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Short Communication

TMSI-mediated Prins-type Reaction of Epoxides with Homoallylic Alcohols: Synthesis of Iodo-Substituted Tetrahydropyrans

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Abstract

The cyclization of epoxides with homoallylic alcohols in the presence of Trimethylsilyliodide generates the 4-iodo-tetrahydropyran derivatives in excellent yield.

Keywords: Tetrahydropyrans, Homoallylic alcohol, Epoxide and trimethylsilyliodide.

Introduction

The Prins-type reaction is one of the most common methods used for the construction of pyran ring system that appears in many natural products[1-13]. Prins reaction is the reaction of aldehydes or ketones with homoallylic alcohol[14-21]. Because of the importance of this reaction as a tetrahydropyran ring formation reaction, various methods have been explored[22-25]. Alternately, the 4-halo tetrahydropyrans can be synthesized by the cyclization of epoxides and homo allylic alcohols[26-28]. Especially, 4-Iodo tetrahydropyrans were became much attention because of the labile Iodo group can easily be displaced by many nucleophiles leading to different biologically active compounds. Sabitha et al reported TMSI mediated Prins cyclization of ketones with homoallylic and homopropargylic alcohols[29].

Due to the importance of tetrahydropyran system as intermediate in many natural products, development of alternate methods are much useful. In view of the emerging importance, we found that iodo-substituted tetrahydropyrans could be synthesized by Trimethylsilyl iodide mediated cross cyclization of epoxides and homoallylic alcohols. Epoxides are the useful intermediates for the preparation of various compounds and very reactive due to the strained ring system[30-35]. All epoxides were prepared by the epoxidation of corresponding olefin compounds[36].

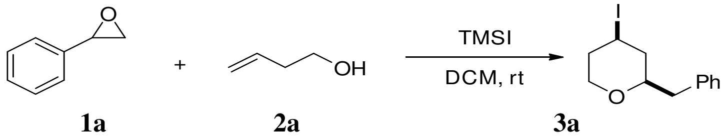
Materials and Methods

^{1}HNMR, ^{13}CNMR spectra were recorded on Bruker 300 NMR spectrometer and Mass spectra were recorded at 70 eV.

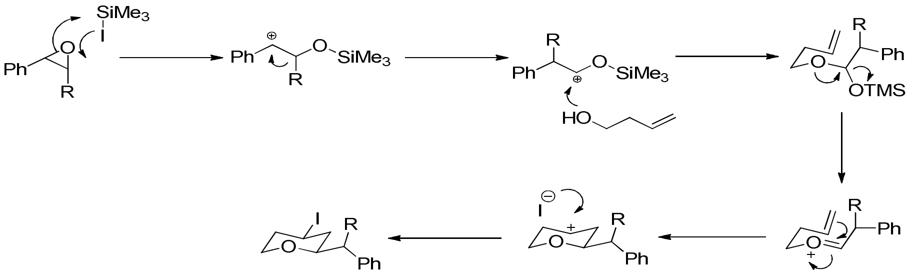
General Procedure: 3-buten-1-ol (500 mg, 6.93 mmol) was taken in anhydrous dichloromethane (15 mL) under stirring. To this solution, was added styrene oxide (1.24 g, 10.4 mmol) and continued stirring for 5 min. Then anhydrous Trimethylsilyl iodide (2.772 g, 13.86 mmol) was added at 25-30 °C under nitrogen atmosphere and stirred for further 1 hour. After 1 hour, TLC indicated the disappearance of both the starting materials. The reaction mixture was quenched with water (20 mL) and the aqueous layer was extracted twice (2 X 20 mL) with dichloromethane. The combined organics were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel (60-120 mesh) by eluting with ethylacetate:hexane mixture (2:7) to afford pure 4-Iodo tetrahydropyran 3a.

Results and Discussion

The initial attempt was made by reacting a mixture of 3-buten-1-ol and styrene oxide with trimethylsilyl iodide in anhydrous dichloromethane under nitrogen atmosphere at 25-30 °C for 1 hour. After workup and purification using silica-gel column chromatography, isolated the product in 78% yield. After characterization of pure compound by spectroscopic analysis and comparing with literature data[37], confirmed as 3a.



Scheme-1
Synthesis of 4-Iodo tetrahydropyran derivative



Scheme-2
Mechanism for the TMSI mediated formation of Tetrahydropyran derivatives

With this result in hand, the method was further extended to stilbene oxide and other homoallylic alcohols to give afford the iodo-substituted tetrahydropyrans yielding from 60-78 % as illustrated in Table-2. In these cases also the reaction preceded same as earlier except the slight variation in reaction time and yield.

Mechanism for the formation of tetrahydropyrans by the reaction of epoxides and homoallyl alcohols using rimethisilyl iodide can be rationalized as the opening epoxide with TMSI to form carbonium species. After migration of hydrogen in the case of **1a** and aryl group in the case of **1b,** the carbonium species is being attacked by homoallylic alcohol and skeletally rearranges to tetrahydropyran carbonium ion. After further reaction of carbonium species with Iodide nucleophile from Trimethylsilyl Iodide gives 4-Iodo-tetrahydropyran derivative. The hypothetical reaction mechanism for the formation of tetrahydropyran with *cis* selectivity is being explained via (*E*)-oxocarbenium ion with chair-like transition state, which is stable due to the electron delocalization. Because of the delocalization, the hydrogen atom at C4 will be placed in a pseudoaxial position. This transition state favors the equatorial attack of Iodide nucleophile (Scheme-2).

Conclusion

In conclusion, the demonstrated method is simple and convenient for the synthesis of iodotetrahydropyran derivatives. Significant advantages of this method is mild conditions, easy handling, cleaner reaction profiles and short reaction times, which will be a useful method for 4-Iodo tetrahydropyrans synthesis.

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