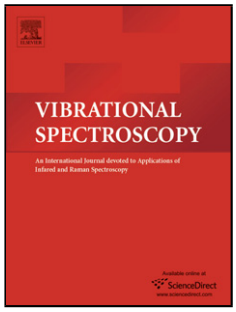

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PII: S0924-2031(16)30300-9
DOI: http://dx.doi.org/doi:10.1016/j.vibspec.2017.02.006
Reference: VIBSPE 2686

To appear in: *VIBSPE*

Received date: 28-10-2016
Revised date: 15-2-2017
Accepted date: 24-2-2017

Please cite this article as: Rukshani Haputhanthi, Ruchika Ojha, Ekaterina I.Izgorodina, Si-Xuan Guo, Glen Deacon, Don McNaughton, Bayden R.Wood, A spectroscopic investigation into the binding of novel platinum(IV) and platium(II) anticancer drugs with DNA, Vibrational Spectroscopyhttp://dx.doi.org/10.1016/j.vibspec.2017.02.006

A spectroscopic investigation into the binding of novel platinum(IV) and platium(II) anticancer drugs with DNA

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Abstract

Platinum(II) complexes have had enormous success in cancer chemotherapy and novel Pt^{IV} complexes show potential for reduced toxic side effects and different mechanisms of action. While the action of Pt^{II} anticancer drugs with DNA has been well characterized with X-ray and many spectroscopic modalities, the mechanisms of binding Pt^{IV} complexes to DNA require further fundamental studies. In the present work using ATR-FTIR spectroscopy, we have extensively analyzed conformational changes in both single-stranded (ss) and double-stranded (ds) calf-thymus DNA, after binding to the Pt^{IV} anticancer complex, [Pt{((p-HC_6F_4)NCH_2)$_2$}$(py)_2(OH)_2$] (py = pyridine) (Pt103$(OH)_2$), and its Pt^{II} analogue, [Pt{((p-HC_6F_4)NCH_2)$_2$}$(py)_2$] (Pt103) in buffered aqueous acetone (55% water), under which conditions no hydrolysis of drugs occurs. To aid in band assignments of the Pt derivatives, DFT calculations using the M062X/cc-pVDZ level of theory were performed. The ssDNA is distorted and its conformation changes more towards the A-like DNA of dsDNA upon binding to both Pt103 and Pt103$(OH)_2$. This conclusion is derived from the changes in the PO_2^- symmetric stretching vibrations (1086 to 1093 cm^{-1}) and C-O (1055 to 1062 cm^{-1}) and C-C