Synthesis of Alkynylaminoazines via Pyridinium N-Aminides using Microwaves

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The Sonogashira cross-coupling reaction of terminal acetylenes with aryl/alkenyl halides or triflates has proved to be a powerful method for the creation of C(sp²)–C(sp) bonds. This methodology has growing applications in diverse areas of chemistry, such as in heterocyclic systems, natural product synthesis and material sciences, allowing access to organic semiconductors and to macrocycles for nanostructures.

Our research programme has been devoted to the study of pyridinium heteroaryl-stabilized aminides (Figure 1), compounds that have proven to be useful intermediates in heterocyclic synthesis due to their particular structure, in which a positively charged pyridinium ring is linked to a negatively charged 2-aminoheteroaryl moiety. The heteroaryl ring of N-azinyl pyridinium aminides (Figure 1) is activated towards electrophiles and, as a result, mono- and di-halogenation process can be accomplished easily and in a selective manner at the 5- and 3-positions of the azine ring. On the other hand, a regioselective N-exoalkylation of heteroaryl-stabilized aminides, followed by reduction of the N–N bond, allows the preparation of 2-alkylaminoazines.

Water has been recognized as an attractive medium for organic reactions not only from environmental and economic points of view but also because other solvents do not have to be dried and products can be easily isolated. In recent years many protocols for Sonogashira coupling reactions in neat water or in aqueous/organic solvents have been reported. The study of the alkynylation of amine 2a was completed by using water as the solvent instead of acetonitrile. Slightly better yields of aminides 3a were obtained with the exception of some compounds where by-products 4 were detected in the reaction mixture.

In previous communications we reported the success of the Suzuki cross-coupling reaction on monobrominated aminides under standard
conditions, which resulted in the regioselective synthesis of 3,5-disubstituted 2-aminopyridines 5a and 2-aminopyrazines 5b.\textsuperscript{15}

![Diagram of reactions](image)

**Fig. 3** - Retrosynthesis of 2-aminoazines

Recently, was carried out the synthesis of alkynylarylamines by reduction of the N-N bond and a Sonogashira coupling in water using MW from the salts 6, that were previously obtained from 6 through a regioselective process (Scheme 2).\textsuperscript{15}

![Scheme 2](image)

**Scheme 2**

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References