Oxidative phosphorylation, the combined activities of the electron transport chain and ATP synthase, has emerged as an important target for drugs to treat tuberculosis (TB). We have developed electron cryomicroscopy (cryoEM) methods that allow high-resolution structure determination of the protein complexes involved in oxidative phosphorylation. Determining structures of these complexes bound to approved and candidate TB therapeutics reveals the mode of action of the compounds and is facilitating development of new mycobacterial oxidative phosphorylation inhibitors.