# Participation of the Protein Ligands in the Folding of Cytochrome c

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Absorption spectral, circular dichroic spectral, and viscosity measurements indicate that the compact low-spin conformation characteristic of native cytochrome c is quantitatively recovered from its extended high-spin conformation at pH 2 by titration to pH 4.0. This conformational transition has a midpoint of 2.5 and is very cooperative. Comparison of the pH transitions of native and various carboxy- methylated derivatives of cytochrome c indicates that recovery of the compact conformation of the protein is coincident with coordination of histidyl-18 and does not require coordination of a second protein ligand. Extensive carboxy-methylation of cytochrome c including histidyl-18 stabilizes an unfolded high-spin conformation of the protein throughout the pH range 2-7.