

Nan SWITCHES based on DNA base pairs.

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The discovery by Kool and co-workers that 2,4-difluorotoluene (F) mimics thymine (T) in DNA replication has led to a controversy about the question if this mimic has the capability of forming hydrogen bonds with adenine (A). In the present study, we address not only the question about the strengths of the hydrogen bonds in AF as compared to those in AT but we focus in particular on the nature of these interactions. Thus, we have analyzed AF and AT at the BP86/TZ2P level of density functional theory (DFT). In line with previous experience, this approach is shown to achieve close agreement with the available data from ab initio computations and experiment: the complexation energy of AF (−3.2 kcal/mol) is confirmed to be much weaker indeed than that of AT (−13.0 kcal/mol). Interestingly, the weak hydrogen bonds in AF still possess a significant orbital interaction component that resembles the situation for the more strongly bound AT, as follows from (1) an analysis of the orbital electronic structure of AF and AT, (2) a quantitative decomposition of the A–F and A–T bond energies, as well as (3) a quantitative decomposition of the charge redistribution associated with the A–F and A–T interactions based on the Voronoi deformation density (VDD) method. The VDD method has been further developed such that the charge redistribution ΔQ per atom can be decomposed into a component associated with the Pauli repulsive orbital interactions and a component associated with the bonding orbital interactions: $\Delta Q = \Delta Q_{\text{Pauli}} + \Delta Q_{\text{oi}}$. Implications of our findings for the mechanism of DNA replication are discussed. Furthermore, with dispersion-corrected DFT computations we reveal the key factors behind the intrinsic affinity of a DNA template–primer complex to select the correct nucleotide.

[1] C. Fonseca Guerra, T. van der Wijst, F. M. Bickelhaupt, *Chem. Eur. J.* **2006**, 12, 3032.

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