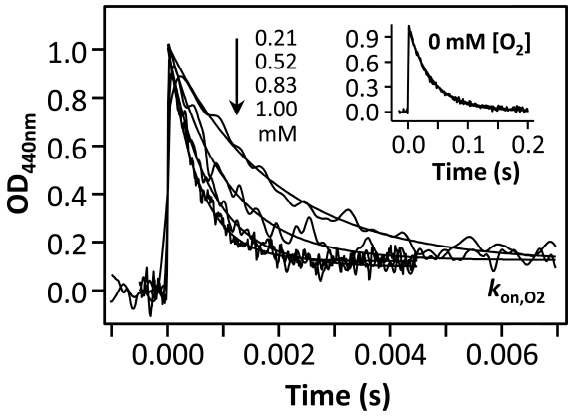

Fig. S1. The O_2 association kinetic traces of the $G8_{WF}$ mutant of Ctb in the presence of various concentration of O_2.

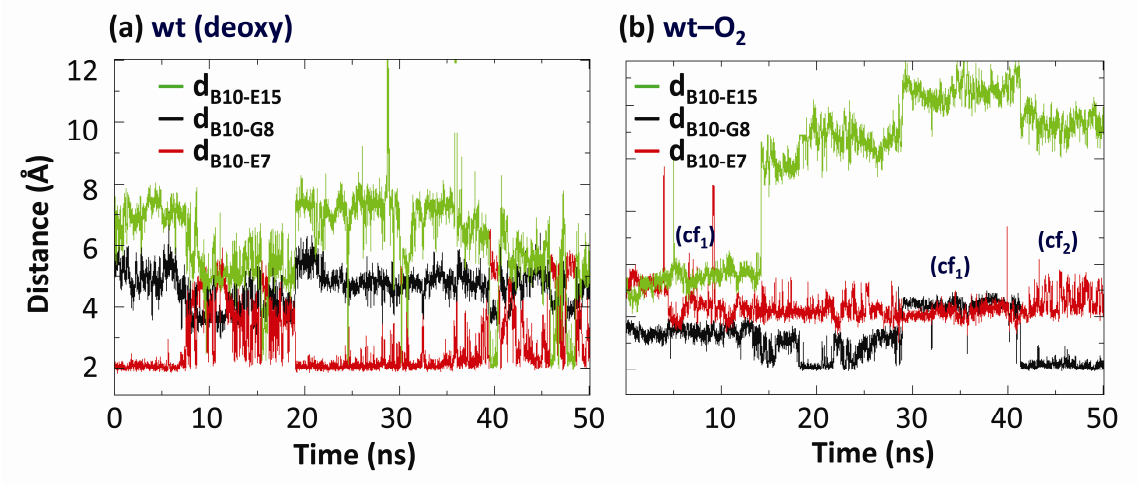

Fig. S2. Time evolution of the various intramolecular distances during the 50 ns MD simulations of the deoxy (a) and O_2-bound derivatives of Ctb. The distances associated with potential H bonds, $d_{B10\text{-}G8}$ and $d_{B10\text{-}E15}$, are defined as the distances between the hydroxylic oxygen of TyrB10 and the indole NH proton of TrpG8 and TrpE15, respectively, while the distance between TyrB10 and HisE7, $d_{B10\text{-}E7}$, is defined as the distance between the hydroxylic hydrogen of TyrB10 and the Nε of HisE7.

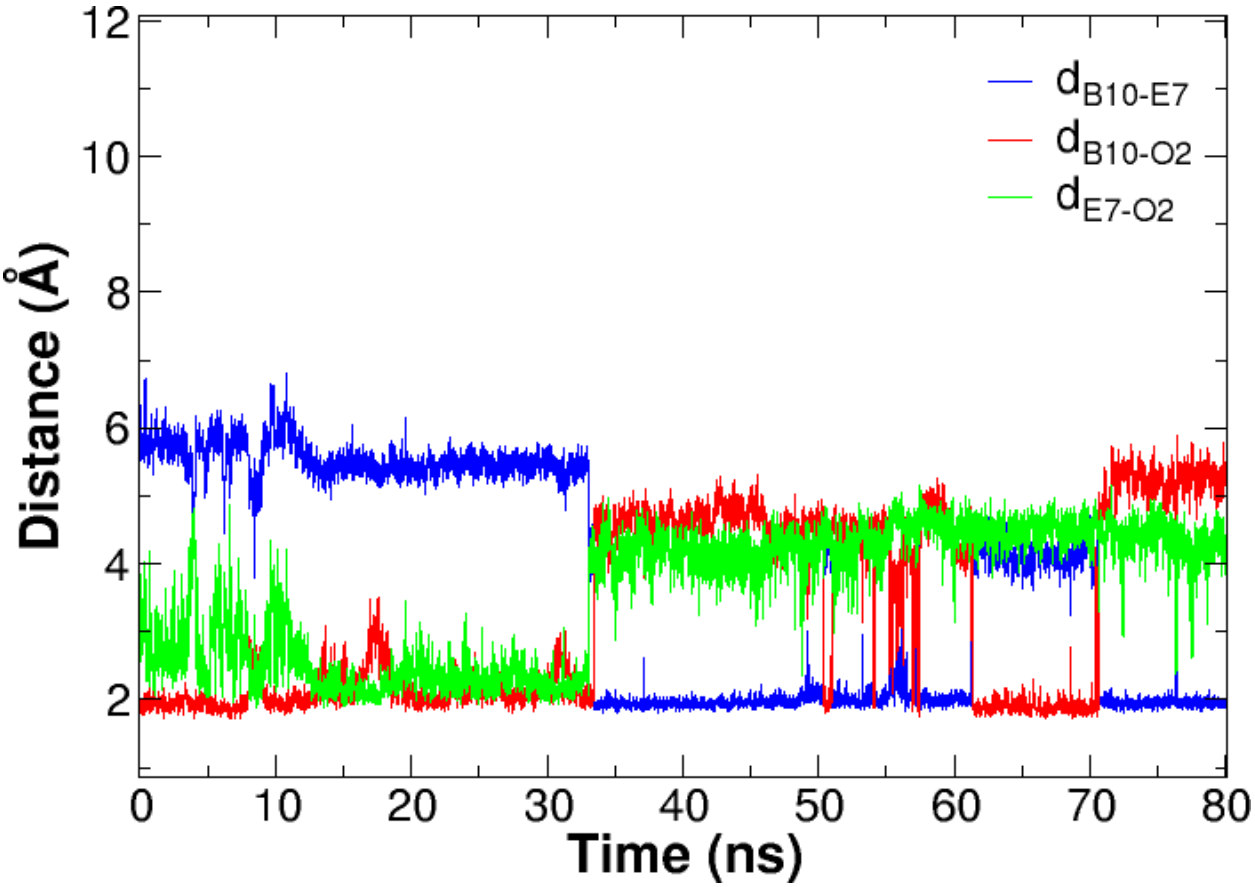

Fig. S3. Time evolution time evolution of $d_{B10\text{-}E7}$, $d_{B10\text{-}O2}$ and $d_{E7\text{-}O2}$ during the 50 ns MD simulations of the O_2-adduct of the $G8_{WF}$ mutant of Ctb. The distances associated with potential HBs, $d_{B10\text{-}E7}$, $d_{E7\text{-}O2}$, and $d_{B10\text{-}O2}$, are defined as the distances between the hydroxylic hydrogen of the TyrB10 and the imidazolic Nδ proton of the HisE7, and between the terminal oxygen of the O_2 ligand and the hydroxylic hydrogen of the TyrB10 and the imidazolic Nε proton of the HisE7, respectively