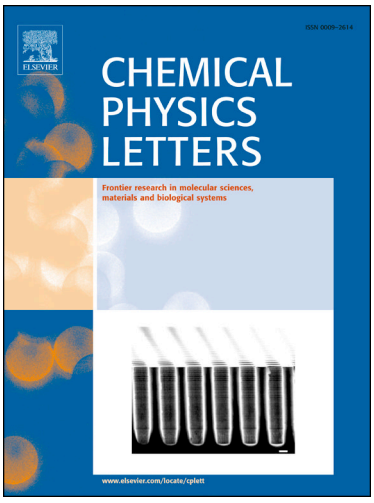

Research paper

First principles prediction of aqueous acidities of some benzodiazepine drugs

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First principles prediction of aqueous acidities of some benzodiazepine drugs

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Abstract

In this study, aqueous acidities of several benzodiazepine (BZD) drugs including Oxazepam, Clonazepam, Nitrazepam, Flunitrazepam, Diazepam, Alprazolam, Estazolam, Temazepam, Medazepam and Bromazepam were successfully computed using two common thermodynamic cycles. To that, calculated gas phase Gibbs free energies at PBE1PBE/6-311+G(d,p) level of theory and computed solvation Gibbs free energies at (CPCM/IEF-PCM: UAKS, UAHF and UA0)/HF/6-31+G(d) levels of theory were combined. The most accurate pK_a values were obtained with thermodynamic cycle involving water and using CPCM-UA0 solvation model with MAD = 0.4. Moreover, for the first time, aqueous pK_a value of Halazepam was predicted using the best method equal to 3.1.

Keywords: Benzodiazepine; pK_a; Thermodynamic cycle; Solvation model; Cavity model.