

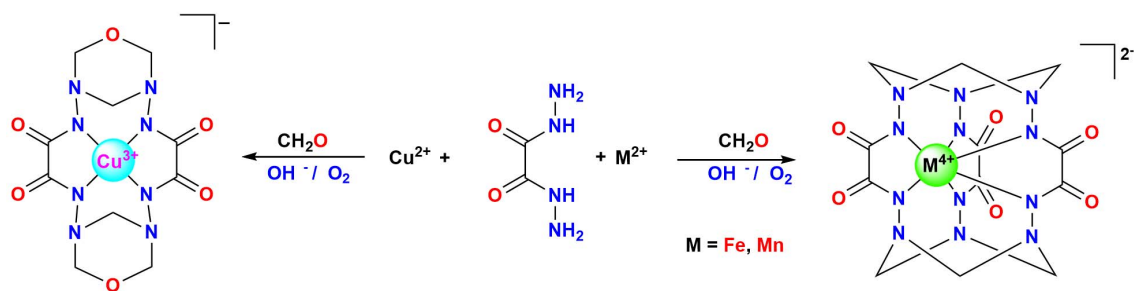
MACRO(BI)CYCLIC ENCAPSULATION OF HIGH-VALENT Fe, Mn AND Cu FOR CATALYSIS AND BIOMEDICAL USE

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Macro(bi)cyclic polyhydrazide ligands provide a unique encapsulation platform that stabilizes high oxidation states of 3d-metals, enabling both catalytic and biomedical applications in aqueous media. Template synthesis with oxalodihydrazide and formaldehyde yields two families of complexes: macrobicyclic clathrochelates encapsulating Fe^{IV} and Mn^{IV}, and macrocyclic tetrazomacrocycles stabilizing Cu^{III} [1]. All complexes form spontaneously under aerobic conditions, demonstrating exceptional thermodynamic stabilization of high-valent ions with extremely low redox potentials for the M^{4+/3+} (M = Mn, Fe) and Cu^{3+/2+} couples:



The encapsulated Fe and Mn clathrochelates exhibit high electrocatalytic activity in water oxidation at pH 8 with low overpotentials (0.39 V). In photochemical water oxidation using a [Ru(bpy)₃]²⁺/Na₂S₂O₈ system, the Fe clathrochelate achieves record TON (365) and TOF (2.27 s⁻¹) for mononuclear iron catalysts, with a trapped Fe^V intermediate identified spectroscopically [1]. The Cu^{III} macrocycles efficiently catalyze cross-coupling of aryl halides with phenols, thiols and amines under mild conditions (120 °C, 0.1–1 mol% loading), achieving up to quantitative conversion. Spectroscopic and DLS experiments confirm the molecular nature of all catalysts without degradation or nanoparticle formation.

The exceptional hydrolytic stability and remarkably low toxicity of the Fe^{IV} clathrochelate (LD₅₀ 5 g/kg) enabled its biomedical application [2]. Formulated as the veterinary drug "Clathroferan", it prevents iron deficiency anemia in piglets: intramuscular administration to pregnant sows increases hemoglobin by 28% and weight gain by 33% in offspring versus controls, with complete renal excretion of the complex. This work demonstrates that macro(bi)cyclic encapsulation of high-valent 3d-metals creates versatile platforms spanning from solar fuel catalysis to antianemic therapy.

[1] S.I. Shylin, J.L. Pogrebetsky, A.O. Husak, D. Bykov, A. Mokhir, F. Hampel, S. Shova, A. Ozarowski, E. Gumienna-Kontecka, I.O. Fritsky, *Chem. Comm.*, **2021**, 57, 11060.

[2] I. Derkach, V. Dukhnitsky, S. Derkach, V. Lozoviy, V. Kostrub, Y. Losa, I. Fritsky, M. Plutenko, *World Vet. J.*, **2021**, 11, 663.