

Systematic calculations were performed to uncover the free energy surfaces for hydrolytic reactions of methyl-diphosphate (in vacuum and implicit solvents) and GTP in EF-Tu active site.

Density functional theory and ONIOM extrapolative QM/MM scheme were adopted for the assay.

In accordance with experiments, the catalytic effect of the sodium cation was mild.

It changes the conformation of GTP attracting its negatively charged oxygen atoms.

hydrolyze GTP.

The Na<sup>+</sup> also equilibrates the charges of all phosphate groups of the GTP mostly by transferring electrons from gamma to beta-phosphate group, which is characteristic for the intermediate states during the hydrolytic reaction.