

[E013]



## Microwave Assisted Organic Synthesis of benzamides with C<sub>3</sub> symmetry



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Microwave assisted organic synthesis (MAOS) of amides by pyrolysis of salts, which was developed in 1993,<sup>[1,2]</sup> constitutes a good example of solvent-free reaction with a minimal environmental impact. This method was applied to the synthesis of imides pharmacologically active, such as thalidomide.<sup>[3,4]</sup> In this work was found that simultaneous formation of several amide groups were possible. Thus, we considered the possibility of using this reaction for the synthesis of triamides with symmetry C<sub>3</sub> (figure 1).

Click on the image to see 3D model<sup>[5]</sup>

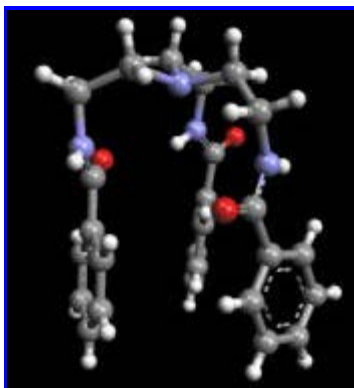
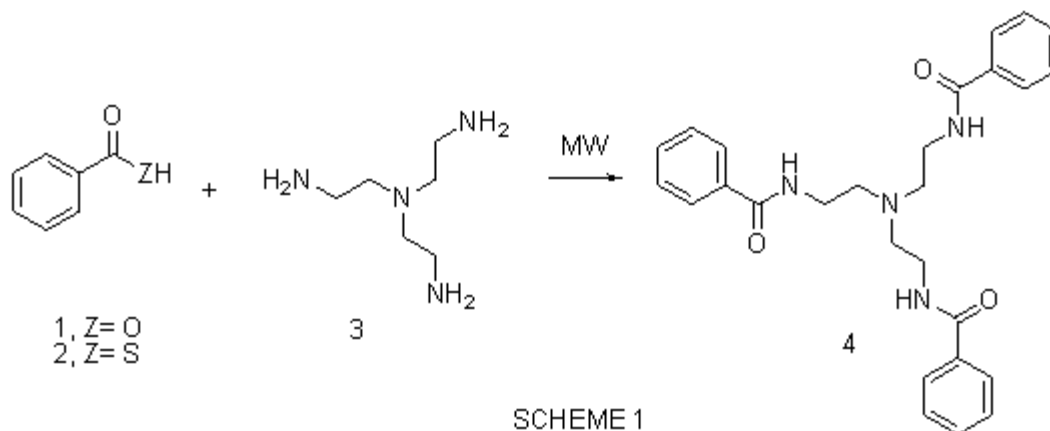


Figure 1

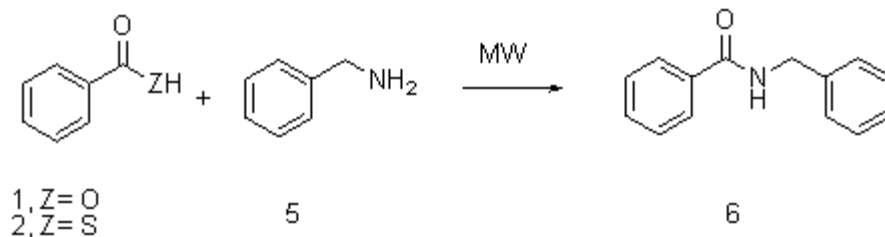
Most of the compounds belonging to this kind of amides are TREN (tris(2-aminoethyl)amine) derivatives, where the amide groups are useful for the stabilization of high valent metals. These tripodal type ligand structures are useful for enforcing trigonal pyramidal geometries in metal complexes, making these triamides useful in metal extraction.<sup>[6]</sup>

Therefore, a mixture of benzoic acid with TREN, in a 3:1 ratio, was heated in a multimode ETHOS-D microwave oven at 800W for 3 minutes, obtaining triamide **4** in 56% yield (scheme 1).



SCHEME 1

This moderate yield led us to study the possibility of improving it by using a more reactive derivative of benzoic acid. There have been reports on the synthesis of amides by microwave irradiation of amines with esters, acid chlorides and anhydrides. Now, the use of thiobenzoic acid, a stable and easily affordable benzoic acid derivative, is reported. As a test to compare the relative reactivity of benzoic acid and thiobenzoic acid, N-benzylbenzamide **6** was prepared both from benzoic acid and thiobenzoic acid (scheme 2). In the first case, the corresponding amide was obtained in 48% after 4 minutes of irradiation, meanwhile in the second one the yield was higher, reaching 82% yield.



SCHEME 2

Analogously, when a 1:3 mixture of TREN and thiobenzoic acid were irradiated at 800W during 4 minutes triamide **4** was produced in 86% yield.

In summary, the possibility of formation by microwave irradiation of three amide bonds in the same reaction is demonstrated. The reaction is carried out under solvent-free conditions and the best performance was achieved with thiobenzoic acid compared to benzoic acid. At the present we are checking the scope of the reaction both for carboxylic acids and thioacids.

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### References

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