

Synthesis of 4-Chloro-5,6-dihydro-2H-pyran Derivatives by NbCl₅ Mediated Cyclization of Epoxides with Homopropargylic Alcohols

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Epoxides undergoes cyclization with homopropargylic alcohols in the presence of niobium pentachloride under mild condition to afford the corresponding dihydropyran derivatives in good yield.

Keywords: Epoxides, Homopropargylic alcohols, Dihydropyrans, Niobium pentachloride.

INTRODUCTION

The dihydro and tetrahydropyran ring present in many natural products represent an important class of six member ring heterocycles of oxygen [1,2]. Especially the dihydropyrans are much useful intermediates due to the presence of olefin functionality, which allows further functionalization to obtain poly substituted tetrahydropyrans [3-6].

Among existing methods, the Prins cyclization is the most common and successful method and has been emerged as a powerful tool in the synthesis of pyran ring system. Although other methods are available [7-11], their numerous applications and increasing demand have prompted us to develop methods, which give access to this structure. Furthermore, the development of efficient and simple methods would be more useful. Epoxides are the most convenient starting materials for the preparation of various compounds due to the strained ring system [12-17]. In recent years, niobium pentachloride has emerged as an efficient Lewis acid in promoting various organic transformations [18,19]. Herein, we report the formation of dihydropyran derivatives by the reaction of epoxides and homopropargylic alcohols using niobium pentachloride.

EXPERIMENTAL

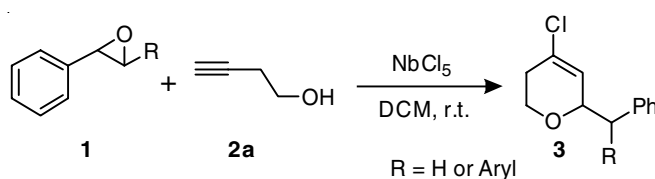
¹H NMR, ¹³C NMR spectra were recorded on Bruker 300 NMR spectrometer and Mass spectra were recorded at 70 eV.

General procedure: To a stirred solution of styrene oxide (500 mg, 4.16 mmol) and 3-buten-1-ol (291 mg, 4.16 mmol) in dry methylene chloride (25 mL) under nitrogen atmosphere,

was added niobium pentachloride (540 mg, 2 mmol) at room temperature. The mixture was stirred under a nitrogen atmosphere for 45 min. After completion by TLC, the reaction mixture was quenched with water and extracted with methylene chloride (2 × 25 mL). The organic extracts were combined, dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel (ethyl acetate-hexane, 3-7) to afford **3a** in 76 % yield.

RESULTS AND DISCUSSION

We initiated our investigation by treating the mixture of styrene oxide and 3-buten-1-ol with niobium pentachloride in anhydrous methylene chloride at room temperature under nitrogen atmosphere. The mixture was stirred at room temperature for 45 min. to achieve the quantitative yield. After work-up, the crude product was subjected to column chromatography on silica gel allowed the isolation of pure product with good isolated yields. By the spectroscopic data, confirmed the product as **3a** and compared with the literature data [11] (Scheme-I).



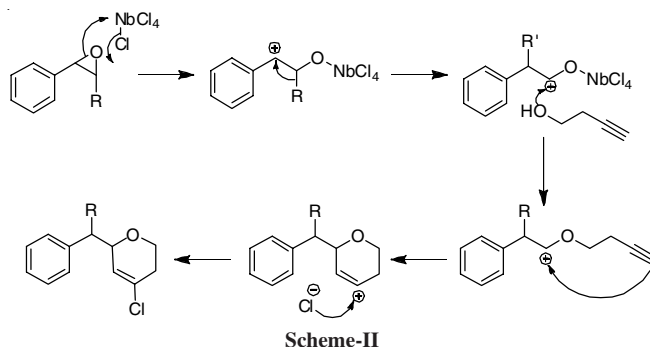
Scheme-I

The scope of the reaction was further studied with variety of epoxides and homopropargylic alcohols under the same reaction conditions. In all the cases, the reaction proceeded well with good yield ranging from 60-76 % showing the generality of the reaction (Table-1).

The role of NbCl₅ in catalyzing the opening of epoxide ring with alcohol and providing chloride nucleophile. The tentative mechanism for the formation of dihydropyrans can be explained by the opening of epoxide ring with niobium pentachloride followed by the migration of hydrogen (in case of **1a**, **1c** and **1d**) and aryl group (in case of **1b**) to generate the carbonium species, which is attacked by the homopropargylic alcohol and skeletally rearranged to the cyclic dihydropyran carbonium species. After further reaction of carbonium species with chloride nucleophile from niobium pentachloride gives 4-chloro-dihydropyran derivative (**Scheme-II**).

Conclusion

In conclusion, the demonstrated method is simple and convenient for the synthesis of dihydropyran derivatives. Significant advantages of this method is mild condition, easy handling, cleaner reaction profiles and short reaction times, which makes as useful method for dihydropyrans synthesis.



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TABLE-1
NbCl₅ MEDIATED CYCLIZATION OF EPOXIDES WITH HOMOPROPARGYLIC ALCOHOLS

Entry	Epoxide	Alcohol	Products ^a	Yield (%) ^b
1				76
2				62
3				70
4				60
5				60
6				60

^aAll the products were characterized by ¹H NMR and mass spectroscopy; ^bYields are after isolation by column chromatography.

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