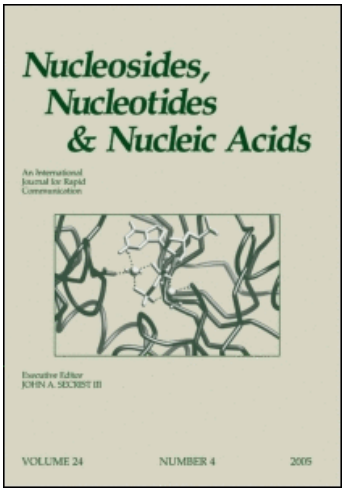

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Combined UV and Liquid Scintillation Detection in HPLC. Formation and Depurination of Substitution Inert Pt(II) Complexes of Purine Nucleosides

Jorma Arpalahti[a]; Rainer Käppi[a]; Pejtti Lehikoinen[a]; Harri Lönnberg[a]
[a] Department of Chemistry, University of Turku, Turku, Finland

To cite this Article Arpalahti, Jorma , Käppi, Rainer , Lehikoinen, Pejtti and Lönnberg, Harri(1990) 'Combined UV and Liquid Scintillation Detection in HPLC. Formation and Depurination of Substitution Inert Pt(II) Complexes of Purine Nucleosides', Nucleosides, Nucleotides and Nucleic Acids, 9: 3, 447 — 448
To link to this Article: DOI: 10.1080/07328319008045168
URL: http://dx.doi.org/10.1080/07328319008045168

NUCLEOSIDES & NUCLEOTIDES, 9(3), 447-448 (1990)

COMBINED UV AND LIQUID SCINTILLATION DETECTION IN HPLC. FORMATION AND DEPURINATION OF SUBSTITUTION INERT Pt(II) COMPLEXES OF PURINE NUCLEOSIDES.

Jorma Arpalahti, Rainer Käppi, Pertti Lehikoinen and Harri Lönnberg*

Department of Chemistry, University of Turku, SF-20500 Turku, Finland

Abstract. Combined UV- and liquid scintillation-HPLC has been applied to study the complexing of purine nucleosides with Pt(II)-diamine ions, and the effect of the complex formation on the acidic depurination.

Pt(II) diamine ions may be competitively coordinated to different nitrogen atoms of purine nucleosides. Formation of these substitution inert nucleoside complexes undoubtedly affects the hydrolytic stability of the N-glycosidic bond, offering a method with which nucleosides may be selectively protected against acidic depurination.

The attachment of cis-$L_2Pt(II)$ ions (L = NH_3, $MeNH_2$, Me_2NH) to the N1 and N7 sites of [8-^{3}H]adenosine was followed by HPLC on a Serva RP-18 column (4x250 mm, 5 μm) using an acetate buffer (0.01M, pH 4.3, $NaClO_4$ 0.05 M) as eluant. The rate constants for the complex formation were calculated from the time-dependent concentration of the uncomplexed nucleoside determined by UV-HPLC. It is noteworthy that the ligand exchange reactions of $L_2Pt(II)$ ions are slow enough to enable chromatographic separation of the complexes and free ligand. The mole fractions of the N1- and N7-coordinated complexes in the product mixture were, in turn, determined by liquid scintillation monitoring of the respective peaks (LKB 1208 Betacord). With each $L_2Pt(II)$ ion, formation of the N7-coordinated species was slightly

favoured, the ratio of the rate constants of N1- and N7-binding being 0.66. Guanosine exhibited under acidic conditions only N7-complexing.

The rate constants for the acidic depurination of the N1- and N7-(dien)Pt(II) complexes of 2'-deoxyadenosine and N7-(dien)Pt(II) complex of 2'-deoxyguanosine were determined by HPLC using UV-detection. While binding of (dien)Pt(II) ion to N7 of 2'-deoxyguanosine was observed to retard the depurination by two orders of magnitude over a wide pH-range, the corresponding complex of 2'-deoxyadenosine was almost as susceptible to hydrolysis as the uncomplexed nucleoside. Similarly, the N1-(dien)Pt(II) complex of 2'-deoxyadenosine was depurinated under acidic conditions only 2 times less readily than 2'-deoxyadenosine. The observed pH-rate profiles were employed to estimate the basicity and leaving-group ability of the N1- and N7-complexed adenine rings.

Comparative kinetic studies with substitution labile (dien)Pd(II) ion showed that complexing with this ion retarded the depurination of 2'-deoxyguanosine by a factor of 65. By contrast, the effect on the depurination of 2'-deoxyadenosine was a small one; an acceleration or retardation depending on pH and the metal ion concentration. The data obtained with (dien)Pt(II) complexes have been employed to explain mechanistically the kinetic effects of (dien)Pd(II) ion.

In summary, the results presented help to understand the known effect of $K_2[PdCl_4]$ on the depurination of DNA.