FP5 apparatus

Preparation of 1,4-bis(triphenylphosphonium)-2-butene Dichloride (BTPBDC): To a solution of 1,4-dichlorobutene (5 mmol) in CHCl₃ (10 mL) in a 50 mL round-bottomed flask equipped with a magnetic

Table 1. Reaction of various epoxides with sodium azide in the presence 1,4-bis(tri phenyl phosphonium)-2-butene dichlorid as a catalysta

No.	Substrate	Product(s)	Time (h)	Yield (%)
1			3.5	85 (15:85) ^b
2			4	88
3			3	91
4			3	93
5			3	87
6			3.5	89
7			4	81
8			3	89
9			4.5	93

^a Products were identified by comparison of their physical and spectral data with those of authentic samples.

^b According to GC analysis.

stirrer and a reflux condenser was added triphenylphosphine (10 mmol). The reaction mixture was refluxed on a water bath for 2.5 h. The solution was cooled to room temperature and then, while vigorously stirred, diethylether was added dropwise until an oily product separated. The ether was removed by decantation and acetone (40 mL) was added. Stirring the acetone solution for 40 min afforded a white

precipitate which was filtered, washed with acetone (20 mL) and dried. Yield (80%), m.p. 278-279 °C. IR (KBr): ν = 3053, 2755, 1613, 1575, 1478, 1437, 1258, 754, 693, 556 (Cm⁻¹). ¹H NMR (CDCl₃): δ 5.7 (dd, 4H), 6.3 (m, 2H), 7.7-8.0 (m, 30H). ¹³C NMR (CDCl₃): δ 20.7, 120.8, 132.15, 134.2, 137.01, 140.17.

Conversion of oxiranes to 2-azido alcohols using sodium azide and BTPBDC: The epoxide (1 mmol), sodium azide (1.5 mmol), BTPBDC (0.4 mmol) and water (15 mL) were stirred at room temperature for the time specified in Table 1. The progress of each reaction was monitored by TLC. The reaction mixture was extracted with diethylether (3×10 mL). The combined organic layer washed with cold water (3×10 mL), dried over sodium sulfate and filtered. The filtrate was subjected to column chromatography to give the desired product.

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4. References

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