

A catalytic bentonitic clay assisted method for the preparation of 2-(R-anilino)-1,4-naphthoquinones

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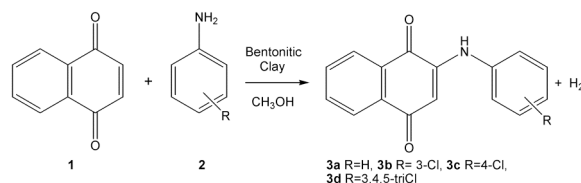
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Introduction.

The quinone structure is found in many synthetic and natural compounds and is associated with diverse biological activities [1]. In most cases, the biological activity of quinones has been related to their capacity to accept one or two electrons to form the corresponding radical-anion or radical-dianion [2]. The electron-accepting capacity of a given quinone can be modified by directly adding a substituent to the quinone structure [3]. The synthesis of alkyl or arylamino derivatives of 1,4-naphthoquinone is of important interest, since these compounds exhibit strong antitumoral, antibacterial, antifungal, and antimalarial [4] action.

The reported general methods for their preparation involve either a direct 1,4-type alkyl or arylamine addition to the 1,4-naphthoquinone structure [5] or a nucleophilic displacement of the readily obtained halogenated derivatives [6, 7]. Both methods usually give very low yields (0-50%) and generate many secondary products, particularly with primary amines [6]. Therefore, these methods are impractical requiring tedious chromatographic purifications. Recently, the use of clays has gained importance in organic synthesis, because they are easy to handle, non-corrosive, selective and inexpensive [8]. A simple, mild and efficient procedure to prepare 2-(R-anilino)-1,4-naphthoquinones **3** by reacting 1,4-naphthoquinone **1** with an aniline **2** in a methanol solution and in the presence of a natural bentonitic clay (Scheme 1).



Scheme 1. Catalytic synthesis of 2-(R-anilino)-1,4-naphthoquinones.

Experimental

A measured amount of 1,4-naphthoquinone **1** was dissolved in methanol (50 mL). The bentonite catalyst was added and allowed to react with the quinone **1** for 30 minutes at room temperature. A solution of the corresponding aniline **2** in methanol was added and the mixture was allowed to react under solvent reflux. After several days of reaction, a crystalline solid precipitated. The solid mixture was separated by filtration and washed several times with cold methanol. The 2-(R-anilino)-1,4-naphthoquinone **3** was dissolved in chloroform and filtered over diatomaceous earth to remove the remaining bentonitic clay.

The solvent was removed by evaporation under and the solid product was further purified by recrystallization. Other anilino derivatives such as 3-chloroaniline, 4-chloroaniline, and 3,4,5-trichloroaniline were also synthesized. With each aniline, the reaction was performed three times to ensure reproducibility.

All the compounds prepared were characterized by melting point, IR, UV-Vis, ¹H NMR and mass spectrometry. IR spectra were determined on a Nicolet 205 FT-IR. UV-Vis spectra were determined on a Shimadzu UV-2401 PC. NMR spectra were obtained on a Bruker 200 AC instrument. Mass spectra were obtained on a VG 70-2505 MS instrument. The commercial bentonite clay has been previously characterized. It has a total acidity of 1.35 mmol of NH₃/g and a BET surface area of 31 m²/g.

Results and discussion

In our experimental procedure, 1,4-naphthoquinone **1** in methanol is first allowed to react with the catalyst and then a solution of the corresponding aniline **2** in methanol is added. The reaction of 1,4-naphthoquinone with aniline at room temperature (25 °C) gave 2-anilino-1,4-naphthoquinone in moderate yields (45%). Lower yields (35%) were obtained under refluxing conditions (65 °C). The reaction of the same quinone with several chloro-substituted anilines gave the corresponding adduct in low to moderate yields (26-35%). Only when the reaction was carried out at room temperature and in the presence of a bentonitic clay there was a high conversion of reactant species and the naphthoquinone derivatives were obtained in very good yields (80-85 %). The ¹H NMR and the MS characterization results confirmed the identity of the following products: 2-(anilino)-1,4-naphthoquinone (**3a**), 2-(3-chloroanilino)-1,4-naphthoquinone (**3b**), 2-(4-chloroanilino)-1,4-naphthoquinone (**3c**) and 2-(3,4,5-trichloroanilino)-1,4-naphthoquinone (**3d**). The role of the clay is explained in terms of a reaction mechanism in which an activated complex is formed by the reaction of 1,4-naphthoquinone with Lewis and Brønsted acid sites of the clay.

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