



Figure 4. Spatial superpositions of S0-TRANS, S1S0-CIS, and S0-CIS structures in the DNA duplex (left) with an unpaired thymine nucleobase and without it (right). The out-of-plane motions of the N3 and N4 atoms of the azobenzene play different roles for the photoisomerization in the two DNA environments.

looks similar in the unmodified and modified DNA duplexes. However, the *trans-cis* photoisomerization path is different in the unmodified and modified DNAs (Figures S5 and S6). Due to the strong steric interaction between the right phenyl group of the azobenzene and the nearby thymine nucleobase (Figure 4), the S_1 energy profile for the *trans-cis* path is much steeper in the unmodified than in the modified DNA (without the thymine nucleobase). This steric interaction is thus the driving force that re-shapes the S_1 *trans-cis* potential energy surface and accelerates the *trans-cis* photoisomerization. This is again confirmed by QM(OM2/MRCI)/MM dynamics simulations. In 200 trajectories, we do not observe any $S_1 \rightarrow S_0$ excited-state decay nor any *trans-cis* photoisomerization during the 500 fs simulations. This is qualitatively different from the situation in the unmodified DNA environment where ca. 90% of the trajectories decay to the S_0 state (see above). Both the electronic structure calculations and the dynamics simulations thus support the motion that the steric interaction between one phenyl group of the azobenzene and the nearby thymine is responsible for the acceleration of the *trans-cis* photoisomerization.

In addition, this steric interaction also makes the *trans-cis* photoisomerization mechanism of the azobenzene in the unmodified DNA different from that in the modified one. Figure 4 shows spatial superpositions of S0-TRANS, S1S0-CIS, and S0-CIS structures in these two DNA duplexes. It is clear from the left panel that in the unmodified DNA the hula-twist photoisomerization process is dominantly driven by the N3 atom of the azo N=N group because the rotational motion along the C1C2N3N4 dihedral angle is less constrained than that along the N3N4C5C6 dihedral angle (as discussed above). Removal of the nearby thymine nucleobase reduces this steric interaction and enables rotational motion along the N3N4C5C6 dihedral angle. As a result, the N4 atom drives the hula-twist motion in the modified DNA (see the right panel). This demonstrates that the two nitrogen atoms can play different roles in the photoinduced hula-twist of the central N=N double bond and that the local environment can be of decisive importance in regulating the excited-state relaxation paths of azobenzene in the confined DNA surroundings.

To summarize, we have employed combined QM/MM electronic structure calculations and nonadiabatic dynamics simulations to study the photoisomerization mechanism and excit-

ed-state decay dynamics of an azobenzene that is covalently tethered to a DNA duplex. We find that the *trans-cis* photoisomerization path in the S_1 state is much steeper in the DNA surroundings than in the gas phase; whereas, the *cis-trans* path is similar in both situations. This enhanced steepness makes the *trans-cis* photoisomerization much faster in the DNA than in vacuum, which is confirmed by our subsequent surface-hopping dynamics simulations. Moreover, we find that the enhanced steepness of the *trans-cis* photoisomerization path in the DNA duplex is mainly caused by the steric interaction between the phenyl group of the azobenzene and the corresponding unpaired thymine nucleobase, which is supported by further electronic structure calculations and nonadiabatic dynamics simulations on an analogous DNA duplex without this unpaired nucleobase. This steric interaction also changes the *trans-cis* photoisomerization mechanism of azobenzene, since the two nitrogen atoms are found to play different roles in driving the hula-twist motion of the central N=N double bond in the unmodified and modified DNA duplexes. Finally, we emphasize that the focus of our present study is on exploring the initial photoisomerization dynamics of two representative DNA-azobenzene complexes^[12c] and the effects of the local DNA environment on the S_1 dynamics; further work is required to address computationally the efficiency of these complexes for DNA photocontrol.

In more general terms, the present study shows that complicated biological surroundings can re-shape excited-state potential energy surfaces of chromophores, thereby tuning and even significantly changing their photodynamics. We hope that these mechanistic insights will advance the understanding and design of azobenzene-tethered DNA/RNAs in biotechnology and nanotechnology.^[4-12]

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Conflict of interest

The authors declare no conflict of interest.

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