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[E012]

P_2S_5 mediated synthesis of benzoxazoles and benzothiazoles by microwave irradiation

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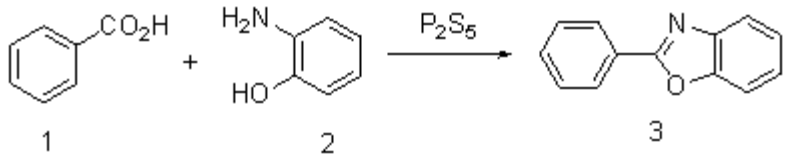
During last years microwave irradiation has become a valuable alternative to the heating by conventional methods. Microwave assisted organic synthesis (MAOS) has demonstrated to be a useful tool for dramatic reduction of reaction times, improvement of yields and in many cases avoid the use of solvent. This makes MAOS one of the most important options for developing synthesis in the field of "green chemistry".

Benzoxazoles are present in the structure of many compounds with biologic activity as antitumorals, antimicrobial and antiviral[1] and they are used as protecting groups for carboxylic function too. For this reason many methods have been developed for their synthesis, some of them using microwaves, those based on the condensation of 1,2-aminophenols and carboxylic acids,[2,3] acid chlorides[4] and S-methylthioamides.[5]

Recently we needed access to an easy route to achieve benzoxazole for several tests, so we reviewed the literature for an easy and clean method for their production. Soufiaoui et al.[2] developed a method from benzoic acids in a monomode Synthewave 402 microwave oven, but this procedure showed to be difficult to reproduce in a Milestone ETHOS-D, even for the same compound reported (i.e. veratric acid). Recently Chakraborti[3] et al. have published similar synthesis in a domestic microwave oven, but the reported yields were low for benzoic acid, and the reaction conditions were not working for our compounds. The other previously described methods assisted by microwaves for benzoxazoles required more labile derivatives of benzoic acids (i.e. acid chlorides) or non commercial starting materials (i.e. S-methylthioamides). So, we started a new procedure to achieve benzoxazoles from carboxylic acids by MAOS, studying the influence of an auxiliary reagent. The reagent chosen was P_2S_5, since it has been used for thionation and safely used under microwave irradiation.[6]

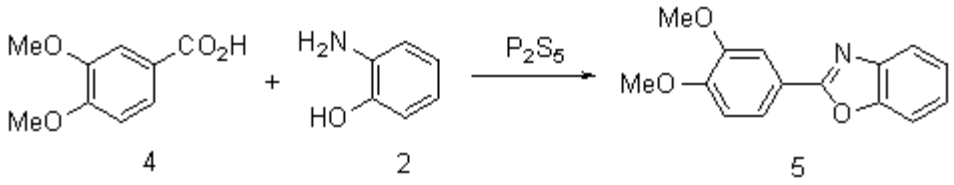
Thus, when a mixture (1:1) of benzoic acid **1** and 1,2-aminophenol **2** were irradiated with microwaves in the presence of P_2S_5 (40% molar) led to the formation of 2-phenylbenzoxazole **3** in 70% yield (14 minutes irradiation in a ETHOS-D microwave oven, 800W). This constituted a good increment compared with Chakraborti's (35% yield for benzoic acid).



1 2 3

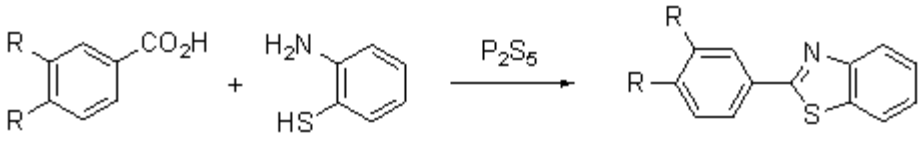
Scheme 1

Similar behaviour was found for veratric acid **4**, obtaining the corresponding benzoxazole **5** in a 68% yield after the same irradiation time.



Scheme 2

This procedure can be extended to the synthesis of benzothiazoles, just by replacing 1,2-aminophenol by 1,2-aminothiophenol **6**. In this way, 2-phenylbenzothiazoles **7** and **8** were obtained in 82% and 79% yields, respectively. In both cases the reaction times suffered an important reduction in reaction times, requiring now 1'5-2 minutes.



Scheme 3

In summary, we present here the preliminary results of a method that allows a clean and fast synthesis of benzoxazoles and benzothiazoles. This method is comparable to Soufiaoui's for benzoic acid using a monomode equipment and clearly superior to Chakraborti's in a multimode one.

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