Study of covalent and non-covalent interactions in [Pd(dien)nucleobase]$^{2+}$/l-tryptophan(N-Acetyl-tryptophan) systems: Formation of metal-tryptophan species by nucleobase substitution under biologically relevant condition.

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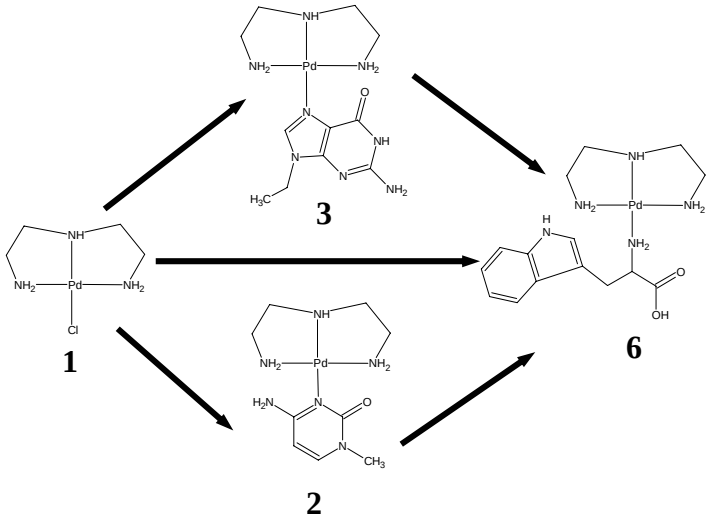
Substitution of the model nucleobases: 1-Methylcytosine (1-MeCyt) and 9-Ethylguanine (9-EtGH) by the amino acid l-tryptophan (Trp) and N-acetyltryptophan (N-AcTrp) was observed in complexes $[Pd(dien)(1\text{-}MeCyt)]^{2+}$ (**2**) and $[Pd(dien)(9\text{-}EtGH)]^{2+}$ (**3**) respectively, under physiological pH. The resulting species $[Pd(dien)(Trp)]^{2+}$ (**6**) and $[Pd(dien)(N\text{-}AcTrp)]^{2+}$ (**7**) were characterized using ^{1}H-, ^{13}C- NMR and ESI-MS techniques as coordinated through the amino and deprotonated amido nitrogen respectively. Complexes (**6**) and (**7**) were also obtained from a solution of [Pd(dien)Cl]Cl (**1**) and Trp or N-AcTrp respectively, to confirm the proposed structure. Substitution reactions did not occur in analogs Pt(II) complexes namely $[Pt(dien)(1\text{-}MeCyt)]^{2+}$ (**4**) and $[Pt(dien)(9\text{-}EtGH)]^{2+}$ (**5**) suggesting that the intrinsic more reactive nature of the Pd(II) center is the responsible for the substitution phenomenon. The association constant of complexes (**2**-**5**) was further investigated towards N-AcTrp under conditions that ruled out covalent bonding to examine both: molecular recognition through π- π stacking of the nucleobases with the indole ring in N-AcTrp, and the effect of the nature of the metal. The solid state structure for (**2**) and (**4**) was also determined and compared with analogous Pt,Pd-cytosine complexes.



Scheme I. Substitution reactions for Pd-nucleobase complexes with l-tryptophan.