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MINI-REVIEW-ARTICLE

Selenocyclization by Formation of Carbon-Nitrogen Bonds

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Abstract: Selenium promoted-cyclization of unsaturated substrates containing internal nitrogen nucleophiles, such as different amines and amides, including the examples of its application in the synthesis of more complex polycyclic compounds is reviewed. Selenocyclization reactions of some more specific polyfunctional substrates, like Biginelli hybrids and hydantoins, are also covered.

Keywords: Selenium reagents, cyclization, cyclic amines, cyclic amides, lactamisation, fused rings.

1. INTRODUCTION

In recent decades, selenium compounds have received considerable attention because of their broad spectrum of biological activities and various applications in the formation of carbon-carbon or carbon-heteroatom bonds. Fundamental applications of organoselenium chemistry have been described in notable books and chapters. [1-4] A number of quite useful review articles have also been published [5-8]. New aspects of carbon-carbon bond formation have been illustrated in addition to reactions of electrophilic selenium reagents. From a synthetic point of view, a selenium atom can be introduced and used as an electrophile, nucleophile or as a radical. Nitrogen-containing heterocyclic groups are very important building blocks in many natural products and biologically important scaffolds. Access to a diverse array of functionalized compounds is critical in drug discovery and for this reason, in the past few decades, operationally simple new methodologies for C-N bond formation have been extensively investigated. Among the various kinds of ring-forming reactions, those based on the reaction of an electrophilic reagent with an alkene holding a suitably positioned nucleophilic group are certainly the most useful. Electrophilic seleno-induced/catalyzed heterofunctionalizations of carbon-carbon multiple bonds [9-16] offer interesting opportunities, considering the growing interest in pharmacological and toxicological properties of selenium-containing compounds [17-22]. The most common reagents/catalysts employed for these mentioned synthetic transformations are PhSeCl, PhSeBr, PhSeSePh, and *N*-phenylselenophtalamide (*N*-PSP) [23, 24]. Some electrophilic reagents can be generated *in situ* by oxidative cleavage of diselenides, consuming inorganic or organic oxidants, persulfates or hypervalent iodine. The ability of selenium reagents to affect ring closure reactions has made them increasingly popular in recent years, mostly due to the high availability of the reagents, mild chemical reaction conditions and numerous chemical manipulations that can be done on the selenium moiety before or during its removal. Selenium promoted cyclization reactions thus provided easy access to a wide variety of heterocyclic compounds in general and especially those that contain oxygen and/or nitrogen heteroatoms. In the recent decade, the focus in selenium chemistry has been to develop selenium catalysts that will be useful for cyclofunctionalizations of various specific substrates into novel heterocyclic motifs. [25] However, examples of intramolecular C-N bond formation are relatively rare compared to the extensively studied cases of C-O bond formation [9, 13, 23, 26-30]. Accordingly, this overview will focus on the state-of-the-art selenium-promoted or -catalyzed amino-cyclofunctionalizations of double bonds, illustrating the versatile synthetic applications of selenium-based compounds.

2. INTRAMOLECULAR AMINOSELENYLATIONS

Mechanistically, phenylselenium-induced cyclization of unsaturated substrates bearing tethered internal nitrogen nucleophiles is initiated by the formation of seleniranium ion intermediates from alkenes and selenium electrophile PhSeX followed by backside nucleophilic attack of internal nitrogen nucleophile. Possible ways of cyclization (*endo* or *exo* mode) depend on the relative position of the nucleophile and the double bond in starting alkene (Scheme **1**). Intramolecular aminoselenylation of alkenes usually occurs with high regio- and stereocontrol under mild reaction conditions. Different regioisomers can be obtained in some cases by simply choosing conditions favorable to kinetic or thermodynamic control.

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