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Synthesis of New phenazine

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Introduction: The phenazines are an important class of heterocyclic that have a wide spectrum of biological activity, such as antimalarial, antimicrobial and antitumor activity. The importance of this class is verified by more 6,000 phenazine compounds identified and reported during the past century. One way of obtaining phenazines is by synthesis from quinones. Methodologies have been previously described to obtain phenazines from quinones in good yields using solid phase synthesis or in solution of acetic acid. Quinones, such as 1,4-naphthoquinone, are largely employed in organic synthesis because of its potential as intermediate in the preparation of heterocycles and because of the different biological properties described in the literature. It has been reported that the addition of amines in the 2 position of 1,4-naphthoquinone also results in products with biological activity. In this context, this study synthesized a new phenazine in moderate yields which can be useful for pharmacological screenings. **Objective:** Exploring the chemical versatility of naphthoquinones and based on methods previously used for the synthesis of phenazines, the purpose of this study was synthesizing a new phenazine scaffold to develop a library of this class of heterocycles. **Methods:** The starting material of the phenazines library is 2,3-epoxy-1,4-naphthoquinone, used in a series of epoxide ring opening reactions, to produce 3-amine-hydroxyquinones derivatives. The amine-quinone was reacted with phenylenediamine, in several conditions, such as solid-phase or in solution, to get the respective phenazine. The structures were confirmed by GC/MS, ^{1}H-MNR and ^{13}C-MNR. **Results:** The use of catalyst allowed a high yields (94.7%) synthesis of 3-hydroxy-4-phenylamine-1,4-naphthoquinone, in a reduced time, once the same yield was previously accomplished by other techniques only after 24 hours of reaction. In this work was possible to synthesize a new phenazine from 3-hydroxy-4-phenylamine-1,4-naphthoquinone in 6.4% of yield. **Conclusion:** The production of this new phenazine may represent an important biologically active drug, once various phenazines and its precursors have biological activity. The 3-hydroxy-4-phenylamine-1,4-naphthoquinone, the precursor of this new phenazine, presented antimalarial activity *in vivo*, with 53% inhibition of parasitemia in the fifth day of infection. Thus, if compared to the mainstream drug cloroquine (97-98% of inhibition) this compound presents a high activity. However, the method of synthesis this new phenazine, showed a low yield, proving that this method have low efficiency, so the improvement of this method and other methods are being tested.

Keywords: naphthoquinone, antimalarial, heterocyclic.

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