Synthesis of 2,5-disubstituted selenazoles by O-Se exchange

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INTRODUCTION

The interest in organoselenium compounds has been growing during the last decades due to its importance in synthetic chemistry. In particular, selenazole heterocycles are being studied because of its interesting biological properties.[1]

As part of our studies involving organoselenium compounds,[2] we explored the cycloisomerization of alkynyl selenoamides. Herein, we report a novel tandem procedure for the synthesis of 2,5-disubtituted selenazoles by cycloisomerization of propargyl selenoamides.

RESULTS AND DISCUSSION

A range of aromatic and some aliphatic terminal propargyl amides were converted to their corresponding selenazoles **4a-h**, as is shown in Scheme 1.

Scheme 1. Synthesis of selenazoles **4a-h**

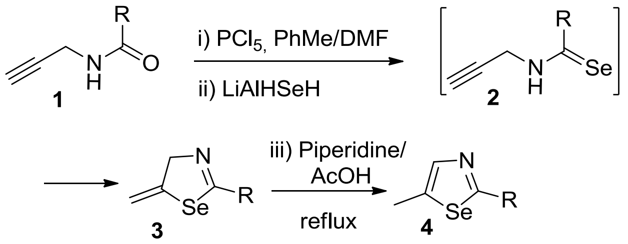


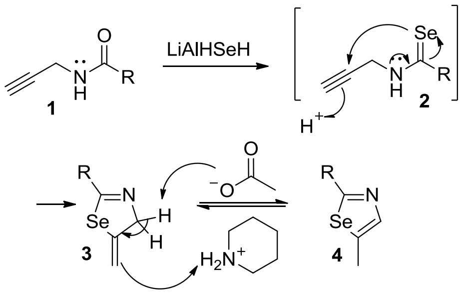
Table 1. Scope of cycloisometization of propargyl amides **1** to 2,5-disubstituted selenazoles **4a-h**.

Comp	R (yield%)	Comp	R (yield%)
4a	Ph (74%)	**4e**	4-isopropyl Ph (61%)
4b	3-Br Ph (70%)	**4f**	*tert*-butyl (20%)
4c	4-CF$_3$ Ph (55%)	**4g**	Propyl (25%)
4d	4-OMe Ph (88%)	**4h**	Isopropyl (23%)

Aromatic propargyl amides provided good yields from 88 to 55%, whereas when using alkyl propagylamides yields were lower, from 20 to 36%, see Table 1.

The proposed mechanism is shown in Scheme 2. Once the selenoamide **2** is formed by O-Se exchange, the Se atom promotes the 5-*endo-trig* cyclization product giving selenazoline **3**. PipAcOH was used to convert compound **3** to aromatic selenazole **4.**

Scheme 2. Plausible mechanism for selenazole **4** formation.



In order to obtain more functionalized heterocycles, selective bromination at position 5 of the methyl selenazole **4a** was studied. Conditions were optimized and further transformations were explored in order to prepare new derivatives.

CONCLUSION

We have developed a catalyst-free pathway for the synthesis of 2,5-disubstituted selenazoles **4** from propargyl amides **1** *via* cycloisomerization of propargyl selenoamides **2.** Conditions for functionalization of 5-methyl selenazole **4a** are being studied.

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