Microwave-assisted synthesis of new 1,2,4-oxadiazole linked to 1,2,3-triazole derivatives.

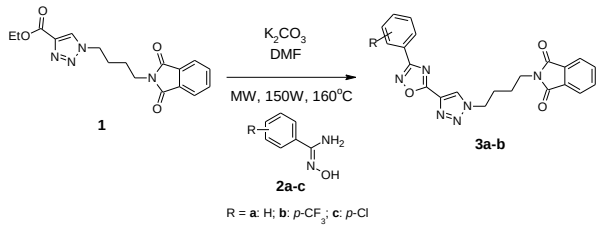
Franciane G. Santos (IC), Valentina Nascimento e Melo (PG), Ronaldo N. de Oliveira (PQ)*

Universidade Federal Rural de Pernambuco, Laboratório de Síntese de Compostos Bioativos
**E-mails: ronaldonoliveira@pq.cnpq.br; francianegs21@hotmail.com*

Keywords: microwave-assisted synthesis, 1,2,3-triazole, 1,2,4-oxadiazole.

Introduction

1,2,4-Oxadiazoles and 1,2,3-triazoles have been described as heterocycles with a wide range of biological activities, such as glycogen phosphorylase, antifungal, and cytotoxic.[1,2] These conjugated nucleus have been little cited in the literature and methodologies to preparing them have had limited scope.[3] Recently, microwave assisted synthesis of 1,2,4-oxadiazole.[4] In this context, here we propose the synthesis of new 1,2,4-oxadiazole-1*H*-1,2,3-triazole derivatives from aryl amidoximes **2a-c** and ester triazolic **1** (Scheme) using MW irradiation.

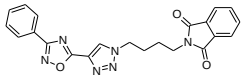
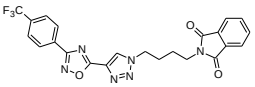
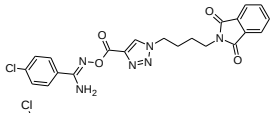
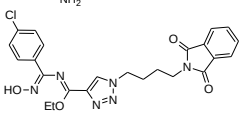


Scheme. Synthesis of new 1,2,4-oxadiazole-1*H*-1,2,3-triazole derivatives

Results and Discussion

The nitriles reacted with $NH_2OH{\cdot}HCl$ using Na_2CO_3 in ethanol to give the amidoximes **2a-c**.[5] The ester triazolic **1** was prepared from corresponding azide phthalimide and ethyl propiolate under click condition.[6] With these compounds in hand, we begin the reaction applying microwave irraditation.[7] Then, was used DMF (1mL), 0.146 mmol of ester, 0.124 mmol of K_2CO_3 and 0.219 mmol of amidoxime **2a** to prepare **3a** in 33% yield under focused microwave irradiation (150W/160°C) for 20 min (4 x 5 min) (Table). Next, was chosen aryl amidoxime **2b** containing electron withdrawing group *p*-CF_3 to obtain **3b** in 27% yield. For our surprise, 1,2,4-oxadiazole using aryl amidoxime **2c** was not formed, but furnished two intermediates **4a** and **4b** in yields of 22 and 24%, respectively. The literature describes in this reaction the compound **4a** as intermediate which after heating can be cyclized to afford 1,2,4-oxadiazole.[1] To our knowledge, by the first time the compound **4b** was isolated as a intermediate. Further the chemical behavior of this reaction is currently being performed in our laboratory.

Table. Reaction between **1** and **2a-c**.

Compds.	Chemical structures	Yield, % [a] (time, min)
3a		33 (20)
3b		27 (5)
4a		22 (10)
4b		24 (10)

[a] After chromatographic column. Starting materials were recovered (no-optimized results).

Conclusion

In summary, new 1,2,4-oxadiazoles linked to 1,2,3-triazole were synthesized in low yields using FMW irradiation; however, optimizations are in progress. New intermediate for this reaction was isolated and this result is being investigated. The structures of the compounds **3a,b** and **4a,b** were assigned by ^1H and ^{13}C NMR spectral analyses.

Acknowledgement

CNPq, FACEPE, CAPES

[1] Jakopin, Z.; Dolenc, M. S. *Curr. Org. Chem.* **2008**, *12*, 850.
[2] Agalave, S. G.; Maujan, S. R.; Pore, V. S. *Chem. Asian J.* **2011**, *6*, 2696.
[3] Sangshetti, J. N.; Shinde, D. B. *Eur. J. Med. Chem* **2011**, *46*, 1040.
[4] de Freitas, J. J. R.; de Freitas, J. C. R.; da Silva, L. P.; de Freitas Filho, J. R.; Kimura, G. Y. V.; Srivastava, R. M. Tetrahedron Lett. **2007**, *48*, 6195.
[5] Barros, C. J. P.; de Freitas, J. J. R.; de Oliveira, R. N.; de Freitas Filho, J. R. *J. Chil. Chem. Soc.* **2011**, *56*, 721.
[6] da Silva, M. T.; de Oliveira, R. N.; Valença, W. O.; Barbosa, F. C. G.; Camara, C. A. *J. Braz. Chem. Soc.* **2012**, *23*, 1839.
[7] Reactions were conducted in a focused microwave (FMW) power delivery system, using a CEM Discover Synthesis (Model 908005, 0-300 W, 2455 MHz, CEM Corporation).