Structural and Functional Comparisons of Ti-TADDOLate Catalyst, R-Selective Imine Reductase and Their Substrates to Asses Reactivities

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ABSTRACT:

Imines previously investigated by the Tanski group for their catalytic reactivity are introduced, stressing the importance of the pro-chiral carbon. Two compounds are studied using Gaussian computations of geometry optimization and partial atomic charges: N-(methylbenzylidene)-benzylamine [N-mbba] and its aniline homolog N-(1-phenylethylidene)-benzenamine [N-peba]. Z-matrices were constructed using Avogadro and two different basis sets were employed to determine appropriate calculations. N-mbba is compared to the X-ray crystal structure data, and both are assessed for their susceptibility to nucleophilic attack. We find that the geometry optimization is highly comparable to the crystal structure showing negligible discrepancies in the C=N bond length (~0.01Å) and two of the bond angles (each ~2°). Further, N-mbba is a more suitable substrate in our catalysis study than its homolog N-peba based on the Mulliken partial atomic charge of the pro-chiral carbon. In a complimentary experiment we studied the structure of the employed titanium-TADDOLate catalysts to the R-selective, enzymatic analog derived from *Streptomyces*. Using a calculated geometry optimization for the Ti-TADDOL complex bound to an imine substrate, the structure is superimposed on a proposed active residue Asp187 of the protein using PyMOL viewer. These studies indicate comparable reactivity between the two catalysts, with a secondary, substrate-stabilizing interaction at Phe221 in place of the TADDOL. Improvements to the experiment are offered, emphasizing the importance of rerunning these experiments using enzyme-imine adduct in structural comparison and molecular-dynamics simulations with a nucleophile.