ABSTRACT

Imaging methods have become an integral part of diagnostic and therapeutic procedures in current medicine. Contrast agents based on metal complexes are often used to improve the final image. Complexes contain radioisotopes in nuclear medicine and gadolinium(III) ion in MRI. These complexes have to show high kinetic and thermodynamic stability and their preparation must not be time consuming.

H_4DOTA and its derivatives are convenient type of ligand for the formation of stable complexes. This work has focused on phosphonate and phosphinate derivatives of the ligand H_4DOTA. The studied compounds can be divided into ligands containing only methylphosphinate/phosphonate (H_4DO3AP^{H}, H_5DO3AP^{OH}) and ligands with a second coordination center (H_6DO3AP^{IDA}, H_5DO3AP^{PIN}, H_4DO3AP^{AM}, H_8DO3AP^{BP} a H_7DOTAM^{BP}).

The work has examined the possibilities of influencing the way and rate of complexation under different conditions. In order to approach the preparation conditions of radio complexes, kinetics measurements were performed not only under the metal ions excess, but also under the ligand excess. The aim was to compare the results of both types of measurements, which often showed to be different. A mechanism for the formation of various types of intermediates formed during complexation has been proposed.

The complexation rate was further affected by the type of pendant arm on the macrocycle. The introduction of an acidic group as another weakly coordinating site in the molecule (e.g. phosphinates on H_5DO3AP^{PIN}) led to complex formation acceleration, on the contrary, the presence of another amino group (H_4DO3AP^{AM}) significantly slowed down the complexation. Another important feature was the stability of the *out-of-cage* complex (i.e., the transition complex formed by the coordination of the metal ion to the coordinating groups of the pendant arm). The presence of a weakly coordinating group accelerated the complexation, but a more strongly coordinating group (e.g. the iminodiacetic group in the ligand H_6DO3AP^{IDA}) significantly slowed down the rate of transition of the metal ion into the macrocycle (formation of the *in-cage* complex).