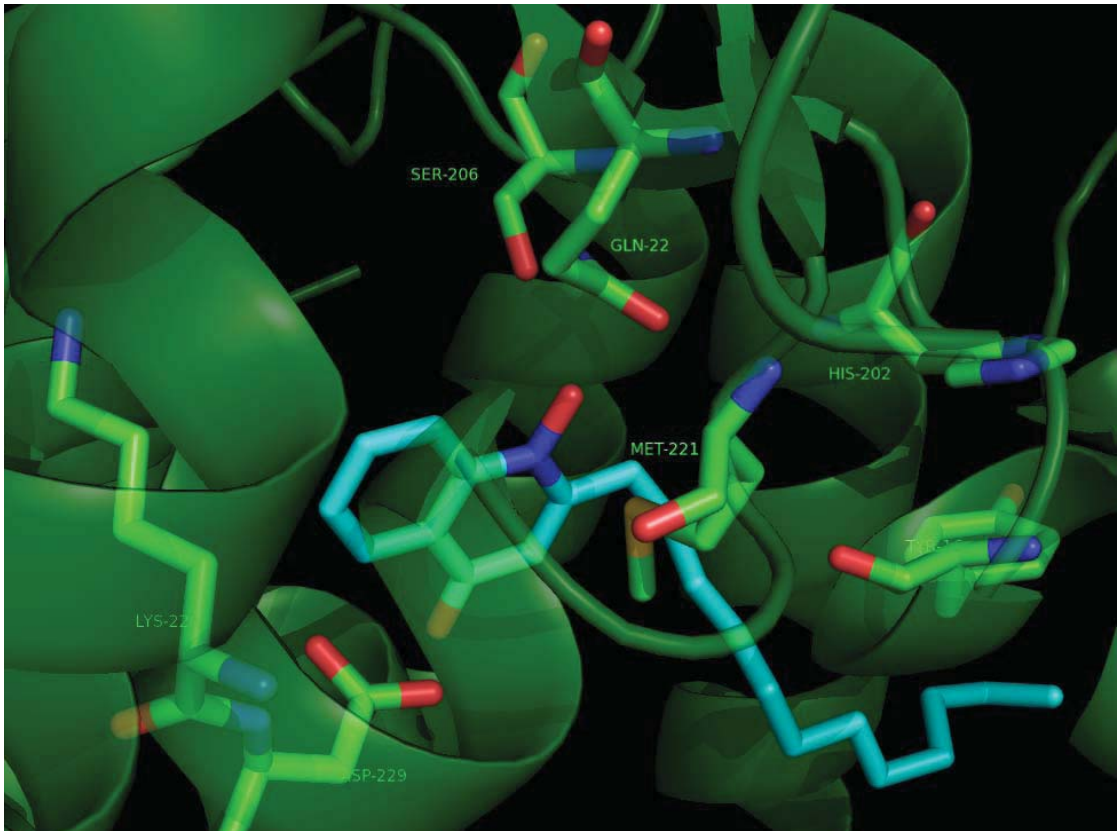

FIG. S2. HDQ docking at the Q_i site. The model of HDQ binding in the Q_i site of yeast bc_1 complex was built as described in Materials and Methods. The protein-HDQ interactions were similar to that of Q_i-bound substrate ubiquinone-6 in PDB entry 1EZV, with the hydroxyl moiety of S34 (transmembrane helix A) forming a hydrogen bond to the carbonyl group of HDQ, with a predicted interatomic distance of 3.0 Å, with a much weaker H-bond between the HDQ *N*-oxide and the hydroxyl moiety of DE-loop residue S206 (3.9 Å separation). An additional H-bond (2.5 Å) was predicted to form between the sidechain of Q22 (a non-conserved residue in the aA loop)) and the N-oxide of the quinolone headgroup. In contrast to the UQ-6 interaction in 1EZV, the carboxyl moiety of D229 (helix E) is unfavourably positioned to H-bond with bound HDQ, despite the close association (2.9 Å) between these groups. Other interactions between HDQ and cytochrome *b* in binding pose *A* are mostly of the hydrophobic van der Waals type, with a significant 79 $Å^2$ interaction (3.3 Å closest approach) between the tyrosyl ring of Y16 (helix a) and the C12 alkyl substituent of HDQ at the mouth of the 'entry channel' of the Q_i site towards the lipidic phase. In addition, the sidechain of M221 (helix E) forms a stabilising hydrophobic contact up against the quinonlone core The closest approach of HDQ to haem b_h in this binding pose is 3.9 Å, between the C18 methyl group of b_h and the carbonyl oxygen of HDQ