Introduction to the Scientific Community – Inorganic Chemistry

Computational DFT study of NHC-Au(I)-complexes used for anti-cancer therapy

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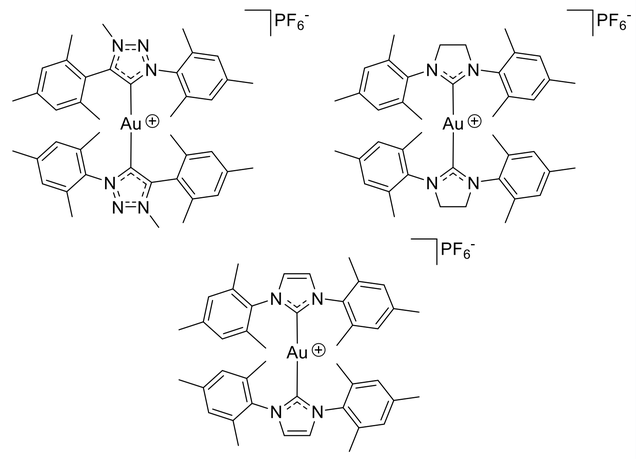
Introduction

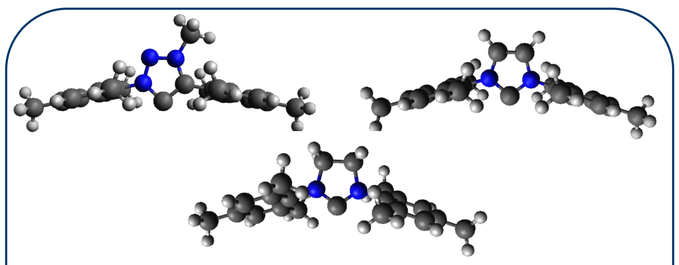
DFT calculations as suitable tool to calculate molecule structures can help to better understand structural and electronic properties of complex chemical systems. In this work, the theoretical investigation and a comparison of different NHC-Au(I)-complexes is presented. In detail, imidazolylidene, 1,2,3-triazole-5-ylidene, and imidazolylidene were chosen bearing a NHC moiety with different wingtips, namely methyl, benzyl and mesityl. These could be used in the future in cancer therapy.[1,2]
Therefore, calculations based on the ωB97X-D functional and the basis set LANL2DZ and 6-311++G* were carried out leading to the calculation of the different HOMO and LUMO orbitals as well as bond lengths, angles and general geometries. As mesityl wingtips turned out to be too complex for reasonable results, the calculation of the imidazolylidene-Au(I)-complex with a methyl wingtips as simplified alternative was the starting point of the herein presented study. In a second step, complexes bearing a benzyl wingtips were investigated mimicking the mesityl wingtips as they also show π-π-interactions. Nevertheless, frequency calculations show negative vibrations leading to incorrect dissociation energies.



Structures of the gold mesityl rest complexes to be calculated triazole (top left), imidazoline (top right), and imidazole (bottom).

Optimization of mesityl ligands

All calculated ligand structures do not deviate from the expected case. Both imidazole and triazole ligands show a more rigid behavior compared to the imidazoline because of their stabilizing π-system. The mesityl rests of the imidazoline are twisted, whereas these moieties are in the same plane for the imidazole and triazole ligands.

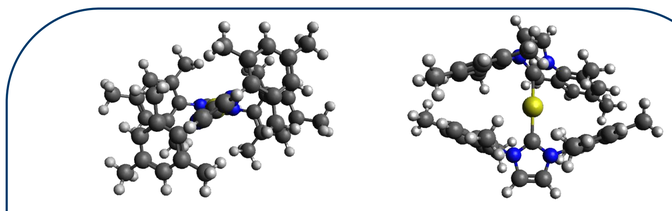


Optimized structures of the mesityl-NHC ligands based on imidazoline (left), imidazole (middle), triazole (right).

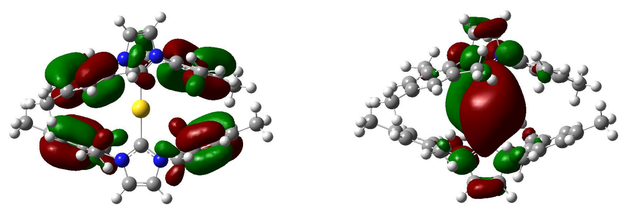
	Bond length NHC-R	Angle carbene-C-N-R	Angle carbene-C
Imidazole	1.44 Å	123°	102°
Triazole	1.44/1.48 Å	126°	100°
Imidazoline	1.43 Å	124°	106°

Optimization of Au(I)-NHC-complexes

Mesityl moieties

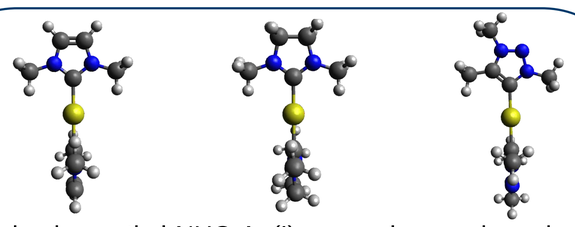


Optimized mesitylimidazoleylidene-Au(I) complex structure.



HOMO (left) and LUMO (right) orbitals of the mesityl-imidazole-Au(I)-complex.

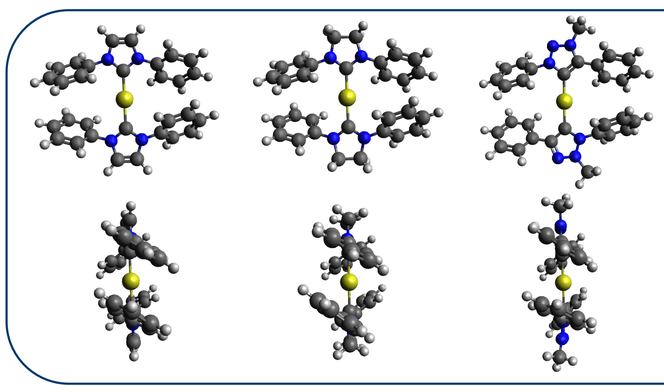
Methyl moieties



Optimized methyl-NHC-Au(I) complexes based on imidazole (left), imidazoline (middle), triazole (right).

	Bond length Au-C	Angle NHC-Au-NHC	Dissociation energy
Imidazole	2.05 Å	179.99°	199 kJ/mol
Triazole	2.06 Å	179.99°	145 kJ/mol
Imidazoline	2.05 Å	178.93°	215 kJ/mol

Benzyl moieties



	Bond length Au-C	Angle NHC-Au-NHC	Dissociation energy
Imidazole	2.04	179.99°	-19162 kJ/mol
Triazole	2.04	178.13°	-23478 kJ/mol
Imidazoline	2.05	179.99	-19168 kJ/mol

Optimized benzyl-NHC-Au(I) complexes based on imidazole (left), imidazoline (middle), triazole (right).

Conclusion

In this work, three different kind of wingtips on three different NHC-Au(I)-complexes (imidazolylidene, imidazolylidene, triazolylidene) were theoretically investigated. The wingtips only allowed calculations with the easiest imidazolylidene complex. It was found that the methyl-complexes are only barely assimilable to the mesityl-complexes because of missing π-π-interactions. However, the benzyl-complexes showed a good comparability to the mesityl complexes, but unfortunately, the dissociation energy could not be calculated due to negative frequency calculations.
For future studies, other computational methods developed for bigger systems could lead to a successful investigation of the herein studied complexes such as Quantum mechanics/Molecular mechanics (QM/MM) or Density Functional based Tight Binding (DFTB).[3,4]

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[2] G. B. C. Nardon, Anticancer Research 2014, 34, 487-492.
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