

Copper Complexes of N-Donor Ligands as Artificial Nucleases



The group of Nora Kulak (second from the right) in “Domäne Dahlem”, a manor in the green neighbourhood of the Freie Universität campus.

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Invited for the cover of this issue is the group of Nora Kulak at Freie Universität Berlin. The cover image shows metal complexes capable of cleaving DNA, so-called artificial metallonucleases based on copper as the central atom and comprising N-donor ligands. Heteroaromatic, macrocyclic, and peptidic ligand systems are adumbrated in the background.

What words would describe your research best?

Interdisciplinary. It is based on rational design, but is always good for a surprise...

Why did you choose this topic for your Microreview?

We synthesize new metal complexes that interact with biomolecules with the aim of developing metal-based therapeutic and diagnostic tools. The first projects of the young group (founded in 2011) dealt with nucleolytic metal complexes, mostly based on copper. When we looked for a common theme in our newly designed molecules, we found that nitrogen donors were included in all of the ligands. Nevertheless, the variety of ligand systems is huge – ranging from macrocyclic amines and heteroaromatic compounds to peptides. This broad variety makes the topic very diverse and interesting, hopefully also to the readers of the Microreview!

How would you describe to the layperson the contents of the Microreview?

DNA encodes the information of our life. Sometimes, however, it might be necessary to cut this big biomolecule into smaller pieces. This happens naturally in some molecular biological processes, but it could also be put to use for preventing cancer cells from growing. Compounds of copper can be used to accomplish this job, either by cleaving the backbone of DNA or by producing reactive species that attack DNA. In this Microreview, several classes of such compounds are described with their structure, properties, and potential applications.

How did each team member contribute to the Microreview?

Christian worked on hydrazone and peptide ligands, Carsten on phenanthroline and bipyridine ligands, their respective PhD topics, and I did the bpa and macrocyclic amine ligands and the rest of the Microreview. Christian, the first author, was responsible for the artwork and the cover design.

What do you consider the exciting developments in the field?

Interesting approaches in the last couple of years have been dealing with oxidative nucleases that do not need external reducing agents like H_2O_2 for activation, so-called self-activating nucleases. This is of particular interest for cell studies that follow DNA cleavage experiments. Although only briefly mentioned in the Microreview, anticancer activity is expected or even proven for

several of the complexes. The connection between copper-dependent DNA cleavage and cell death has yet not been uncovered.

What other topics are you working on at the moment?

We are fascinated not only by molecules that are able to cleave DNA, but also another class of biomolecules – proteins. We have recently developed a system that can cleave proteins, which is based on amphiphilic Cu^{II} complexes.

