Rapid synthesis of di-1,2,4-oxadiazoles pyridyl compounds

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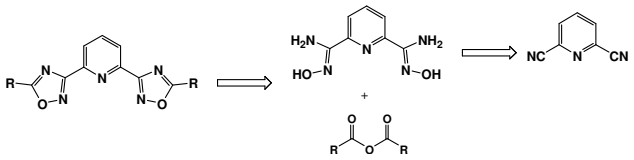
Keywords: di-1,2,4-oxadiazoles pyridyl, microwave, 2,6-di-amidoxime pyridyl

INTRODUCTION

The 1,2,4-oxadiazoles derivatives are compounds that exert a variety of important biological activity, such as anti-inflammatory, antiviral, and cardiovascular activities[1]. These compounds have also been applied as ligands on metal complexes[2] and liquid crystal materials.[3]

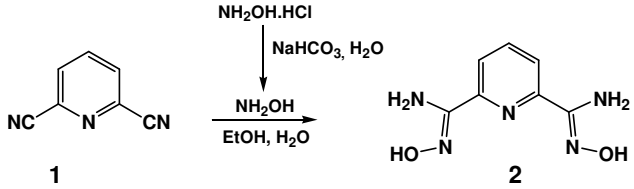
In this work, we have investigated the rapid synthesis of some new di-1,2,4-oxadiazoles pyridyl compounds by two different methods between as shower the scheme 1.



Scheme 1. Retrosynthesis of di-1,2,4-oxadiazoles pyridyl compounds

RESULTS AND DISCUSSION

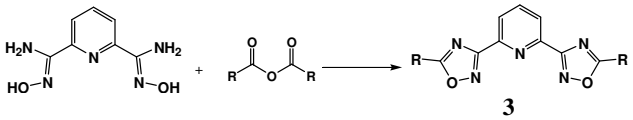
Initially, 2,6-diamidoxime pyridyl (**2**) was synthesized in quantitative yield from commercially available 2,6-dicianopyridine (**1**) and hydroxylamine hydrochloride in H_2O (Scheme 2).



Scheme 2. Synthesis of 2,6-diamidoxime pyriyl

Two methods for preparing 1,2,4-dioxadiazoles pyridyl compounds via reaction between 2,6-diamidoxime pyridyl and an anhydride were compared, namely the standard thermal method (**Method A**) and that by microwave irradiation (**Method B**). The results are shown in Table 1.

Table 1. Yield comparison for the syntheses of di-1,2,4-oxadiazoles pyridyl by the methods A and B.



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Compounds	R	Method A		Method B	
		Time (min)	Yield (%)	Time (min)	Yield (%)
3a	Methyl	120	94	10	>99
3b	trifluoromethyl	90	96	10	>99
3c	n-propyl	150	90	10	>99
3d	n-hexyl	150	90	10	94
3e	Phenyl	240	0	60	0

Conditions: The anhydrides were used as solvent. Yield refers to isolated yields. The purification was done by recrystalization from ethyl acetate. The products were characterized by ^{1}H and ^{13}C NMR, GC-MS and ESI-TOF-MS. Experiments with microwave were carried out in a Discover reactor.

The compounds synthesized from alkyl anhydrides were rapidly obtained in excellent yields (**3a-3d**) by using a microwave reactor. The product **3e** was not obtained by either the two methods tested.

CONCLUSION

We obtained several new 1,2,4-dioxadiazoles pyridyl compounds in good yields and short reaction time by a method using microwave irradiation. Biological activity of these compounds are under investigation in our laboratory.

ACKNOWLEDGEMENTS

CNPq, CAPES, UFPB.

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