The facultative anaerobe Escherichia coli transitions between aerobic and anaerobic metabolism using an oxygen-sensing transcription factor, known as Fumarate and Nitrate Reduction (FNR) regulator protein. The presence or absence of molecular oxygen is communicated through an Fe-S cluster, such that FNR dimerization and DNA binding occur only when oxygen is not abundant in the cell. Until now, this structural change had not been directly observed. Anoxic (<30 ppm oxygen) small angle X-ray scattering (anSAXS) techniques were developed at the Cornell High Energy Synchrotron Source (CHESS) ID-7A to provide the first structural evidence of the dependence on anaerobic conditions for the dimeric form to bind DNA and to demonstrate oxygen-induced dissociation from dimer to monomer in E. coli FNR. This novel experimental setup combines anaerobic technique with chromatography-coupled SAXS, opening new opportunities for the study of highly oxygen-sensitive metalloenzymes with medical and environmental importance.