

IONIZATION MECHANISM OF CITRIC ACID IN WATER.

An *AB INITIO* STUDY AND statistical-mechanism treatment of NMR TITRATION DATA

Sergio Madurga,^{*a} Jose Lu s Garc s^b, Miroslawa Nedyalkova^c, Francesc Mas^a

^a Physical Chemistry Department and IQTCUB, University of Barcelona, Barcelona, Spain.

^b Chemistry Department, University of Lleida, Lleida, Spain.

^c Faculty of Chemistry and Pharmacy, University of Sofia, Sofia, Bulgaria.

e-mail: s.madurga@ub.edu

Citric acid is a three carboxylic molecule biologically and environmentally relevant that is widely used^[1]. In addition to its natural abundance, citrate is a common stabilizer used in the synthesis of gold nanoparticles^[2]. However, there is still controversy about the population of the protonation microscopic states compatible with the macroscopic equilibrium constants. One of the challenges that present this small molecule is its great flexibility making a coupling of protonation and conformational processes. Here, we show *ab initio* MP2 calculations using the SMD polarizable continuum model for solvent^[3] and statistical-mechanism treatment^[4] of accurate NMR titration data to elucidate the sequence of deprotonation states when changing from acid to basic pH. From *ab initio* calculations, we study the coupling between conformational and ionization properties. In addition, NMR data of citric acid^[5] has been analysed with the cluster expansion method^[4,6] to obtain all microscopic ionization constants as well as the probabilities of the different microstates. The information obtained from both approaches allows discussing ionization mechanism of this molecule in full detail. It is concluded that the first ionization of citric acid take place at the central carboxyl group. For the di-ionized form, it is obtained that the most probable state is that corresponding to two consecutive negative charges. This result is counter-intuitive if the molecule is analysed ignoring the conformational structure^[7]. Regarding the conformational details, it is shown that the most extended conformation is the most stable at low pH values, whereas at high pH values a more compact conformation is the most stable.

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