

# **Properties of the Ternary (Dien)Pt(PMEA-*N7*) Complex Containing Diethylenetriamine (Dien) and the Antiviral 9-[2-(Phosphonomethoxy)ethyl]adenine (PMEA). Synthesis, Biological Screening, Acid-Base Behaviour, and Metal Ion-Binding in Aqueous Solution**

Gunnar Kamp<sup>a,b</sup>, Marc Sven Lüth<sup>a,b</sup>, Jens Müller<sup>b</sup>, Antonín Holý<sup>c</sup>,  
Bernhard Lippert<sup>b</sup>, and Helmut Sigel<sup>a</sup>

<sup>a</sup> Institute of Inorganic Chemistry, University of Basel,  
Spitalstrasse 51, CH-4056 Basel, Switzerland

<sup>b</sup> Department of Chemistry, University of Dortmund,  
Otto-Hahn-Strasse 6, D-44227 Dortmund, Germany

<sup>c</sup> Institute of Organic Chemistry and Biochemistry, Academy of Sciences  
of the Czech Republic, CZ-16610 Prague 6, Czech Republic

Reprint requests to H. Sigel (Fax: +41-61-2671017, E-mail: Helmut.Sigel@unibas.ch) or  
B. Lippert (Fax: +49-231-7553797, E-mail: Lippert@pop.uni-dortmund.de), or  
A. Holý (Fax: +42-022-4310090, E-mail: Holy@uochb.cas.cz)

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The synthesis of (Dien)Pt(PMEA-*N7*), where Dien = diethylenetriamine and PMEA<sup>2-</sup> = dianion of 9-[2-(phosphonomethoxy)ethyl]adenine, is described. No useful biological activity could be discovered for this complex which is in contrast to the known antiviral properties of PMEA itself. The acidity constants of the twofold protonated H<sub>2</sub>[(Dien)Pt(PMEA-*N7*)]<sup>2+</sup> complex were determined (UV spectrophotometry and potentiometric pH titration): The release of the proton from the -P(O)<sub>2</sub>(OH)<sup>-</sup> group is only slightly affected by the N7-coordinated (Dien)Pt<sup>2+</sup> unit, whereas the acidity of the (N1)H<sup>+</sup> site is strongly enhanced. The stability constants of the M[(Dien)Pt(PMEA-*N7*)]<sup>2+</sup> complexes with the metal ions M<sup>2+</sup> = Mg<sup>2+</sup>, Ca<sup>2+</sup>, Mn<sup>2+</sup>, Co<sup>2+</sup>, Ni<sup>2+</sup>, Cu<sup>2+</sup>, Zn<sup>2+</sup>, and Cd<sup>2+</sup> were measured by potentiometric pH titrations in aqueous solution at 25 °C and I = 0.1 M (NaNO<sub>3</sub>). Application of previously determined straight-line plots of log K<sup>M</sup><sub>M(R-PO<sub>3</sub>)</sub> versus pK<sup>H</sup><sub>H(R-PO<sub>3</sub>)</sub> for simple phosph(on)ate ligands, R-PO<sub>3</sub><sup>2-</sup> where R represents a non-inhibiting residue without an affinity for metal ions, proves that the primary binding site of the complex-ligand, (Dien)Pt(PMEA-*N7*), with all the metal ions studied is the phosphonate group; in most instances the expected stability is actually reduced by about 0.4 log units due to the N7-bound (Dien)Pt<sup>2+</sup> unit. Only for the Cu[(Dien)Pt(PMEA-*N7*)]<sup>2+</sup> and the Zn[(Dien)Pt(PMEA-*N7*)]<sup>2+</sup> systems the formation of some 5-membered chelates involving the ether oxygen atom of the -CH<sub>2</sub>-O-CH<sub>2</sub>-PO<sub>3</sub><sup>2-</sup> residue could be detected; the formation degrees are 52 ± 9% and 32 ± 14%, respectively. The metal ion-binding properties of (Dien)Pt(PMEA-*N7*) differ considerably from those of PMEA<sup>2-</sup>, yet they are relatively similar to those of pyrimidine-nucleoside 5'-monophosphates. The structures of the various complex species in solution are discussed and compared.