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Crystallization of the complex of cathepsin K with inhibitor **4**

Crystals of mature activated cathepsin K complexed with the inhibitor grew from a solution of 28% MPD, 0.1 M MES at pH 7.0 and 0.1 M tris buffer at pH 7.0. Crystals of the complex are orthorhombic, space group $P2_12_12_1$, with cell constants of a=38.84, b=50.99 and c=103.58 Ångstroms. The crystals contain one molecule in the asymmetric unit and approximately 40% solvent with a V_m value of 2.18 A^3/Dalton. X-ray diffraction data were measured from a single crystal using a Siemens two-dimensional position-sensitive detector on a Siemens rotating anode generate operating at 5 KW. The structure was determined by molecular replacement using X-PLOR. The structure was determined by rigid body refinement with the protein atoms of cathepsin K using X-PLOR at 2.5 Ångstroms resolution.[1] Fourier maps with coefficients $|F_O-F_C|$ and $|2F_O-F_C|$, were used to the atomic model of the inhibitor using the molecular graphics program FRODO. Conventional positional refinement was used to refine the structure during model building using X-PLOR. Several cycles of map fitting and refinement were carried out to a final R_C of 0.193.

Crystallization of the complex of cathepsin K with the inhibitor **14**

Crystals of mature activated cathepsin K complexed with the inhibitor grew from a solution of 30% MPD, 0.1 M MES at pH 7.0 and 0.1 M tris buffer at pH 7.0. Crystals of the complex are isomorphous with those described above. Diffraction data were collected as described above. The structure was determined by rigid body refinement of the cathepsin K protein atoms with X-PLOR as described above at 2.3 Ångstroms resolution. Conventional positional refinement was used to refine the structure during model building using X-PLOR. Several cycles of map fitting and refinement were carried out to a final R_c of 0.26.

(1) Zhao, B., Janson, C.A., Amegadzie, B.Y., D'Alessio, K., Griffin, C., Hanning, C.R., Jones, C., Kurdyla, J., McQueney, M., Qiu, X., Smith, W.W. & Abdel Meguid, S.S. (1997). Crystal structure of human osteoclast cathepsin K complex with E-64. *Nat. Struct. Biol.* **4**, 109-111.