Synthesis and Characterization of Compounds Obtained by Biginelli-Type Reaction: 4-(4-fluorophenyl)-6-phenyl-3,4-dihydropyrimidine-2(1*H*)-thione and of 4-(4-chlorophenyl)-6-phenyl-3,4-dihydropyrimidine-2(1*H*)-thione

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Introduction

The intended compounds in this work are possible candidates to be used like drugs with anticancer activity, once it has a structure related to the Monastrol.[1] The synthesis of 4-(4-fluorophenyl)-6-phenyl-3,4-dihydropyrimidine-2(1*H*)-thione and of 4-(4-chlorophenyl)-6-phenyl-3,4-dihydropyrimidine-2(1*H*)-thione were carried out using a multicomponent reaction of Biginelli-type, once just Biginelli reaction does not present synthetic efficiency to the desired compound.[2] The starting reactant used were: 4-fluorobenzaldehyde and 4-chlorobenzaldehyde with acetophenone and catalyzed by NaOH in ethanolic medium. The intermediary obtained, chalcone, was added to thiourea, NaOH and EtOH under microwave heating conditions, resulting in the dihydropyrimidinethiones as the final product. The compounds were characterized by NMR and GCMS.

Results and Discussion

The intermediary obtained in the first step was identified by thin layer chromatography. The fluoro and chloro chalcone presented a yielding of 86.7% and 96.3%, respectively. The respective thiones 70.4% and 73.3%. The NMR analysis showed to the fluoro dihydropyrimidinethione a singlet at δ = 5.189 to the hydrogen from CH unsaturated group, with a integration for one hydrogen. For the 4-(4-chlorophenyl)-6-phenyl-3,4-dihydropyrimidine-2(1*H*)-thione compound, the NMR spectrum showed a singlet at δ = 5.199, once integrated corresponds to two hydrogen being each one assigned to CH saturated and unsaturated group. The NMR analysis demonstrated for both compounds the free five position. The GCMS analysis of fluorinated compound resulted in the mix of two products, the first with 24.71% and the second (fluoro thione) with 75.29%. For this latter observed two relevant peaks mass/charge equals to 284.1 e 224.1. This information is coherent with the chemical structure of the molecular formula $C_{16}H_{13}N_2SF$ that presented molar mass of 284.4 g/mol and with chemical structure of fluorinated chalcone $C_{15}H_{11}OF$, with a loss of hydrogen, of molecular mass of 226.2 g/mol. Also GCMS analysis for the chloro thione resulted in a mix of two products, the first one with 32.77% and the chloro thione with 67.23%. The chromatogram showed two abundant peaks of mass/charge equals to 299.99 and 240.0, thus such information confirms the chemical structure of chloro thione that showed molecular formula of $C_{16}H_{13}N_2SCl$ and molecular mass of 300.8 g/mol and the chloro chalcone $C_{15}H_{11}OCl$ with molar mass of 242.7 g/mol.

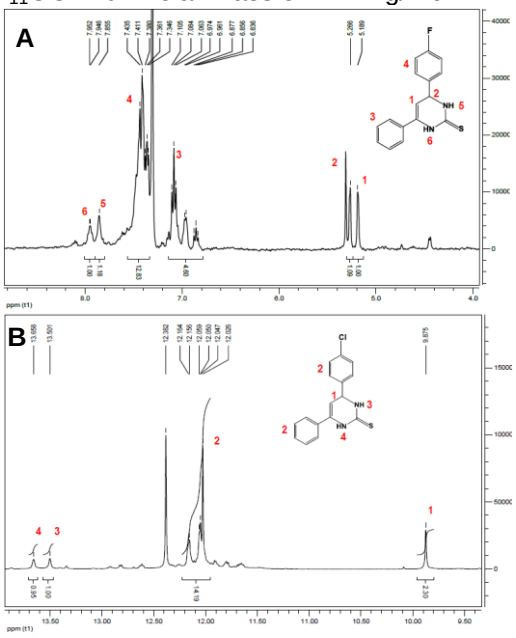

Figure 1. NMR analysis of dihydropyrimidinethiones: **A**) fluoro thione and **B)** chloro thione.

Conclusions

According to results obtained the synthesis used for this purpose, Biginelli-type, was considerably efficient as well easy, fast and cheap of the point of view to prepare dihydropyrimidinethiones with free five position.

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