Synthesis of Diselenide Based Novel Amide Derivatives: A potential Anti-Alzheimer Compounds.

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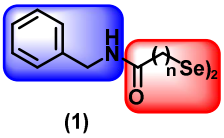
Introdução

Interest in synthetic organoselenium compounds has been growing since the 1970s, when many reports described the identification of various selenoproteins, which are involved in a wide number of physiological processes in mammals, such as antioxidant defense, thyroid hormone production and immune responses.[1-4] There are many reports regarding the biological importance of diselenides having amide bond. The presence of amide bond in close proximity of selenium not only improves the biological activity but also improves the stability of the compound.[2-5]

Thus, according to our interest in bioactive organoselenium compounds,[2-4,6] herein, we describe the synthesis of diselenide based amides **1** (Fig. 1), as a potential anti-alzheimer compound.

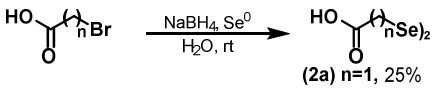


(1)

Fig 1. Diselenide based amide

Resultados e Discussão

Initially, aliphatic diselenides containing free carboxylic acid **2a-c** were prepared, from the reaction of the corresponding bromo carboxylic acids with Na_2Se_2, generated *in situ,* from $NaBH_4$ and selenium (Scheme 1).

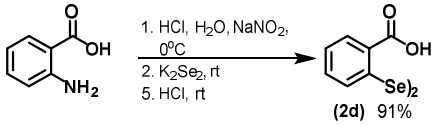


(2a) n=1, 25%
(2b) n=2, 50%
(2c) n=3, 37%

Scheme 1. Synthesis of aliphatic diselenides containing free carboxylic acid

The 2,2'-diselenobisbenzoic acids **2d** was prepared through diazotization of anthranilic acid followed by reaction with K_2Se_2 (obtained by reaction of KOH with selenium) (Scheme 2).

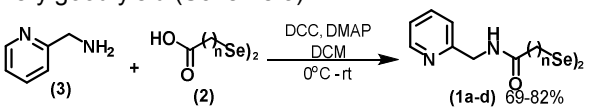
In the following step, the amidation reaction was carried out, by reacting diselenides of **2a-d** with picolylamine **3** using different coupling conditions.



(2d) 91%

Scheme 2. Synthesis of 2,2'-diselenobisbenzoic acids

Best results were achieved by using DCC-DMAP in anhyd. DCM, resulted the desired diselenides **1** in very good yield (Scheme 3).



(3) **(2)** **(1a-d)** 69-82%

Scheme 3. Synthesis of seleno-picolylamides

Initial experiments shows that these diselenide **1a-d** will be an excellent candidate to act a potential anti-alzheimer compounds. For example, in case of **1c** the inhibition in acetyl choline sterase assay was 97 %.

Conclusões

In the present study, a number of novelamide containing diselenides **1a-d** were synthesized through the coupling reaction of diselenides containing free carboxylic acid **2a-d** with amine **3**. According to the initial results diselenide **1c** can act as anti-alzheimer compound, in case of **1c** the inhibition in acetyl choline sterase assay was 97 %. Moreover, the amides 1a-d will also be evaluated in other biological assays (*in-vivo* & *in-vitro*).

Agradecimentos

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