Details from First Principles of the SN1(P)-like mechanism for the cleavage of p-nitrophenyl phosphate.

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Introdução

Reactant state destabilization[1] and Transition state stabilization[2] theory (**Fig. 1**) have both been considered as contributing to the high efficiency of enzyme catalysis.

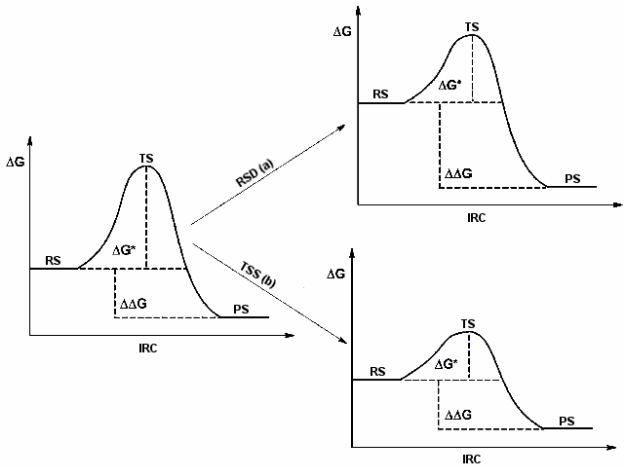

Figure 1. Simplified free energy barrier schemes for an enzymatic catalytic process. (a) In reactant state destabilization (RSD) the free energy of the bound reagents is increased in the active site. (b) In transition state stabilization (TSS), the free energy of the bound transition state is decreased.

To address fundamental questions concerning dielectric effects on the cleavage of phosphate monoesters through zwitterionic transition states, we have used first principles ab initio methods to analyze in detail the cleavage of p-nitrophenyl phosphate by ammonia oxide, as a non-mimetic enzymatic model.

Resultados e Discussão

First Principles were used do probe such mechanism, where all calculations were made using GAMESS package[3]. Our molecular electrostatic potential (ESP) results, derived from the application of Spackman algorithm[4], reveal a SN1(P)-like mechanism with preassociative character, in which the departure of a delocalized quinonoid leaving group (**Fig. 2**) departs more readily than the attack of the nucleophile.

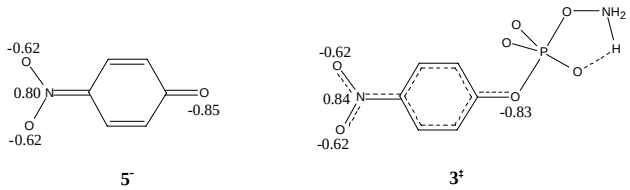

Figure 2. Charge comparison between the p-nitrophenolate (5^-) and the transition state of the attack of ammonia oxide to PNPP ($3^{\ddagger}$). The ESP was calculated using DFT/B3LYP//HF/6-31+G* method. The charges on leaving group oxygens and nitrogen reveals the similarities on both species.

The calculated energy parameters quantify the stabilization of both reactant and transition states by solvent, where better results are obtained using DFT/B3LYP methodology, compared with fourth order perturbation theory method (MP4).

Conclusões

Based in the First Principles, the ESP map for the intrinsic reaction path is shown to be an important tool for the mechanistic analysis, and is considered to be an efficient way to extract information for more complex systems from QM/MM approaches. And all data are in good agreement with representative experimental results.

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