MS5-P50

TMPA capped calixarene as mononucleotide binding agent

Ivana Nikšić-Franjić[1], Aleksandar Višnjevac[1], Ivo Piantanida[1], Benoit Colasson[2] and Olivia Reinaud[2]

1) Ruđer Bošković Institute, Bijenička cesta 54 10000, Zagreb, Croatia

2) Université de Paris, Rue des Saints Pères 45 75006, Paris, France

iniksicf@irb.hr

Studies of interactions of calixarene derivatives featuring short, triazole-attached positively charged substituents and their neutral analogues with polynucleotide chains and mononucleotides have shown encouraging results [1]. Inspired by these results, we have undertaken an interdisciplinary study, using the computational methods and the single crystal X-ray study, on the TMPA capped calixarenes **1** and its charged analogue **2**, as well as with their copper (II) complexes.

Molecular dynamics simulations revealed that calixarene **2**, Cu^{2+}-**1** and Cu^{2+}-**2** bind non-covalently in the minor groove by a combination of electrostatic, van der Waals and hydrogen bonding interactions. Neutral calixarene **1** does not show any interaction towards AT-DNA but its copper(II) complex fits into the DNA minor groove. Calixarene **2** due to its positively charged trimethylammonium moieties forms electrostatic interactions with negatively charged phosphate backbones of the DNA. The negative electrostatic potential of A, T sequence in the minor groove suggest that these sites are likely target for positively charged ligands or cationic complexes. The copper(II) in both complexes stays in TMPA cap surrounded with pyridine nitrogen atoms. CD experiments have confirmed that **2**, Cu^{2+}-**1** and Cu^{2+}-**2** efficiently displace DAPI from AT-DNA minor groove.

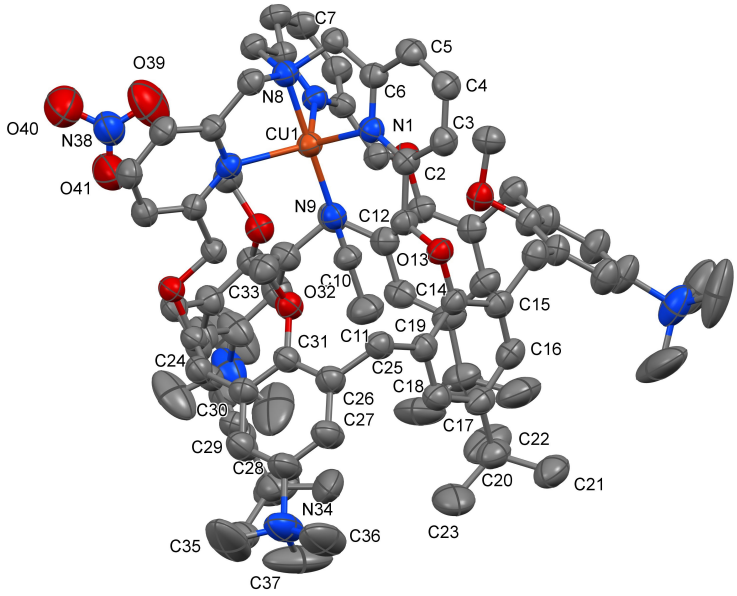

Figure 1.
ORTEP drawing of the complex **2** + **Cu** + **CH_3CN** with atom numbering. Thermal ellipsoids are given at the 50% probability level. Hydrogen atoms as well as two symmetrically generated nitrate anions are omitted for clarity.

Complex **2** crystallizes easily, in the presence of MeCN, in the rhombohedral space group *R*-3 with six molecules per unit cell and one third of a molecule in the asymmetric unit (Figure 1). Copper (II) lies in a center of only slightly distorted axially compressed trigonal bipyramid formed by the central TMPA nitrogen N8 and N9 from the intracavity bound acetonitrile (occupying two apical positions), as well as three pyridine nitrogen atoms in the equatorial positions. There are no classic H-bonds found in the structure of **2**.