A DFT Examination of Iron Binding in the PKIH Series of Chelating Agents.

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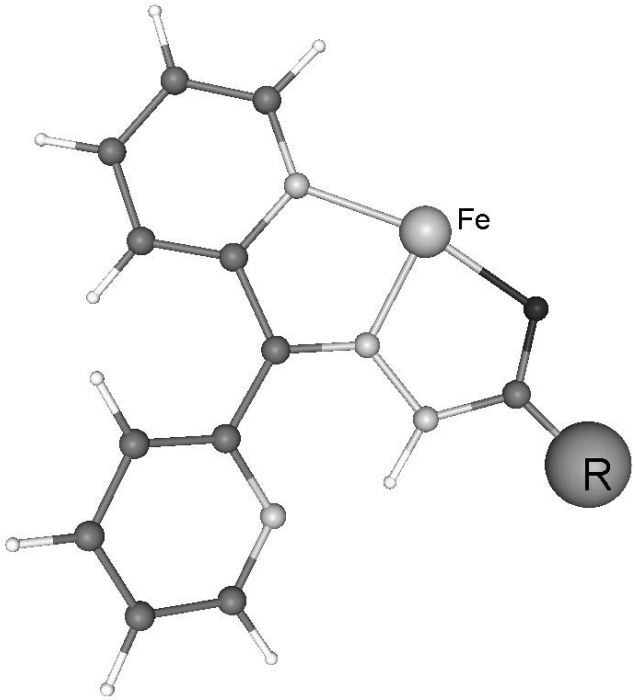
Abstract

Iron chelation therapy is important in treating iron overload diseases and cancer. One class of agent of current interest is the di-2-pyridylketone isonicotinoyl hydrazone (PKIH) series. Binding energies of Fe^{2+} to a series of PKIH chelators have been calculated by density functional theory using the BPW91 functional with numerical basis sets to determine effectiveness of substituent groups at enhancing chelation. The series has been generated by adding bromobenzoyl, pyridyl, benzoyl, phenoyl, and anilinyl functional groups to the basic PKIH structure. Besides energies, population analysis has been employed to determine exceptional charge distribution effects accompanying the substitutions.



Structure of the backbone of the PKIH chelating agents, showing Fe^{2+} bound.