

Efficient synthesis of β -hydroxy thiocyanates from epoxides and ammonium thiocyanate 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 thiocyanate ion to give β -hydroxy thiocyanates in high yields under mild conditions.

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

Introduction

Nucleophilic addition to epoxides plays a pivotal role in the stereoselective preparation of 1,2-disubstituted products and it has been certainly the most thoroughly studied reaction of these compounds.[1] thiocyanates are useful and important intermediates in agricultural, pharmaceutical and synthetic chemistry.[2-3] Unfortunately, some of the synthetic methods available for the synthesis of thiocyanohydrin, suffer from disadvantages such as long reaction times, use of volatile organic solvents and expensive reagents, low regioselectivity and high temperature reaction conditions.[4-5]

Organic reactions in water have recently attracted great interests [6]. 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 a polar 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 [7]. Extensive reviews both on chemistry and engineering viewpoints of phase

transfer catalysts (PTC)s have been published in the last few decades [8]. 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.

In continuation of our studies on the use of phosphonium salts in organic synthesis [9], we describe our successful results that led to an extremely convenient method for preparation of β -hydroxy thiocyanates from epoxides using ammonium thiocyanate and in the presence 1,4-bis(triphenylphosphonium)-2-butene dichloride as an efficient homogeneous PTC in aqueous media in high isolated yields.

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 ^{13}C NMR spectra were taken on a 400 MHz Bruker spectrometer. Melting points were measured on a Mettler FP5 apparatus.

Preparation of 1,4-bis(triphenylphosphonium)-2-butene Dichloride (BTPBDC):

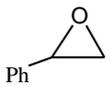
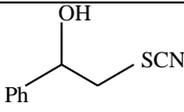
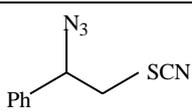
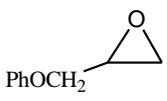
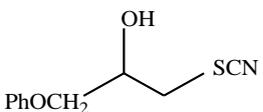
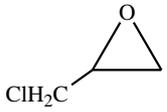
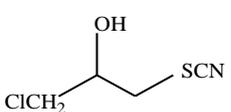
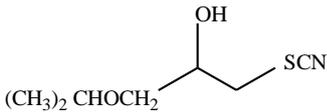
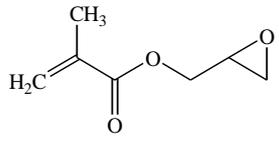
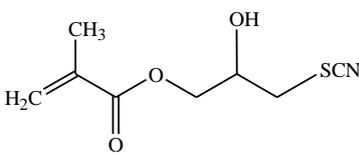
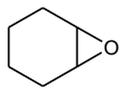
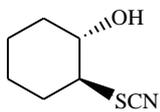
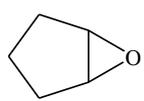
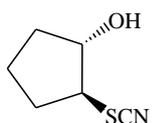
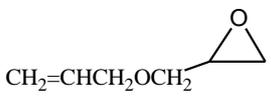
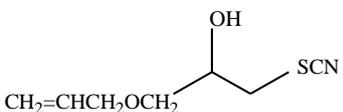
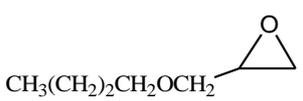
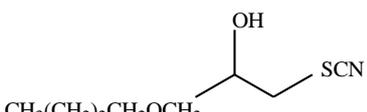
To a solution of 1,4-dichlorobutene (5 mmol) in CHCl_3 (10 mL) in a 50 mL round-bottomed flask equipped with a magnetic stirrer and a reflux condenser was added triphenylphosphine (10 mmol). The reaction mixture was refluxed on a water bath for 2.5 h. The solution was cooled to room temperature and then, while vigorously stirred, diethyl ether 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): $\nu = 3053, 2755, 1613, 1575, 1478, 1437, 1258, 754, 693, 556$ (cm^{-1}). ^1H NMR (CDCl_3): δ 5.7 (dd, 4H), 6.3 (m, 2H), 7.7-8.0 (m, 30H). ^{13}C NMR (CDCl_3): δ 20.7, 120.8, 132.15, 134.2, 137.01, 140.17.

Conversion of oxiranes to β -hydroxy thiocyanates using BTPBDC:

The epoxide (1 mmol), ammonium thiocyanate (2 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 \times 10 mL). The combined organic layer washed with cold water (3 \times 10 mL), dried over

sodium sulfate and filtered. The filtrate was subjected to column chromatography to give the desired product.

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

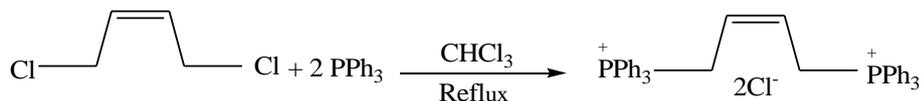
No.	Substrate	Product(s)	Time (min)	Yield (%)
1		 + 	90	85 (15:85) ^b
2			120	87
3			60	92
4			60	90
5			90	82
6			100	83
7			110	87
8			60	84
9			90	90

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

^b According to GC analysis.

Result

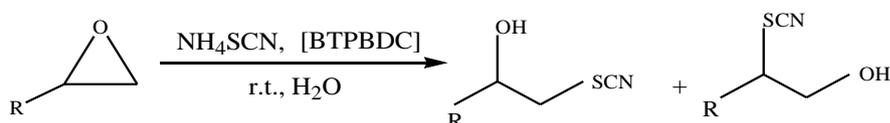
1,4-bis(triphenylphosphonium)-2-butene dichloride [BTPBDC] was easily prepared by reacting 1,4-dichlorobutene with triphenylphosphine in chloroform under reflux condition (Scheme 1). The reaction is very clean and phase transfer catalyst can be easily precipitated in acetone. This reagent is stable and 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 β -hydroxy thiocyanates from oxiranes and NH_4SCN 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 Et_2O , CH_2Cl_2 , CHCl_3 , EtOAc , CH_3CN , and H_2O . 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 NH_4SCN (2 mmol) in the presence of BTPBDC. TLC analysis was showed at room temperature, conversion was completed after 120 min and corresponding product was produced in 87% 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 β -hydroxy thiocyanates in high isolated yields (Scheme 2).



Scheme 2: Synthesis of β -hydroxy thiocyanates from oxiranes, NH_4SCN and 1,4- bis(triphenylphosphonium)-2-butene dichloride as a new catalyst.

In all cases, a very clean reaction was observed and careful examination of the ^1H NMR spectra of the crude products clearly indicated the formation of only one regioisomer in each case. Also in the ^1H NMR spectra of cyclic epoxides such as cyclohexene oxide, the coupling

constant of the ring protons adjacent to the –SCN and –OH groups clearly suggested their trans configuration ($^3J_{12}=15$ Hz).

It is generally accepted that the epoxide ring-opening reaction proceeds under neutral or basic conditions via S_N2 mechanism giving inversion at the attacked C atom, generally the less substituted one and furnishing 1,2- disubstituted products with a trans or anti relationship of the nucleophile to the oxygen leaving group (entry 2-9). In styrene oxide (entry 1), the positive charge on the oxygen appears to be localized on the more highly substituted benzylic carbon leading to the major product.

It is noteworthy that no evidence for the formation of side-product such as diol or thiirane was observed and the products were obtained in pure form without further purification.

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

Acknowledgements

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