Volume: 14
Year: 2025
ISSN: 2239-2459

ISMEC GROUP SERIES
Symposium Edition: XXXV
https://www.ismecgroup.org/ismec-acta/

Acta of the International Symposium on Thermodynamics of Metal Complexes

The **Acta of the International Symposium on Thermodynamics of Metal Complexes 2025** (ISSN: 2239-2459) is published annually online open access by the **ISMEC Group**.

Editors:

Montserrat López-Mesas (President of the ISMEC Group)

Department of Chemistry (GTS)

Unversitat Autònoma de Barcelona

Facultat de Ciències, 08193 Bellaterra (Cerdanyola del Vallès), SPAIN

montserrat.lopez.mesas@uab.cat

Alicia Domínguez-Martín (Chair of the Organizing Committee ISMEC 2025)

Department of Inorganic Chemistry

University of Granada

Campus Cartuja s/n 18071 Granada, SPAIN

adominguez@ugr.es

Acta of the International Symposia on Metal Complexes

ISMEC GROUP SERIES, VOLUME: 14, YEAR: 2025

ISSN: 2239-2459

https://www.ismecgroup.org/ismec-acta/

International Scientific Committee of ISMEC 2025:

Montserrat López-Mesas	Universitat Autònoma de Barcelona, Spain President of ISMEC Group
Natalia Busto	Universidad de Burgos, Spain Deputy president of ISMEC Group
Demetrio Milea	Università degli Studi di Messina, Italy Former president of ISMEC Group
Antonio Bianchi	Università degli Studi di Firenze, Italy
Elzbieta Gumienna-Kontecka	Uniwersytet Wrocławski, Poland
Enrique García-España	Universitat de València, Spain Chair of ISMEC 2022
Vieri Fusi	Università di Urbino, Italy Chair of ISMEC 2023
Maria Rosa Beccia	Université Côte d'Azur, France Chair of ISMEC 2024
Alicia Domínguez Marín	University of Granada, Spain Chair of ISMEC 2025
Andrea Melchior	University of Udine, Italy Chair of ISMEC 2026

Local Organizing Committee of ISMEC 2025

Alicia Domínguez Martín
University of Granada, Spain. Chair of ISMEC 2025

Juan Niclós-Gutiérrez
University of Granada, Spain. Co-Chair of ISMEC 2025

Duane Choquesillo Lazarte
Consejo Superior de Investigaciones Científicas, Spain

Ricardo Navarrete Casas
University of Granada, Spain

Miguel Ángel Galindo Cuesta
University of Granada, Spain

Cristobal Verdugo Escamilla
Consejo Superior de Investigaciones Científicas, Spain

Jeannette Carolina Belmont Sánchez
University of Granada / Consejo Superior de Investigaciones Científicas, Spain

Estephany Muñoz Hernández
University of Granada / Consejo Superior de Investigaciones Científicas, Spain

Francisco Javier Acebedo Martínez
Consejo Superior de Investigaciones Científicas, Spain

Joaquín Criado Reyes
Consejo Superior de Investigaciones Científicas, Spain

Metal-induced amide deprotonation and binding of model peptides to Cu(II), Zn(II) and Fe(II) metal ions

Silvia LEVERARO,[a,b] Valentyn DZYHOVSKYI,[b] Kinga GARSTKA,[b] Agnieska SZEBESCZYK,[c] Fabio ZOBI,[d] Denise BELLOTTI,[a] Kamila STOKOWA-SOŁTYS,[b] Maurizio REMELLI,[a] Magdalena ROWIŃSKA-ŻYREK [b]

[a]) Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, via Luigi Borsari 46, 44121, Ferrara, Italy
[b]) Faculty of Chemistry, University of Wroclaw, ul. F. Joliot-Curie 14, 50-383, Wroclaw, Poland
[c]) Institute of Health Sciences, University of Opole, Katowicka str. 68, 45-060 Opole, Poland
[d]) Department of Chemistry, Fribourg University, Chemin Du Muséè 9, 1700, Fribourg, Switzerland
silvia.leveraro@unife.it

The elucidation of metal-peptide interactions is an extremely important aspect of bioinorganic chemistry, also in the view of designing novel therapeutic agents. While Cu(II)/peptide coordination chemistry is extensively documented [1,2], the coordination behaviour of Zn(II) and Fe(II), particularly concerning the backbone amide deprotonation and binding, still remains controversial [3,4]. In fact, in the case of Cu(II) ions, histidine imidazole often acts as an anchoring site, at acidic pH and, increasing the alkalinity of the solution, the metal coordination might involve the backbone amides towards the N- and/or C-terminal directions. A similar behaviour is also possible, but not fully established, for Zn(II) and Fe(II) metal ions (Fig. 1) [5].

In the present investigation, we studied three model peptides protected at both terminal ends: Ac-AAAHAAA-NH_2, Ac-AAPHAAA-NH_2, Ac-AAPHPAA-NH_2. In the second peptide, an alanine has been substituted with a proline residue in position 3, while in the third peptide, a double substitution has been done in position 3 and 5. Proline is the only natural amino acids having a secondary amino nitrogen. The introduction of proline acts as a sort of "breaking point" in progressive coordination of metal ion to the backbone, since it does not contain replaceable amide protons, thus making the typical stepwise coordination of consecutive amide nitrogens impossible.

The thermodynamic and spectroscopic characterization of the formed metal complexes has been achieved by means of potentiometry, UV-Vis spectrophotometry, circular dichroism, electron paramagnetic resonance, calorimetric titrations, mass spectrometry and DFT calculations.

The results show distinct coordination behaviors for Zn(II) and Fe(II), compared to Cu(II). Both experimental and computational results agree that the metal-induced amide deprotonation and binding are not likely for the three model peptides in the case of both Zn(II) and Fe(II).

Financial support of the Polish National Science Centre (UMO-2020/37/N/ST4/03165) and of the National Recovery and Resilience Plan (NRRP), Mission 4 Component 2 Investment 1.1 – NextGenerationEU (grant PRIN PNRR 2022-P2022EMY52; CUP F53D23008960001; project title: "EnzyMime – Biocompatible and sustainable enzyme mimics based on metal complexes with peptide derivatives: synthesis, characterization and potential biological applications") is gratefully acknowledge.

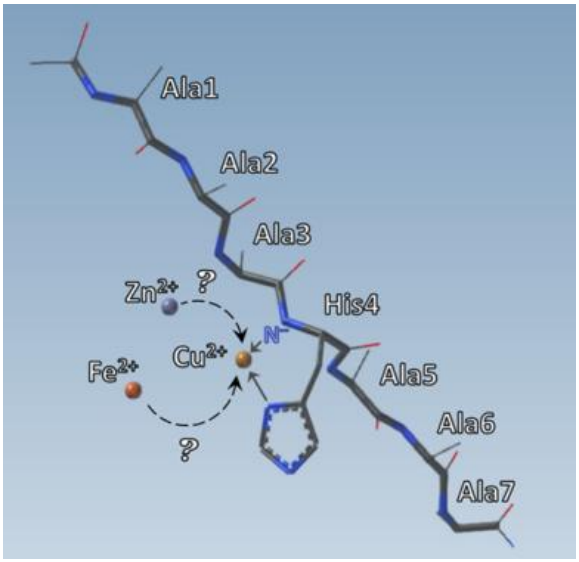

Fig. 1 – Coordination hypotheses of backbone amide nitrogens to divalent metal ions.

References:

[1] D. Bellotti, M. Rowińska-Żyrek, M. Remelli, *Dalton Transaction* **2020**, *49* (27), 9393-9403.
[2] H. Kozłowski, T. Kowalik-Jankowska, M. Jezowska-Bojczuk, *Coordination Chemistry Reviews* **2005**, *249* (21-22), 2323-2334.
[3] K. Garstka, V. Dzyhovskyi, J. Watły, K. Stokowa-Sołtys, J. Świątek-Kozłowska, H. Kozłowski, M. Barcelò-Oliver, D. Bellotti, M. Rowińska-Żyrek, *Molecules* **2023**, *28* (10), 3985.
[4] V. Dzyhovskyi, M. Remelli, K. Stokowa-Sołtys, *Journal of Inorganic Biochemistry* **2025**, *263*, No. 112769.
[5] S. Leveraro, V. Dzyhovskyi, K. Garstka, A. Szebesczyk, F. Zobi, D. Bellotti, K. Stokowa-Sołtys, M. Remelli, M. Rowińska-Żyrek, DOI: 10.1021/acs.inorgchem.5c00672