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ORIGINAL PAPER

The influence of cobalt(II) and tin(II) chloride on regioselectivity and kinetics of phenylselenocyclization of 6-methyl-hept-5-en-2-ol

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Abstract

The reaction of the Δ^4-alkenols with PhSeX can follow three possible reaction pathways: two pathways lead to the formation of two regioisomeric cyclic ether products through the process of intramolecular cyclization, while the third represents the addition of the reagent to the double bond of an alkenol. As there are relatively few literature data on the kinetics of these reactions, we have chosen 6-methyl-hept-5-en-2-ol as a substrate of interest in order to obtain valuable results that will enable better understanding of the mechanism of phenylselenoetherification reactions. 6-Methyl-hept-5-en-2-ol is a particularly interesting model-substrate due to its substitution pattern of functional groups involved in the cyclization process. In this research, through synthetic and kinetic studies, we aimed to resolve key questions concerning the influence on kinetics, chemo- and regioselectivity of the reagent's counter ion, steric hindrances in substrate functional groups and the presence of additives.

Keywords Cobalt(II) chloride · Tin(II) chloride · Cyclization · Kinetics · Selenium

Introduction

The distinct position of organoselenium compounds in the field of biologically active molecules is well established, due mainly to their antioxidant and antitumor activity, but also their antimicrobial and antiviral properties [1–5]. The unique features of organoselenium compounds and their modular nature make them versatile sources of nucleophilic, electrophilic and radical species. Furthermore, once introduced into a molecule, selenium can be removed easily from the carbon skeleton through several convenient processes, which can result in a vast number of functionalities [6, 7]. The pronounced reactivity of electrophilic selenium(II) reagents towards unsaturated compounds is highly exploited in ring-closure reactions. The functional necessities of substrates used for the cyclization process are a double bond and a suitably oriented pendant nucleophilic part of the molecule. In such an environment, the addition of the selenium reagent to the double bond results in the formation of a seleniranium intermediate, with subsequent attack of the nucleophilic part and formation of the cyclic products. Selenocyclization reactions have found great utility in natural product synthesis, as the proper choice of pendant nucleophiles can lead to a variety of heterocycles [8, 9]. Despite the immense number of studies devoted to the synthetic application of selenium-promoted ring-closure reactions, our understanding of the processes that influence the mechanism and kinetics of these reactions is still vague.

Selenocyclization reactions are stereospecific *anti*-addition processes, initiated through the formation of a seleniranium intermediate (Scheme 1, **A**), whose three-membered ring can be opened to afford two different regioisomers (**C** and **D**). The regiochemistry is usually under thermodynamic control, favoring the Markovnikov adduct, although many factors can lead to the formation of the anti-Markovnikov product. In most cases, selenocyclizations yield five- or six-membered ring products as a result of 5-*endo-trig*, 5-*exo-trig* or 6-*endo-trig* cyclizations. The presence of the external nucleophile can interfere with the chemoselectivity of these reactions, affording the concurrent reaction of addition (**B**). Therefore, a very delicate product ratio balance is influenced by the structure and properties of the reagent, its counter ion, solvent, reaction temperature, the presence of external additives, structural pattern of the substrate and the nature of its internal nucleophile [10–13]. In order to achieve better insight into the mechanism of phenylselenoetherification reactions, we

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