Human immunodeficiency virus type 2 infects approximately 2 million people worldwide, primarily those in or around West Africa. Due to its crucial role in the maturation of the virus, HIV-1 protease has been commonly used as a target for developing anti-retroviral drugs for the more prevalent HIV-1 infection. Hence, HIV-2 infections are currently being treated with HIV-1 protease inhibitors, often with decreased efficacy. Here, in order to evaluate potential new inhibitors, the HIV-2 protease is prepared for enzyme inhibition assays and structural studies by X-ray crystallography. Protein was prepared by bacterial overexpression of HIV-2 protease and purified using fast-protein liquid chromatography (FPLC) and high-pressure liquid chromatography (HPLC). Once purified this protein will be assayed with different potential inhibitors and crystallized for structural analysis to determine the key interactions between the inhibitor and the protease. New tight-binding inhibitors will have potential as antiviral agents for patients with HIV-2 infections.