Abstract ID: *ASRS2019-13* *Chemistry*

AN NMR SPECTRAL STUDY INVESTIGATING POTENTIAL ANTICANCER ACTIVITY OF A Pt(II) SULFONAMIDE COMPLEX

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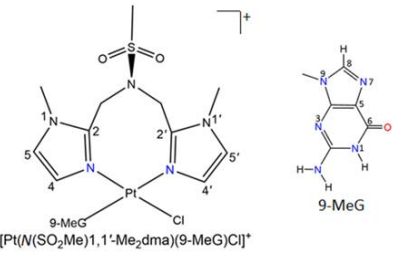
Chelate ligands in anticancer-active Pt(II) complexes greatly influence anticancer activity by affecting DNA structural distortions after the Pt(II) ion binds preferentially at N7 of guanine (G) residues of DNA. During the preliminary studies of novel Pt(II) complexes intended for therapeutic use, simpler G adducts of single guanine derivatives such as 9-methylguanine (9-MeG) or guanosine, can be utilized to evaluate the reactivity of the metal complexes towards biological molecules. In those "model adducts", the metal-bound-G molecules can rotate around the Pt−N7(G) bond. If the in-plane bulk of the carrier ligand is high enough to restrict this rotation of the bound G on the NMR time scale, two or more H8(G) signals should be observed corresponding to different rotamers of the adduct. Existence of rotamers in the model adducts suggests that when the complex is bound to actual DNA, the carrier ligand potentially could have enough bulk to sterically disturb the G residues of DNA, a key feature of an anticancer agent. In this study, NMR spectroscopy is used to analyze the in-solution reactivity of bifunctional Pt(*N*(SO_2Me)1,1′-Me_2dma)Cl_2 complex with 9-methylguanine. The reaction progress is monitored by obtaining ^{1}H NMR spectra in a timely manner. The resultant product was characterized by using 2D NMR data (^{1}H-^{1}H ROESY). Even though Pt(*N*(SO_2Me)1,1′-Me_2dma)Cl_2 is bifunctional, the reaction with 9-MeG resulted in a mono G adduct, [Pt(*N*(SO_2Me)1,1′-Me_2dma)(9-MeG)Cl]$^+$. The observation of only one H8(G) signal for the adduct indicates that the rotation of the guanine derivative is not highly impeded in the new adduct. However, the broadness of the H8(G) peak indicates that the interconversion of the two rotamers could be somewhat slow. Therefore, it is conceivable that by a slight adjustment to the structure of *N*(SO_2Me)1,1′-Me_2dma, the ligand bulk required to impede the bound G rotation could be achieved.



Keywords: *Anticancer activity, G Adducts, Rotamers*