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Preparation of 3-Aryl-5-phenylselenomethyl 1, 2, 4-Oxadiazole and their Further Deselenenylation Reaction

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Abstract: A mild Porco's two-step, one-pot condensation reaction for the preparation of 3-aryl-5-phenylselenomethyl 1, 2, 4-oxadiazole through phenylseleno acetic acid and benzamidoxime was reported. And further deselenenylation of 3-aryl-5-phenylselenomethyl 1, 2, 4-oxadiazole was studied.

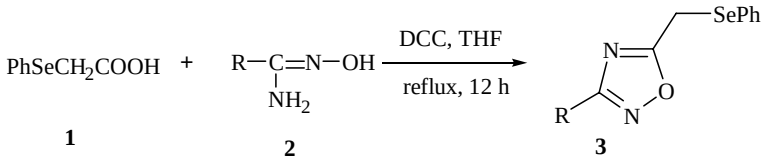
Keywords: Porco condensation, 1, 2, 4-oxadiazole, benzamidoxime.

Oxadiazoles are important bioisosters for esters and amides in drug discovery with reported muscarinic agonist, benzodiazepine receptor agonist, 5-HT agonist, and antirhinoviral activities[1]. Diorganic selenides have attracted considerable interest because of their potential use as anticancer and antioxidant agents[2]. However, the incorporation of selenide and oxadiazole into the molecule, which we believe could be a useful agent with potential biological activities, has rarely been investigated.

Our research group[3] has been interested in the application of selenium in organic synthesis for several years. Here we reported a mild Porco condensation[4] to prepare 3-aryl-5-phenylselenomethyl 1, 2, 4-oxadiazoles. Phenylselenoacetic acid **1** (1.0 mmol), easily prepared from diphenyl diselenide and bromoacetic acid, was mixed with benzamidoxime **2** (1.1 mmol) and DCC (2.5 mmol) (**Scheme 1**). The mixture was refluxed in THF for 12 h. 3-Aryl-5-phenylselenomethyl 1, 2, 4-oxadiazole **3** was obtained in good yield and the results are summarized in **Table 1**.

The obtained 3-(4-methylphenyl)-5-phenylselenomethyl 1,2,4-oxadiazole **3a** reacted with LDA and allyl bromide smoothly to afford alkylated product **4a**, which followed by selenoxide *syn*-elimination to obtain **5a** in 94% yield (**Scheme 2**).

Scheme 1



1 **2** **3**

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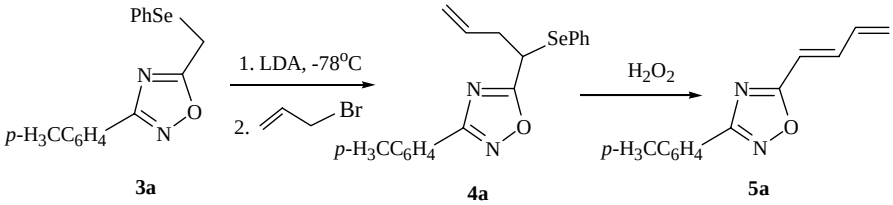
Table 1 Synthesis of 3-aryl-5-phenylselenomethyl 1, 2, 4-oxazoles

Product	R	Yield [a]	Product	R	Yield [a]
3a	4-$CH_3C_6H_4$	88	**3d**	4-ClC_6H_4	83
3b	4-$CH_3OC_6H_4$	84	**3e**	4-FC_6H_4	78
3c	C_6H_5	91	**3f**	4-BrC_6H_4	88

a Isolated yield

Scheme 2



3a **4a** **5a**

Yield: 86% Yield: 94%

In summary, we report a mild Porco condensation reaction for the preparation of 3-aryl-5-phenylselenomethyl 1, 2, 4-oxadiazole, which further undergo deselenenylation reaction to obtain 3, 5-disubstituted 1, 2, 4-oxadiazole.

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References

1. G. D. Diana, D. L. Volkots, T. J. Nitz *et al.*, *J. Med. Chem.*, **1994**, *37*, 2421.
2. K. El-Bayoumy, *Nutr. Cancer*, **2001**, *40*, 4.
3. (a) W. M. Xu, E. Tang, X. Huang, *Synthesis*, **2004**, 2094. (b) X. Huang, W. M. Xu, *Chin. Chem. Lett.*, **2004**, *11*, 1279.
4. T. L. Deegan, T. J. Nitz, D. Cebzanov *et al.*, *Bioorg. Med. Chem. Lett.*, **1999**, *9*, 209.

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