Electrophilic Cyclization of 2-Chalcogen-*N*-Alkynylimidazoles: Versatile Access to Imidazo[2,1-*b*]Chalcogenazoles

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INTRODUCTION

The synthesis of imidazole derivatives and their properties have been thoroughly reported in the literature.[1] The synthetic methods to obtain multiple substituted imidazoles can be basically divided into two classes.[2] The first approach is based on a construction of the imidazol nucleus after the substituents have been installed and properly functionalized.[2] The second approach is based on a preformed imidazol to which carbon substituents are attached in successive order. In this context, electrophilic cyclizations of suitable unsaturated systems have been frequently utilized to construct a wide range of carbocycles and heterocycles.[3] In this study, we optimized the preparation of imidazo[2,1-*b*]chalcogenazoles **2a** via eletrophilic cyclization of 2-chalcogene-*N*-alkynylimidazoles **1a** (Figure 1).

RESULTS AND DISCUSSION

The synthesis of the starting material **1a** was facile and scalable, starting from standard *N*-alkynylation of 1*H*-imidazole via copper salt and 1-bromoalkyne[4] followed by selenation of the 2-position of the *N*-alkynylimidazole using *n*-BuLi/*n*-BuSeBr sequence.[5] After the successful in the preparation of 2-chalcogene-*N*-alkynylimidazoles, we then turned our attention to use these compounds in the electrophilic cyclization reactions. For this purpose, the reaction of 2-chalcogene-*N*-alkynylimidazole **1a** with iodine was chosen as a model system. Thus the careful analysis of the optimized reactions revealed that the optimum condition for the cyclization reactions was the mixture of **1a** (0.25 mmol) with iodine (1.1 equiv) at room temperature in EtOH under air atmosphere (Figure 1).

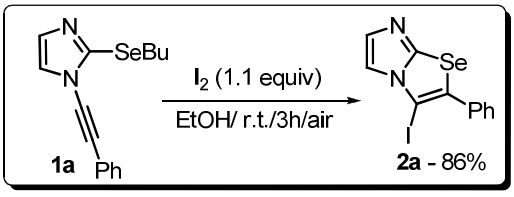

Figure 1. Optimized reaction conditions

The results demonstrated that the cyclization efficiency was not sensitive to electronic effects of the aromatic ring. For example, aromatic ring with a MeO, an electron-donating group, gave similar yields than aromatic ring with a Cl, an electron-withdrawing group. Meanwhile, with the purpose to evaluating the possibility to introduce one more different function at C-3 of the selenazole ring, we tested the behavior of **1a** using PhSeBr as electrophile source. It is also worth noting that this reaction can be performed using a sulfur group at C-2 of the starting *N*-alkynylimidazole **1a** (Figure 2).

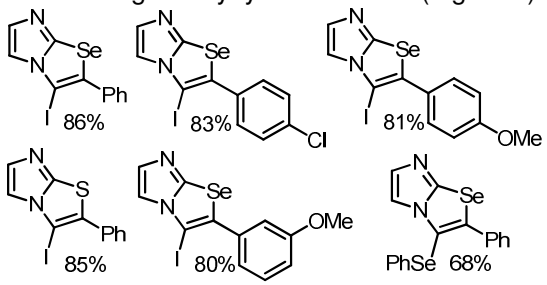

Figure 2. Imidazo[2,1-*b*]chalcogenazoles prepared

CONCLUSION

In summary, we have explored the electrophilic cyclization of easily accessible 2-chalcogene-*N*-alkynylimidazoles establishing a route to imidazo[2,1-*b*]chalcogenazole derivatives in good yields. Further studies are in progress in our laboratory to extend the scope of the reaction and to fully exploit the biological potential of these compounds.

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