

Transition Metal-Free Direct C–H Bond Selenation of 1,3,4-Oxadiazoles

Jamal Rafique (PG)*, Sumbal Saba (PG), Marcelo Godoi (PG) and Antonio L. Braga (PQ)

LabSelen – Laboratório de Síntese de Substâncias Bioativas de Selênio, Departamento de Química - CFM, Campus Universitário, Universidade Federal de Santa Catarina, CEP 88040-900, Florianópolis, SC, Brasil.

*e-mail corresponding author: jamal.chm@gmail.com

Palavras Chave: Carbon-Hydrogen Bond Functionalization, Selenides, Oxadiazole, Catalyst Free.

Introdução

The formation of C-Se bonds represent a very important and a key step in the synthesis of a wide range of biologically active molecules and functional materials.¹⁻³ From the last decade, the cross-coupling of aryl halides and diselenides has become one of the dominant methods for the construction of C-Se bonds.⁴ But these traditionally coupling reactions are effective in constructing various C-Se bonds either metal-ligand combinations and/or prefunctionalized reaction partners are required, which significantly restricts potential applications of these methods.

Recently, major advances have been achieved in C-H bond functionalization of 1,3,4-oxadiazoles.⁵ These are relevant heterocycles because of their interesting properties in medicinal chemistry and material sciences.⁶ Interestingly, so far there is no report regarding selenation of 1,3,4-oxadiazoles. Keeping in mind that the oxadiazoles family has pharmacological and material science applications and considering our interest^{1,4}, and that transition metal-free C-Se bond-forming reactions between diorganyl diselenide and 1,3,4-oxadiazoles are unknown, herein we report for the first time a method for direct selenation of 1,3,4-oxadiazoles C-H bonds using diaryl diselenides, Fig. 1.

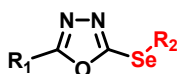
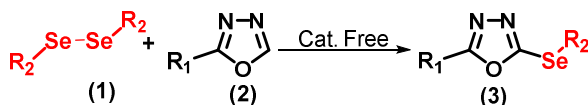


Fig 1. Selenated 1,3,4-oxadiazole

Resultados e Discussão

In order to optimize our methodology, we initiated our studies by evaluating the reaction between diphenyl diselenide **1** and 2-substituted 1,3,4-oxadiazole **2**, as shown in scheme 1.



Scheme 1. Selenation of 1,3,4-oxadiazole

We checked several reaction parameters as depicted in Table 1. It is noteworthy that the best reaction condition was established by using DMF as

solvent and K₂CO₃ as base at 100°C for 12 hours reaction time, affording the desired product **3** with 84% yield (entry 7).

Table 1. Optimization of the reaction conditions^a

Entry	Solvent 3ml	Base 1eq.	Temp. °C	Time hr	Yield ^b %
1	DMSO	K ₂ CO ₃	100	24	65
2	DMF	K ₂ CO ₃	100	24	77
3	THF	K ₂ CO ₃	100	24	NR
4	DMF	Na ₂ CO ₃	100	24	40
5	DMF	Cs ₂ CO ₃	100	24	48
6	DMF	<i>t</i> -BuOK	100	24	NR
7	DMF	K ₂ CO ₃	100	12	84
8	DMF	K ₂ CO ₃	120	12	71
9	DMF	K ₂ CO ₃	80	12	60

^a Reaction conditions: diselenide (0.25 mmol), oxadiazole (1 eq.), Base (1 eq.). ^b Isolated yields.

Conclusões

In the present studies, we developed a facile procedure for the synthesis of oxadiazole selenides under catalyst free condition through a direct C-H bond functionalization. Reaction condition was optimized for the selenation of 2-Substituted 1,3,4-oxadiazole at C5 in excellent yield using diselenide as selenide source. Further work in this direction is in progress in our group.

Agradecimentos

CNPq, TWAS, UFSC, and INCT-Catálise

¹ Braga, A. L e Rafique, J. Chapter 13-*The chemistry of organoselenium and tellurium compounds. V.4*, ed. Rappoport, Z, **2013**, 989.

² Braga, A. L e Rafique, J. Chapter 14-*The chemistry of organoselenium and tellurium compounds. V.4*, ed. Rappoport, Z, **2013**, 1053.

³ Braga, A. L e Rafique, J. Chapter 15-*The chemistry of organoselenium and tellurium compounds. V.4*, ed. Rappoport, Z, **2013**, 1119.

⁴ a) Singh, D.; Deobald, A. M.; Camargo, L. R. S.; Tabarelli, G.; Rodrigues, O. E. D. e Braga, A. L. *Org. Lett.* **2010**, *12*, 3288. b) Chatterjee, T. e Ranu, B. C. *J. Org. Chem.* **2013**, *78*, 7145.

⁵ Kawano, T.; Hirano, K.; Satoh, T. e Miura, M. *J. Am. Chem. Soc.* **2010**, *132*, 6900.

⁶ Boström, J.; Hogner, A.; Llinàs, A.; Wellner, E. e Plowright, A. T. *J. Med. Chem.* **2012**, *55*, 1817.