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Interactions of cisplatin with nucleobases and nucleotides: an IRMPD study

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Cisplatin (cis-diamminedichloroplatinum(II)) is a widely used anticancer drug that has been particularly successful in treating small cell lung, ovarian, or neck tumors.[1,2] Although cisplatin is one of the most successful anticancer drugs, side effects, natural and acquired resistance of patients toward the drug have motivated searches for structurally and/or functionally analogous alternatives.[2] Unfortunately, finding analogous compounds that outperform cisplatin has proved to be difficult. In this context, a better understanding at the molecular level of the interactions between the Pt and the nucleobase moieties is thought to be helpful in establishing a rational strategy to design cisplatin analogues. Experimentally, the coupling of mass spectrometry to InfraRed Multiple Photon dissociation (IRMPD) spectroscopy has proven to be a powerful method for probing the structure of gaseous metal cationized complexes.[3] We presently use this approach to characterize to structure of the cisplatin/guanine and cisplatin/dGMP complexes generated in the gas phase by electrospray ionization.

IRMPD spectra in the mid-infrared region (900 cm-1-1900 cm-1) were recorded by means of a Bruker Esquire 3000+ ion trap mass spectrometer coupled with the tunable IR beam provided by the CLIO free electron laser (Centre Laser Infrarouge Orsay). Theoretical calculations were carried at the B3LYP/6-31G(d,p) level, the LANL2DZ effective core potential and basis set being used to describe the platinum atom.[4,5] Harmonic vibrational frequencies were estimated at this level in order to classify the optimized structures as local minima or saddle points, and to compare computed and experimental infrared spectra.

Bibliography

[1] Rosenberg, B.; Van Camp, L.; Krigas, T. Nature 1965, 205, 698.
[2] Jung, Y. W.; Lippard, S. J. Chem. Rev. 2007, 107, 1387.
[3] Fridgen, T. D. Mass Spectrom. Rev. 2009, 28, 586.
[4] Wadt, W. R.; Hay, P. J. J. Chem. Phys. 1985, 82, 284.
[5] Hay, P. J.; Wadt, W. R. J. Chem. Phys. 1985, 82, 299.