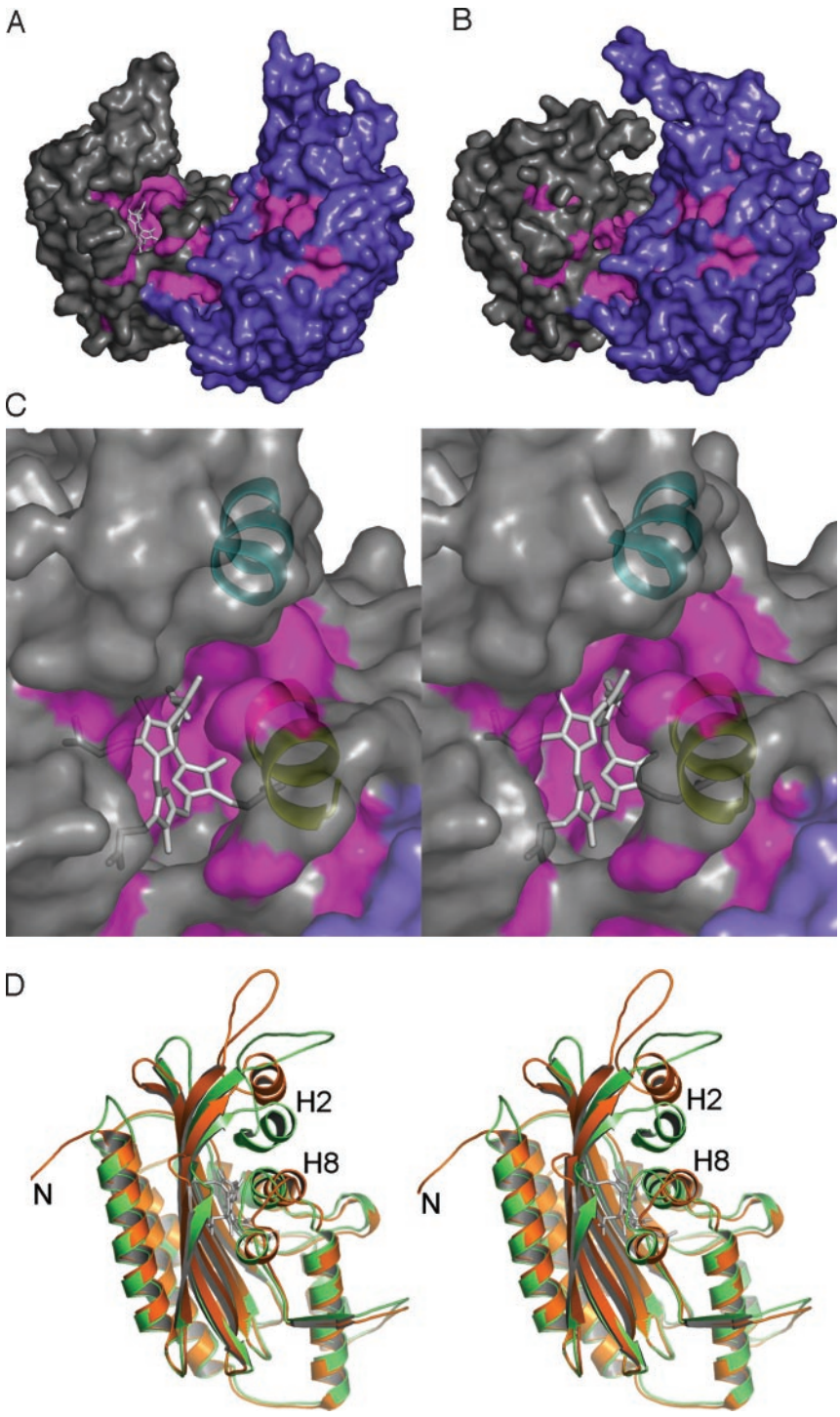

FIG. 5. **Active-site cleft/cavity.** *A*, form I crystal structure. Shown is the molecular surface of the odCPO/Hem13p dimer. Monomers are colored *gray* and *slate*. Invariant residues are colored *magenta*. The substrate modeled into active site is colored *white*. The view direction is similar to that of Fig. 4B, but with the 2-fold axis tilted from the vertical to show the cleft. *B*, same as *A*, but for the form II crystal structure. The modeled substrate is completely sequestered in the active-site cavity and hidden from view. As shown, the projections at the top of this figure (loop between helix H2 and strand S4) have been built in very different conformations in form I and II structures. To some extent, this results from displacement of helix H2 upon closing the active-site cavity (see "Results and Discussion"), although these residues are highly flexible and have been assigned zero occupancy in the refined models. *C*, stereo view of the form I active-site cleft from *A*. A semitransparent surface is displayed, with helices H2 (*cyan*) and H8 (*yellow*) below. These helices close together to seal the active-site cavity in the form II structure. *D*, stereo view ribbon diagram showing open conformation (form I; *orange*) and closed conformation (form II; *green*). The helices that move to enclose the active-site cavity (helices H2 and H8) are labeled.

though this form was important for structure determination of the full-length protein, it lacks more than half of the residues that are visible in the form I and II crystals and does not form the physiologically relevant dimer (discussed below). The two monomers in form I crystals overlap with a root mean square deviation (r.m.s.d.) of 0.6 Å on all pairs of Cα atoms, and the six monomers in form II crystals overlap on each other with r.m.s.d. of 0.7–1.0 Å over all Cα atoms. Form I and II monomers overlap with a r.m.s.d. of ~1.5 Å on all pairs of Cα atoms except those before Arg^{13} and between Gln^{77} and Lys^{110}, inclusive. The 12 N-terminal residues project in very different directions in the two crystal forms, apparently because of different lattice constraints. The Gln^{77}–Lys^{110} loop appears to move significantly between the two crystal forms, in part because, as discussed below, helix H2 serves as a lid that moves to cover the active-site cavity in the form II structure.

odCPO/Hem13p crystallizes as a dimer in which the β-sheets face each other and project above their surrounding helices (Fig. 4). This is consistent with multiple reports that the enzyme is dimeric in solution (3, 9, 15, 16). The dimeric interface buries a total of 2638 $Å^2$ of solvent-accessible surface area and includes 11 direct hydrogen bonding interactions between protein atoms. There are also five water molecules buried at the interface, although most of the contact surface is hydrophobic. The 28 residues that lose accessible surface area upon dimerization are derived from helices H5, H7, H8, and H9; strands S1, S2, S3, and S8; and connecting segments. At the center of the interface, strand S8 forms an antiparallel β-ladder with its