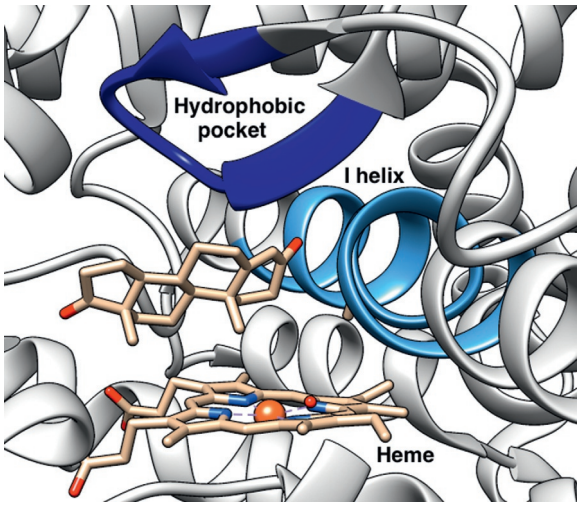

FIGURE 3.22

Androstenedione at the active site of human placental aromatase.[40] The structure was generated from Protein Data Bank reference 3EQM and displayed with Chimera 1.8.1.

model compound for describing the interaction of azole derivatives with aromatase. The N-2 atom of fadrozole is involved in a coordinate bond with the heme iron of aromatase, having also favorable interactions with the side chains of Ileu-305, Ala-306, and Thr-310, whereas the cyano group appears to be hydrogen-bound to the Ser-478 hydroxyl. Three-dimensional quantitative structure–activity relationship (QSAR) data for fadrozole derivatives and other studies support the presence of hydrogen bonding and hydrophobic interactions in the active site of the enzyme (Figure 3.23)[41a], although more recent molecular docking studies do not fully agree with this conclusion.[41b]

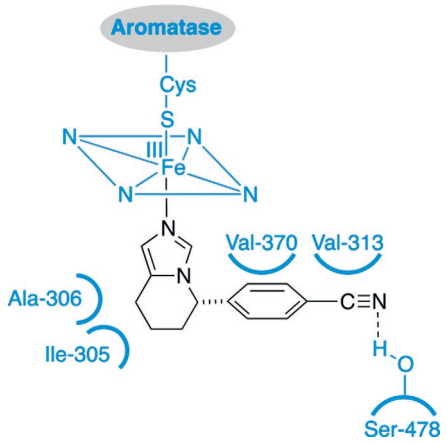

FIGURE 3.23

Interaction of fadrozole with the aromatase active site.