

Evaluation of α -lapchones Reduction Sites through DFT and QTAIM calculations

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Abstract: Quinones are a class of organic compounds which participate on a wide range of vital biochemical processes.[1] They have also been studied for their anticancer, anti-inflammatory, trypanocidal, and antimicrobial activity.[2] The ease of reduction is an important feature in the chemistry of quinones, and in some cases their redox potential correlates with the biological activity.[3,4] Thus, a molecular description of the reduction mechanism of quinones may prove useful to understand their role on many biochemical processes. In a recent study, two α -lapachone isomers (01 and 02, Figure 1) have been synthesized and their electrochemical properties have been evaluated.[5] Analysis of compound 01 electrogram suggests that the reduction site for the first and third reduction happen at the quinone moiety while the second reduction takes place at the nitro group. Although 01 and 02 differ only by the position of nitro group, they exhibited very different electrograms, and the reduction mechanism for 02 is still unclear. In this work, we study the reduction mechanism of compounds 01 and 02 by calculating the first three reduction intermediates and assessing the reduction site in each reduction. Full optimization and frequency calculations were performed for the neutral, -1, -2 and -3 anionic forms of compounds 01 and 02. Calculations were carried out using DFT and QTAIM approaches at M11-L/6-31+g(d,p) level and DMF as implicit solvent using PCM model. Both singlet and triplet states have been calculated for -2 forms, and both duplet and quartet for -3 forms. It has been found that singlet and duplet were the most stable states for -2 and -3 forms respectively. QTAIM charges points the quinone moiety as the first reduction site for both 01 and 02, as shown by the net charge difference between the neutral and -1 forms. In addition, NO₂ group and the quinone moiety are likely to be the second and third sites respectively for compound 01. Compound 02, on the other side, shows a similar change in the net charge over the quinone and nitro regions of about -0,3 for the second reduction. Therefore, the electron density change on going from -1 to -2 form is highly delocalized. It is unclear either the reduction site is spread along the structure or the anion undergoes an intramolecular charge transfer following the second reduction. Finally, the third reduction of compound 02 seems well localized at the quinone moiety. Results agree with experimental evidence of quinone and nitro groups being the most likely electroactive groups for these compounds and the reduction mechanism for compound 01. It also suggests that compound 02 dianion is partially stabilized by charge delocalization.



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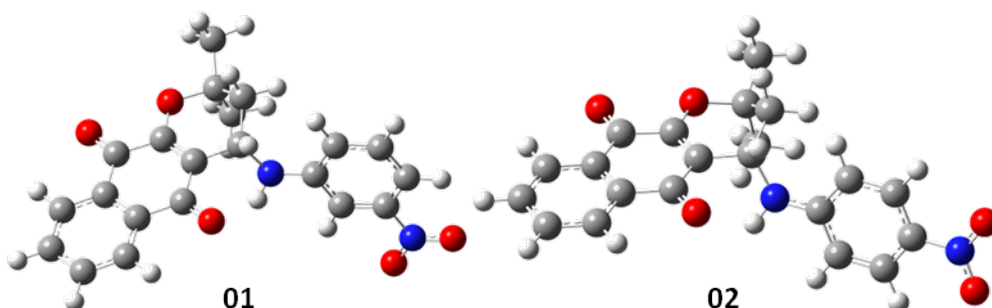


Figure 1 α -lapachones isomers 01 and 02

Keywords: Quinones, Redox Potential, Density Functional Theory, Quantum Theory of Atoms in Molecules

Support: CENAPAD-SP, CAPES, CNPq

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