Introduction to the Scientific Community – Inorganic Chemistry

Synthesis and characterization of lipophilic cationic gold(I) bis(NHC) complexes for biomedical applications

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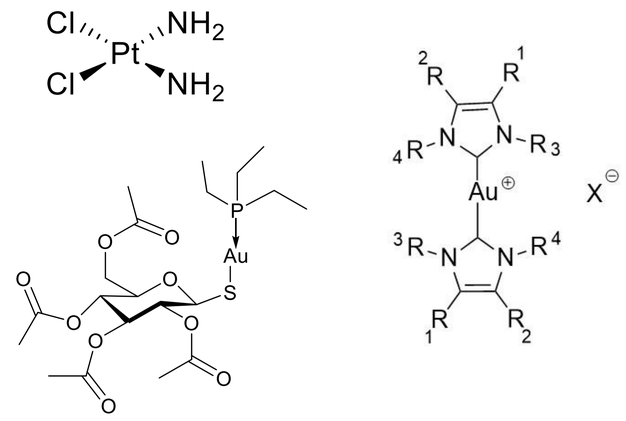
Introduction

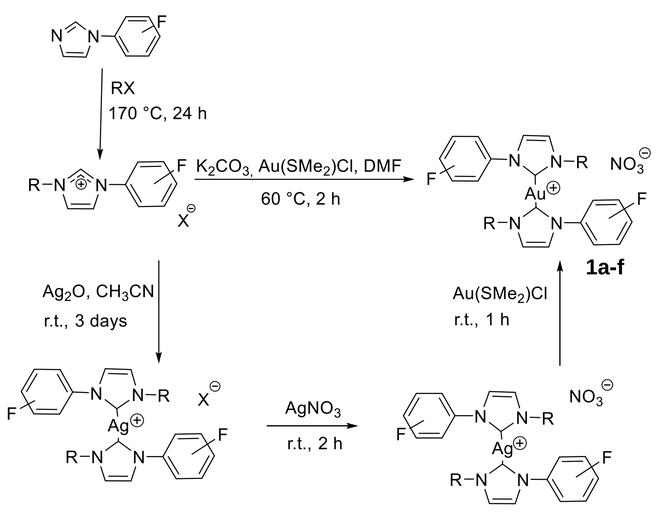
Cancer is a major health problem in the world. Many current used anti-cancer drugs as for example cisplatin present non negligible side effects besides other disadvantages such as low selectivity.[1] The development of new drugs with less side-effects is therefore important. Organometallic complexes are promising compounds in this research field. Good anti-cancer activity for diverse gold complexes such as auranofin has been reported during the last years.[2,3] Lipophilicity is a possible key point for anti-cancer activity of gold NHC complexes (NHC = *N*-heterocyclic carbene).[4] Thus, this poster presents the synthesis of new lipophilic cationic gold(I) bis(NHC) complexes with fluorinated ligands as well as their characterisation by NMR spectroscopy and X-ray measurements. In total, six complexes could be successfully synthesized with yields between 45 % and 80 %.



Molecular structures of cisplatin (left, top), auranofin (left, bottom) and general structure of a cationic gold(I) bis(NHC) complex (right).

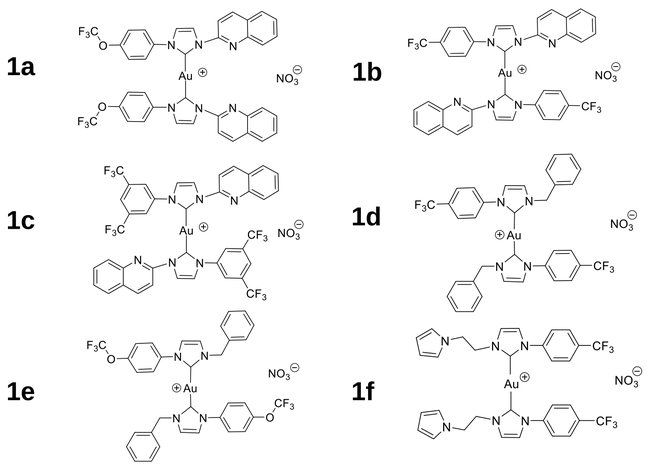
Synthesis of the complexes

Synthetic access to the gold(I) bis(NHC) complexes is provided by a two step synthesis. In a first step, *N,N*-difunctionalized imidazolium salts were generated. The final products were formed either by direct reaction with a gold(I) salt, or by transmetalation, passing by the corresponding silver complex.



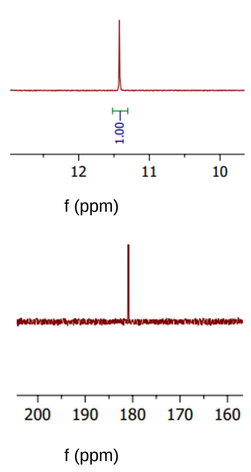
Overall reaction scheme of the synthesis of the gold(I) bis(NHC) complexes.
X= Cl^-, Br^-
R = benzyl, quinoline-2-yl, 2-(1*H*-pyrrol-1-yl)ethyl.

Synthesized complexes

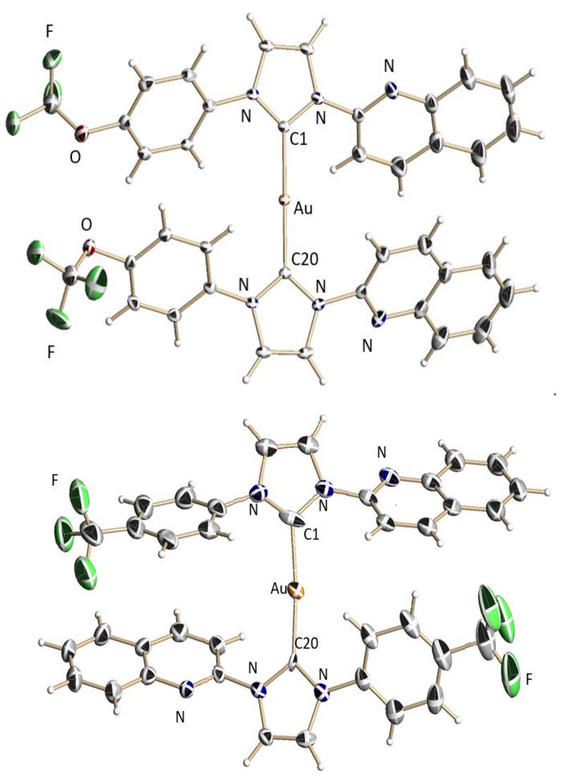


NMR experiments

The ^{1}H NMR spectra of the imidazolium salts show a characteristic peak of the imidazolium proton between 11 and 12 ppm.
The ^{13}C NMR spectra of the complexes show the characteristic carbene singlet at approximately 180 ppm.



X-ray structures



Crystal structure of the cationic part of **1a** (top) and **1b** (bottom) depicted as ellipsoid plot at 50% level. Noncoordinating anions have been omitted for clarity. Selected bond lengths [Å] and angles [°]:
1a: Au-C1 2.0152(18), Au C20 2.0153(18), C1-Au-C20 179.74(10).
1b: Au-C1 2.025(6), Au-C20 2.054(7), C1-Au-C20 174.5(3).

Conclusion

New anti-cancer drugs are needed and as it is still hard to determine a leading species with the best structure-activity relationship, the synthesis of new complexes is important. A range of fluorinated imidazolium salts and their cationic gold(I) bis(NHC) complexes could be successfully synthesised and their structures could be investigated by NMR measurements. For two complexes, X-ray structures could be obtained, proving the formation of the desired products. The *in vitro* and *in vivo* anti-cancer activity of the synthesised complexes still has to be investigated in future studies. Based on previous results, the synthesized complexes are expected to present a high cytotoxicity due to their lipophilicity that was induced by fluorinated ligands.

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[1] S. Gómez-Ruiz, D. Maksimović-Ivanić, S. Mijatović and G. N. Kaluđerović, *Bioinorg Chem Appl* **2012**, 140284.
[2] B. Dominelli, J. D. G. Correia and F. E. Kühn, *J Organomet Chem* **2018**, 866, 153-164.
[3] M. Porchia, M. Pellei, M. Marinelli, F. Tisato, F. Del Bello and C. Santini, *Eur J Med Chem* **2018**, 146, 709-746.
[4] C. Zhang, M. L. Maddelein, R. Wai-Yin Sun, H. Gornitzka, O. Cuvillier and C. Hemmert, *Eur J Med Chem* **2018**, 157, 320-332.