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Highly Regioselective Conversion of Epoxides to β-Hydroxy Nitriles with Cyanide Exchange Resin

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ABSTRACT

A simple and regioselective method is described for the efficient conversion of epoxides to β-hydroxy nitriles using Amberlite IRA-400 supported cyanide. The reactions occur in the absence of catalyst and furnish the corresponding β-hydroxy nitriles in high yields.

Key Words: Functionalized polymer; Polymer supported cyanide anion; β-Hydroxy nitrile; Epoxide.

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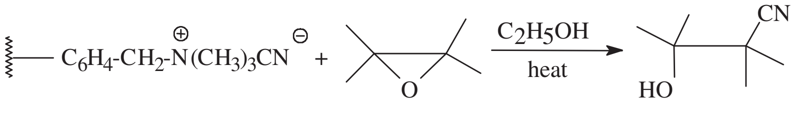
INTRODUCTION

β-Hydroxy nitriles are considered as important intermediates in organic synthesis for the preparation of 1,3 amino alcohols.[1] The ring opening addition reactions of 1,2 epoxides with hydrogen cyanide or with cyanides in the presence of different catalysts is one of the most widely used methods for β-hydroxy nitrile synthesis.[1–6] Although the direct reaction is well applied for simple aliphatic epoxides, it shows poor performance for more complex epoxides and the reactions usually suffer from long reaction times.[7] Cyanation of epoxides with either HCN or an alkali metal cyanide has also been performed in protic solvents under homogeneous conditions.[8–10]

As far as we know, there has been no report in the literature on the use of polymer supported cyanide anion for the ring opening of epoxides. Here, we report the preparation and use of Amberlite IRA-400(CN^-) as an efficient functionalized polymer for the conversion of different epoxides into their corresponding β-hydroxy nitriles, avoiding the use of Lewis acid catalyst and aqueous condition (Sch. 1).

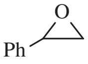
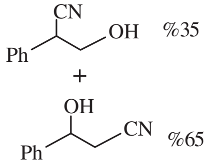
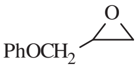
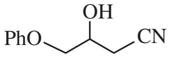
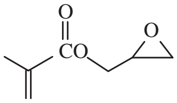
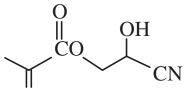
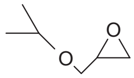
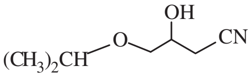
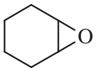
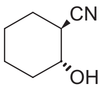
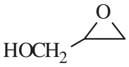
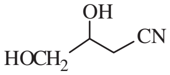
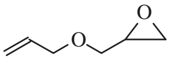
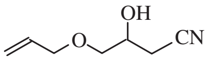
RESULTS AND DISCUSSION

The Amberlite IRA-400 cyanide anion resin was easily prepared by the reaction of Amberlite IRA-400 (Cl^- form) with aqueous sodium cyanide. This polymer supported cyanide resin was found to be a highly effective reagent for the conversion of epoxides to β-hydroxy nitriles (Table 1). Among different solvents such as, CCl_4, benzene, *n*-hexane, ethanol, and DMSO used for this reaction, ethanol was found to be the most suitable media and gave the best results. The optimum molar ratio of the polymer supported cyanide reagent to the epoxide was found to be 3:1. The reaction product can be obtained by simple filtration of the resin and evaporation of the solvent with no neutralization or separation problems. Additionally, the resin can be readily regenerated by treating with dilute sodium chloride and subsequent sodium cyanide solutions.



Scheme 1.

Table 1. Reaction of epoxides with amberlite IRA-400 supported CN^- in ethanol.

Entry	Epoxide	Time (h)	Product[a]	Yield[b] (%)
1		4		85
2		4		83
3		4		80
4		4		80
5		3.5		83
6		4		84
7		4		85

[a] Products were identified by comparison of their IR and NMR spectra and/or physical data with the known samples.[11]

[b] Yield refers to the isolated product.

Except for the reaction of styrene oxide which produced two regioisomers with ratio of 65/35, the reaction of other epoxides were found to be highly regioselective and only one isomer was obtained. With cyclohexene oxide, the *tran*-isomer was produced as the only product.

The advantages of this method over some of those reported in the literature, are its relatively short reaction time, clean conversion of epoxides to nitriles, high regioselectivity and the neutral reaction conditions.

In addition, unlike most reported cases no catalyst is required for the occurrence of the reaction.

EXPERIMENTAL

Material and Techniques

Epoxides were purchased from Merck and Amberlite IRA-400(Cl^-) from Fluka chemical companies. Products were characterized by comparison of their physical data with those of known samples. Gas chromatography was recorded on a Shimadzu GC 14-A. IR spectra were recorded on Perkin Elmer 781 spectrometers. ^1H and ^{13}C NMR spectra were recorded on Bruker Avance DPX 250.

Preparation of Polymer Supported Cyanide Anion

Amberlite IRA-400 (chloride form) (10 g) was washed several times with distilled water to remove foreign materials. The resin was stirred in a 20% aqueous sodium cyanide solution (100 mL) for 5 min. It was then, filtered and washed several times with water until no cyanide anion was detected in the filtrate ($AgNO_3$ test). The resin was finally dried over anhydrous P_2O_5 for 5 h under vacuum at 50°C.

The exchange capacity of polymer supported cyanide anion reagent was found to be in the range 1.0–1.2 mmol/g of dry resin. The regeneration of the used resin can be easily achieved by washing it first with 1 M aqueous sodium chloride and subsequently with NaCN solution.

General Procedure for Preparation of β-Hydroxy Nitriles

A mixture of Amberlite IRA-400 cyanide anion resin (3 mmol/g), epoxide (1 mmol) and ethanol (10 mL) were stirred at 50°C for 4 h. The progress of reaction was followed by T.L.C. and/or G.C. On completion of the reaction, the resin was filtered off and washed with ethanol. The filtrate was dried with sodium sulfate and solvent evaporated. β-Hydroxy nitriles were identified by comparison of their spectral data with those of the known samples.[11]

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