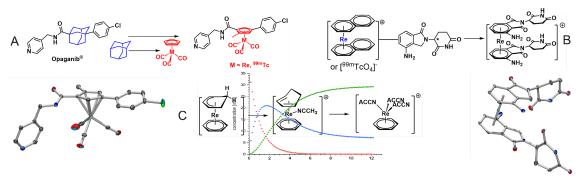
ADVANCES IN TECHNETIUM AND RHENIUM CHEMISTRY: STILL RELEVANT FOR MOLECULAR IMAGING?

Roger Alberto, Robin Bolliger, Henrik Braband, Federica Battistin

Department of Chemistry, University of Zurich, Winterthurerstr. 190, CH-8057 Zurich Switzerland

The application of ^{99m}Tc complexes in molecular imaging is the thrust for investigating fundamental aspects of the chemistry of Tc, but not the only one. Fundamental studies are usually done with the long-lived ⁹⁹Tc isotope, available in grams, or with Re where appropriate [1]. Knowledge from macroscopic chemistry (⁹⁹Tc) is transferred to the microscopic level (^{99m}Tc), often yielding different results. Despite the motivation of bringing a compound from bench to bedside, a fading out of technetium chemistry is observed over the past decade or more [2]. This is surprising as Tc chemistry is widely unexplored in many directions, for potential applications or for basic reasons such as the comparison with its neighboring elements. Reasons why this is so will be discussed.



Organometallic chemistry of Tc and, more recently, of Re have found their roles in bioorganometallic chemistry. For combining either of these elements with a targeting functionality, a complex is combined with a pharmaceutical. Extrapolating from our basic organometallic research, we proposed other approaches, which do not require bifunctional chelators but rely on replacing a phenyl ring in the lead structures with a Cp-ring (A) [3]. Alternatively, the 99m Tc complex is bound directly to the phenyl ring in the intact lead structure (B), leading to sandwich complexes with two pharmaceuticals bound to 99m Tc. [4] This concept leads to a plethora of new complexes and reactivities (C), for application or not. The chemistry around $[(\eta^5\text{-Cp-pharm})^{99m}\text{Tc}(CO)_3]$ complexes and the sandwich complexes $[^{99m}\text{Tc}(\eta^6\text{-pharm})_2]^+$ will be presented [5]. Reactivity aspects going beyond applications in molecular imaging will be shown. A key preparing such unusual complexes in water and in quantitative yields accessible is kinetics, an aspect making chemistry with ^{99m}Tc and ^{99}Tc or rhenium often different.

^[1] Alberto, R., Organometallic Chemistry of Drugs Based on Tc and Re. In *Comprehensive Organometallic Chemistry IV*, Parkin, G.; Meyer, K.; Eds. Elsevier: Oxford, **2022**; pp 226-260.

^[2] Alberto, R., Qaisar, N., 99mTechnetium-Based Imaging Agents and Developments in ⁹⁹Tc Chemistry. In *Metal Ions in Life Sciences*, Walter de Gruyter GmbH: Berlin, **2020**; Vol. 22, pp 195-238.

^[3] Lengacher, R., Alberto, R., Coord. Chem. Rev. 2021, 437.

^[4] Nadeem, Q., Meola, G., Braband, H., Bolliger, R., Blacque, O., Hernandez-Valdes, D., Alberto, R., *Angew. Chem. Int. Edit.* **2020**, *59*, 1197-1200.

^[5] Lengacher, R., Wang, Y. C., Braband, H., Blacque, O., Gasser, G., Alberto, R., *Chem. Commun.* **2021**, *57*, 13349-13352.