Synthesis of Hidroxamic acid and Proline derivatives of Diselenide as Mimetics Enzyme to GPx.

Daiane Gobbatto de Liz* (PG) [1], Gustavo P. silveira (PQ) [2], Antonio Luiz Braga (PQ) [1]

[1] *Universidade Federal de Santa Catarina, UFSC, Florianópolis – Santa Catarina, Brasil*

[2] *Universidade Federal do Rio Grande do Sul, RS, Brasil*

* *daiane.liz@gmail.com*

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INTRODUCTION

Seleno amino acids and peptides are promising agents that mimic the enzyme glutathione peroxidase (GPx). Recently, our research group prepared a library at new selenide and diselenide derivatives of amino acids. They were able to promote the catalytic reduction of H_2O_2 to water at the expense of oxidation of thiols at the speed higher than the already known mimetic of GPx, diphenyl diselenide[1]

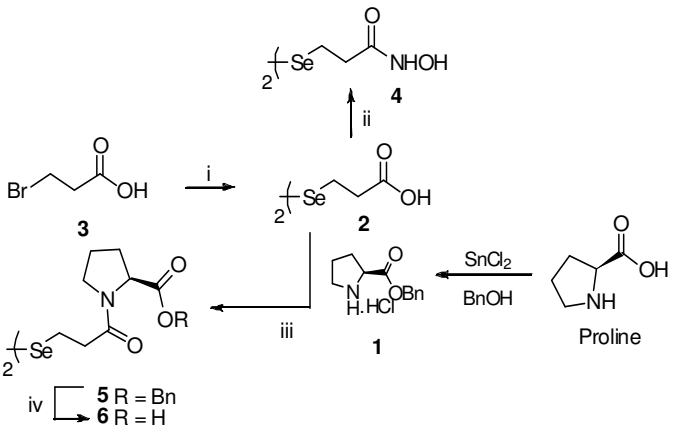
Numerous natural products contains the pyrrolidine ring in their structure, showing significant biological activities and used as therapeutic agent.[2] Similary hydroxamic acids got recent focus in chemistry due its biological its aspect.[3]

The present work shows the synthesis of new diselenide derivatives of the proline and hydroxamic acids as potential mimetics GPx.

RESULTS AND DISCUSSION

The reaction between proline and benzyl alcohol in the presence of thionyl chloride led to formation of benzyl proline hydrochloride **(1)** with 80% yield. The 3,3'-diselanediyldipropanoic acid **(2)** was prepared by reaction of 3-bromo propionic **(3)** and disselenolato lithium, which was generated *in situ* by treatment at Se^0 elemental and superhydride (lithium triethylborohydride) in anhydrous THF. Subsequently reaction of **2** with ethyl chloroformate resulted an anhydride intermediate which on reaction with hydroxylamine and triethylamine led to generate 3,3'-diselanediylbis(N-hydroxypropan-amide) (**4**) with 60% yield.

Continuing the synthesis of the desired compounds a reaction coupling was carried out between **2** with proline derivative (**1**), using EDC and DMAP led to the formation of diseleno proline derivative (**5**) with 40% yield. Finally, deprotection of benzyl group by catalytic hydrogenation, using Pd-C 10%, 150 psi for 24 hours at room temperature, led to proline acid derivative of diselenide **(6)** with 80% yield (Scheme).



Scheme . *i)* Se^0, $LiEt_3BH$/THF, 0^0C, 12h, 80%; *ii)* $C_3H_5O_2Cl$, Et_3N, THF, DMF, $NH_2OH.HCl$ *iii)* EDC, DMAP, NMM, DCM, r.t., 24h, 40%; *iv)* H_2 (150 psi), Pd-C 10%, MeOH, r.t., 12h, 80%.

Thus the compounds synthesized in this work are being studied as GPx mimetics by kinetic evidence.

CONCLUSION

We prepared a new diselenide of proline acid derivative **(6)** and 3,3'-diselanediylbis(N-hydroxypropan-amide) (**4**) by using an optimized synthetic route with good yields (80% and 60% respectively). From the proposed synthetic rout a library of new diselenide will be propared and will be evaluated for as mimetics to GPx.

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