Synthesis of New Diselenide Based Ester Derivatives: Biologically Potential Compounds

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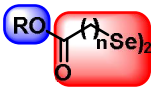
INTRODUCTION

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, 2]. There are many reports regarding the biological importance of diselenides having amide bond[2, 3]. However, ester derivatives with diselenide moiety have not been explored.

Thus, according to our interest in bioactive organoselenium compounds[4] as well as the versatile biological activities of esters, herein, we describe the synthesis of diselenide based esters **1** (Figure 1), as potentially bioactive molecules.

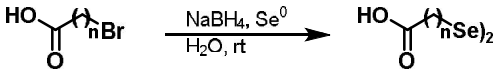


(1)

Figure 1. Diselenide based esters

RESULTS AND DISCUSSION

Initially, aliphatic diselenides containing free carboxylic acid **2a-b** were prepared, from the reaction of the corresponding bromo carboxylic acids **3a-b** with Na_2Se_2, generated *in situ,* from $NaBH_4$ and selenium (Scheme 1).



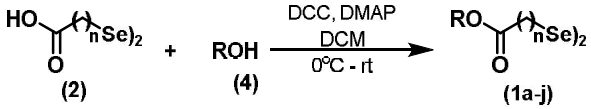
(3a) n=1
(3b) n=2

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

Scheme 2. Synthesis of diselenides of carboxylic acid

In the following step, esterification of diselenides containing free carboxylic acid **2a-b** with different alcohols **4** was carried out, using different coupling conditions. Best results were achieved by using DCC-DMAP in anhyd. DCM, resulted the desired diselenides **1** in very good yield (Scheme 2).

A number of diselenide based ester derivatives **1** were synthesized using various naturally occurring biologically active alcohols **4** (Table 1).



(2) **(4)** **(1a-j)**

Scheme 2. Synthesis of diselenide based ester

Table 1. Reaction of diselenide containing acid **2** and alcohol **3**

Entry	Acid **2**	ROH **4**	Ester **1**	Yield (%)
1	**2a**	*β*-Citronellol	**1a**	79
2	**2a**	Cholesterol	**1b**	75
3	**2a**	Cinnamyl alcohol	**1c**	75
4	**2a**	2-Hydroxymethylfurfural	**1d**	62
5	**2a**	Methyl (*S*)-(+)-mandelate	**1e**	65
6	**2b**	*β*-Citronellol	**1f**	83
7	**2b**	Cholesterol	**1g**	80
8	**2b**	Cinnamyl alcohol	**1h**	78
9	**2b**	2-Hydroxymethylfurfural	**1i**	68
10	**2b**	Methyl (*S*)-(+)-mandelate	**1j**	75

Initial experiments shows that these diselenides **1a-j** will be an excellent candidate to act as GPx-mimic. For example, in case of **1h**, the time required to reduce the concentration of thiol to 50% was 11.83 min at 100 *μ*M concentration.

CONCLUSION

We have prepared the desired diselenide based ester derivatives in very good yields using DCC-DMP as coupling reagents. According to the initial results diselenide **1h** can act as GPx-mimic, which reduce the concentration of thiol to 50% in 11.83 min at 100 *μ*M concentration.

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