

Departamento de Química

Fluorine-19 Chemical Shifts as Structural Probes of Orange Protein

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Post doctoral fellow since 2010, working on metalloprotein, mainly focused on iron-sulfur protein and synthesis of NMR structural probe of the Orange Protein.

Objectives

In Orange Protein (ORP),^[1] the trinuclear mixed metal sulfide cluster ($[\text{S}_2\text{MoS}_2\text{CuS}_2\text{MoS}_2]^{3-}$) (see Figure 1) is non-covalent interaction with protein matrix but its location is obscure. Our current interest is to elucidate the position of the metal-cofactor in this protein using external NMR-structural probes. For that purpose, we recently reported small thiol containing tetrathiomolybdate-copper clusters, which gave ^1H NMR,^[2] but in a narrow 10 ppm range. The fluorine-19 chemical shifts can be used as an alternative NMR structural probe, since it has a wide range of chemical shift (+ 400 to - 400 ppm), no background signal and more sensitive than ^1H -NMR.^[3] Therefore, some discrete tetrathiomolybdate-copper with fluorinated thiol complexes were synthesized and characterized in an effort to develop a ^{19}F -NMR structural probe for metal-binding proteins.

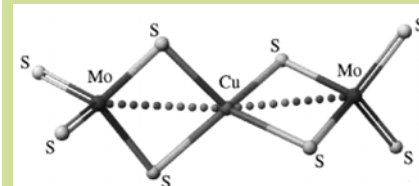
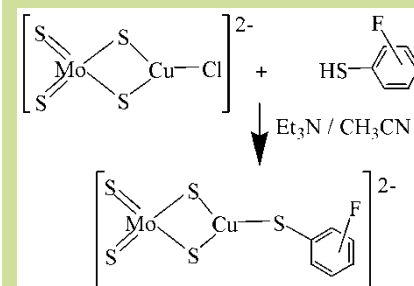


Fig. 1 - EXAFS structure of ORP

Methodology

Synthesis: Complexes $[\text{M}]_2[\text{S}_2\text{MoS}_2\text{Cu}(\text{SR}_F)]$, $[\text{M} = \text{Ph}_4\text{P}^+$ or Et_4N^+ ; $\text{SR}_F = 2$ -Fluorothiophenol, 3-Fluorothiophenol and 4-Fluorothiophenol] were obtained by treating with $[\text{PPh}_4]_2[\text{MoS}_4\text{CuCl}]$ and the corresponding fluorothiols in presence of triethylamine in acetonitrile solvent (scheme 1).

^{19}F NMR: The convergence or divergence of these isomeric ligands of the fluorothiophenol are used in this Mo-Cu complexes for tuning the ^{19}F -NMR signal. The complexes exhibit ^{19}F resonances at -108 (for ortho-F), -116 (for meta-F) and -125 ppm (for para-F). The ^{19}F -NMR signals of complexes showed a variation in the degree of chemical shift due to associate with a very subtle change in the position of fluorine atom in their benzene ring.



Scheme 1: Reaction with fluorinated-thiols.

Expected Results

The ability to design and evaluate in particular small-size model systems, which may provide a powerful tool for studying the metal reconstitution of the protein. The small fluorinated thiol binders displayed wide range of ^{19}F -NMR signals, which may provide a blueprint for the location of the metal-cofactor in the Orange Protein.

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[3] C. Belle, C. Beguin, S. Hamman, J.L. Pierre, *Coord. Chem. Rev.* **2009**, 253, 963.