Synthetic Chemistry and Chemical Precedents for Understanding the Structure and Function of Acetyl Coenzyme A Synthase

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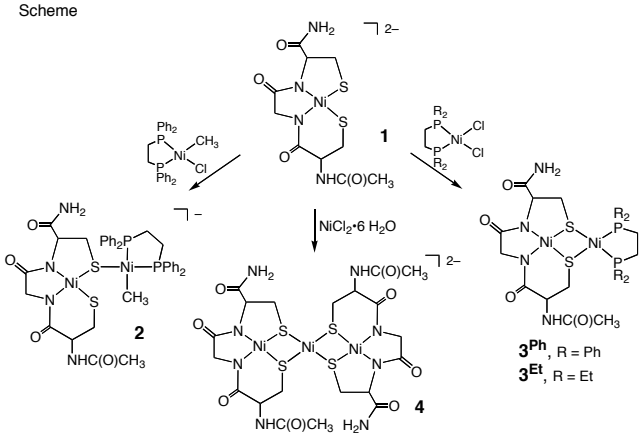
Recent protein crystallographic investigations of acetyl coenzyme A synthase (ACS) revealed a surprising active site (A cluster) composition not anticipated based on prior biophysical and enzymology studies.[1] Specifically, the physiologically relevant cluster is of $Ni_2Fe_4S_4$ composition with one Ni ligated in a CysGlyCys motif (Ni_d) and the other Ni (Ni_p) bound through only three μ–Cys residues, one of which links the Fe_4S_4 cuboid. Using small molecule synthetic and mechanistic chemistry we are developing an understanding of the activity of ACS with particular regard to understanding the formation and properties of organonickel intermediates relevant to catalysis. Herein we present the synthesis, characterization and physical properties of binuclear complexes, Scheme, designed to establish the fundamental reactivity of these small molecules relevant to ACS catalysis.[2]

Scheme



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