Microwave assisted synthesis of biologically relevant selenosemicarbazones

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INTRODUCTION

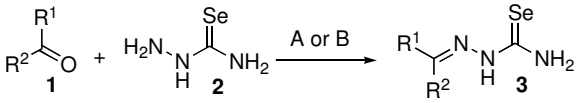
The synthesis of compounds containing selenium has caught much attention due to their biological and pharmaceutical properties.[1] It has been widely reported that organoselenium compounds can be used as antioxidant, antiinflammatory, antibacterial, antiviral, and antitumor agents.[2]

Cruzipain is the native enzyme responsible for the mayor proteolytic activity in all stages of *Trypanosoma cruzi* parasite, the causative agent of Chagas disease.[3] Thiosemicarbazones have been developed as reversible cruzipain inhibitors.[4] In this order, since selenium shares similar electronic properties with sulfur, an isosteric replacement could turn the selenocarbonyl group into more nucleophilic specie compared to thiocarbonyl moiety and consequently be active against cruzipain.

RESULTS AND DISCUSSION

Selenosemicarbazones **3a-f** were synthesized according to a general reaction sequence. Scheme 1,Table 1.

Table 1. Synthesis of Selenosemicarbazones **3a-3f**



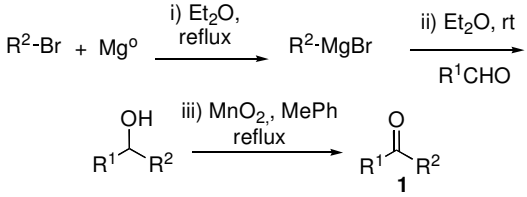
Compound	R^1	R^2	Yield (%)
E-**3a**	*m*-Br Ph	Me	53[a]
Z/E-**3a**	*m*-Br Ph	Me	43[b]
3b	*m*-Br Ph	H	46[a]
3c	*m,p*-diCl Ph	H	77[a]
3d	*m*-CF_3 Ph	H	52[b]
3e	*m*-Br Ph	*m*-Br Ph	27[b]
Z/E-**3f**	*m,p*-diCl Ph	Butyl	55[b]

Table 1. [a]AcOH (cat.), EtOH, reflux 4h; [b]*p*-TsOH (cat), EtOH, µw 6 min, 90°C.

Selenosemicarbazones derived from ketones presented *Z/E* isomerism around the C=N group. The mayor difference between thermal and microwave heating lies not in the yields but in the isomer proportion obtained. In fact, when **3a** and **3f** were prepared using microwave irradiation, a mixture of *Z/E* isomers was isolated. Whereas, conventional heating led to a single isomer *E*-**3a.**

Ketones **1a**, **1e** and **1f** were synthesized in good yields (55 - 70 %), according to Table 2.

Table 2. Synthesis of ketones **1a**, **1e** and **1f**



Compound	R^1	R^2	G.Yield (%)
1a	*m*-BrPh	Me	69
1e	*m*-BrPh	*m*-BrPh	70
1f	*m,p*-diCl Ph	Butyl	55

CONCLUSIONS

Selenosemicarbazones were easily synthesized following the reaction sequence described. Although microwave assisted reaction was an easy methodology due to lower time reaction and minimization of solvent waste, it was not as selective as reflux conditions, were a single *E* isomer was obtained. These compounds will be evaluated as anti cruzipain and anti *T.cruzi* agents.

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REFERENCES

[1] Xi, Y.; Liu, J.; Li, J. *Tetrahedron Lett.* **2011**, *52*, 932–935.
[2] Nogueira, C.W.; Zeni, G.; Rocha, J. *Chem Rev.* **2004,** *104*, 6255-6285.
[3] de Cazzulo, F. BM.; Martinez, J.; North, MJ.; Coombs, GH.; Cazzulo, JJ. *FEMS Microbiol Lett.* **1994**, *124*, 81-88.
[4] Du, X.; Guo, C.; Hansell, E.; Doyle, P.; Caffrey, C.; et al. *J. Med. Chem.* **2002**, *45*, 2695-2707.