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Complex Formation Between Gadolinium(III) Porphyrins and Some Nucleic Bases or their Nucleoside Derivatives in Aqueous Solutions

S. Radzki[1] and **P. Krausz**[2]

[1] Department of Chemistry, Maria Curie-Skłodowska University, PL-20031 Lublin, Poland
[2] Laboratorie de Chimie des Substances Naturelles, Université de Limoges, F-87060 Limoges Cedex, France

Summary. The mutual interactions of Gd(III)tetraphenylporphyrin (Gd*TPP*), Gd(III)tetramethylpyridylporphyrin (Gd*TMePyP*), and the free base tetramethylpyridylporphyrin (H_2*TMePyP*) with some nucleic bases (adenine, thymine, uracil, and cytosine) and their N-glycoside derivatives (adenosine, thymidine, uridine, and cytidine) have been studied by spectrophotometric titration in mixed methanol-ammonia-water solutions. It has been found that tetramethylpyridylporphyrin and its gadolinium complex form 1:1 complexes with nucleic bases and their nucleoside derivatives. The equilibrium constants were estimated using curve fitting procedures. The interactions are stronger for nucleoside derivatives than for nucleic bases. They are also stronger for metallated than for non-metallated porphyrins.

Keywords. Gadolinium; Interaction; Porphyrin; Nucleic Bases; Nucleoside.

Komplexbildung zwischen Gadolinium(III)porphyrinen und einigen Nucleinbasen oder ihren Nucleosidderivaten in wäßrigen Lösungen

Zusammenfassung. Die Wechselwirkungen von Gd(III)tetraphenylporphyrin (Gd*TPP*), Gd(III)-tetramethylpyridylprophyrin (Gd*MePyP*) und der freien Base Tetramethylpyridylporphyrin (H_2*TMePyP*) mit einigen Nucleinbasen (Adenin, Thymin, Uracil, Cytosin) und ihren N-glycosidierten Derivaten (Adenosin, Thymidin, Uridin, Cytidin) wurden in Methanol-Ammoniak-Wasser – Mischungen mittels spektrophotometrischer Titration untersucht. Tetramethylpyridylporphyrin und sein Gadoliniumkomplex bilden 1:1-Komplexe mit Nucleinbasen und ihren Nucleosidderivaten. Die Gleichgewichtskonstanten wurden über *curve-fitting* – Algorithmen bestimmt. Die Wechselwirkungen sind für Nucleosidderivate stärker als für Nucleinbasen und für metallierte Porphyrine stärker als für nichtmetallierte.

Introduction

The intercalation of the water-soluble cationic *tetrakis*-(4-N-methylpyridyl)-porphyrine with *DNA* was first described by *Field et al.* [1, 2]. Since that time the interaction between nucleic acids and cationic porphyrins or their metal complexes has been investigated by many groups and by various techniques [3–7]. Also, the

interaction of tetramethylpyridylporphyrine and its divalent (Cu and Zn) and trivalent (Mn, Fe and Co) metal complexes with the building blocks of nucleic acids (nucleosides and nucleotides) has been further examined by UV/Vis, fluorescence, RR and NMR spectroscopy [8–14]. It was established that porphyrins without axial ligand or with one axial ligand interact stronger with nucleotides or nucleosides and intercalated *DNA* than porphyrins having two axial ligands which are bound nonintercalatively to *DNA*. Furthermore, the interaction of porphyrins with molecules of biological interest is important because of the selective accumulation of porphyrins in diagnosis and photodynamic treatment (PDT) of cancer [15, 16]. Gadolinium(III) porphyrins are particularly interesting due to the paramagnetic properties of Gd^{3+} ions inserted into the N_4 porphyrin plane. Such compounds could operate as so called biological probes [17–19] and as potential MRI (magnetic resonance imaging) contrast agents [20].

The present paper describes the result assessing the interaction of the cationic free base *tetrakis*-(4-N-methylpyridyl)-porphyrine ($H_2TMePyP$) and their Gd(III) complex with some nucleoside bases (adenine, thymine, uracil, and cytosine) and their N-glycoside derivatives (adenosine, thymidine, uridine, and cytidine) in terms of UV/Vis absorption spectroscopy. Also, the interaction of these compounds with the Gd(III) complex of non-ionic tetraphenylporphyrin (Gd*TPP*) is analysed. A mixture of methanol, ammonia, and water was applied as a solvent. Use of this solvent was determined by the solubility of the compounds. The calculated association constants and the deviation from *Beer-Lambert*'s law were studied to elucidate the power of the interaction. The nature of the complexation between porphyrin and nucleic bases and their derivatives, and the question of whether Gd(III) as central metal is involved in complex formation are also considered. Fixing of the Gd(III) porphyrins into the building blocks of nucleic acid and further to material of biological relevance could be used as a paramagnetic probe in EPR diagnosis. This phenomenon could be also important if Gd(III) porphyrins are considered as photosensitizers in the PDT method.

Results and Discussion

The $H_2TMePyP$, Gd(III)*TMePy*(*acac*), and Gd(III)*TPP*(*acac*) solutions with a concentration range of 10^{-6}–10^{-5} mol·dm^{-3} in a 1:1 mixture of MeOH with 28% NH_3 in water were prepared just before measurements and spectrophotometrically titrated with saturated solutions of nucleic bases or their nucleoside derivatives in the same solvent. As it was difficult to find a common solvent for the analysed set of compounds, a study of the interaction with free-base tetraphenylporphyrin was neglected. Applying the buffers commonly used as a solvents in such a study was not possible as the charged gadolinium prophyrin complex is soluble in other solvents than neutral gadolinium porphyrin.

It is commonly assumed that porphyrins in a concentration range of 10^{-6}–10^{-5} mol·dm^{-3} do not agglomerate and follow *Beer-Lambert*'s law even in water solutions [8, 21, 22]. Examples of the spectra upon titration are depicted in Figs. 1 and 2. The spectra shown here were recorded from the measurement in a spectrophotometrical cell purged with nitrogen to prevent atmospheric CO_2 absorbtion by the solvent. Nucleic bases and their nucleoside derivatives do not have any bands

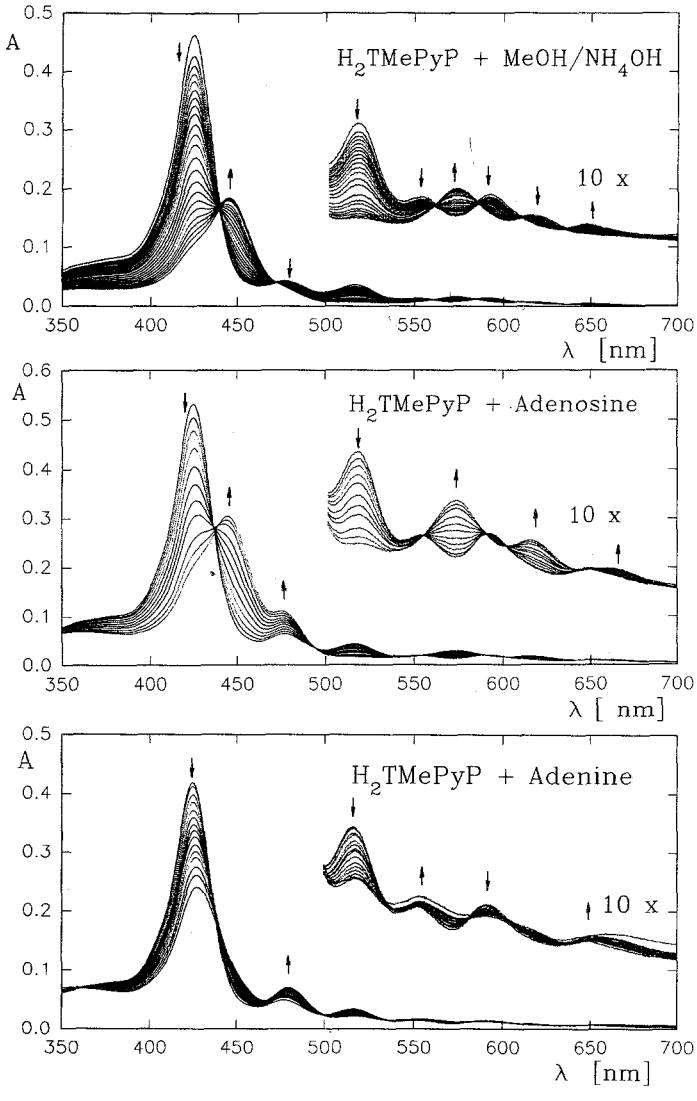


Fig. 1. Evolution of the absorption spectra occurring upon titration of: i) $2.8 \cdot 10^{-6}$ mol·dm^{-3} methanol-ammonia-water solution of $H_2TMePyP$ with solvent, ii) $3.3 \cdot 10^{-6}$ mol·dm^{-3} methanol-ammonia-water solution of $H_2TMePyP$ with 0.02 mol·dm^{-3} adenosine in MeOH/NH_4OH, iii) $2.6 \cdot 10^{-6}$ mol·dm^{-3} methanol-ammonia-water solution of $H_2TMePyP$ with 0.07 mol·dm^{-3} adenine in MeOH/NH_4OH

either in the *Soret* or in the Q-band region of the porphyrin spectra. Figure 1 shows the UV/Vis spectral changes that occur upon titration of a MeOH/NH_4OH solution of $H_2TMePyP$ with adenosine and adenine solution in the same solvent compared with titration of the pure solvent. It is known that the spectrum of $H_2TMePyP$ strongly depends on *pH*. The *Soret* band moves from 422 nm ($pH = 4$–7) to 450 nm ($pH = 14$) [23]. The evolution of $H_2TMePyP$ upon a MeOH/NH_4OH titration looks like a *pH* dependence; however, upon titration the porphyrin with the solvent the *pH* does not change. The variations of the spectra going through the isosbestic points are due to the porphyrin monoanion formation as described by *Hambright* [24] for the titration of $H_2TMePyP$ with NaOH in water: $H_2P + OH^- \leftrightarrow HP^- + H_2O$.

The same reaction takes place after dissolving crystals of $H_2TMePyP$ in MeOH/NH_4OH. In fact, the dependence of the spectra upon solvent titration is essentially the same as the dependence of the spectra obtained in the "time run" of

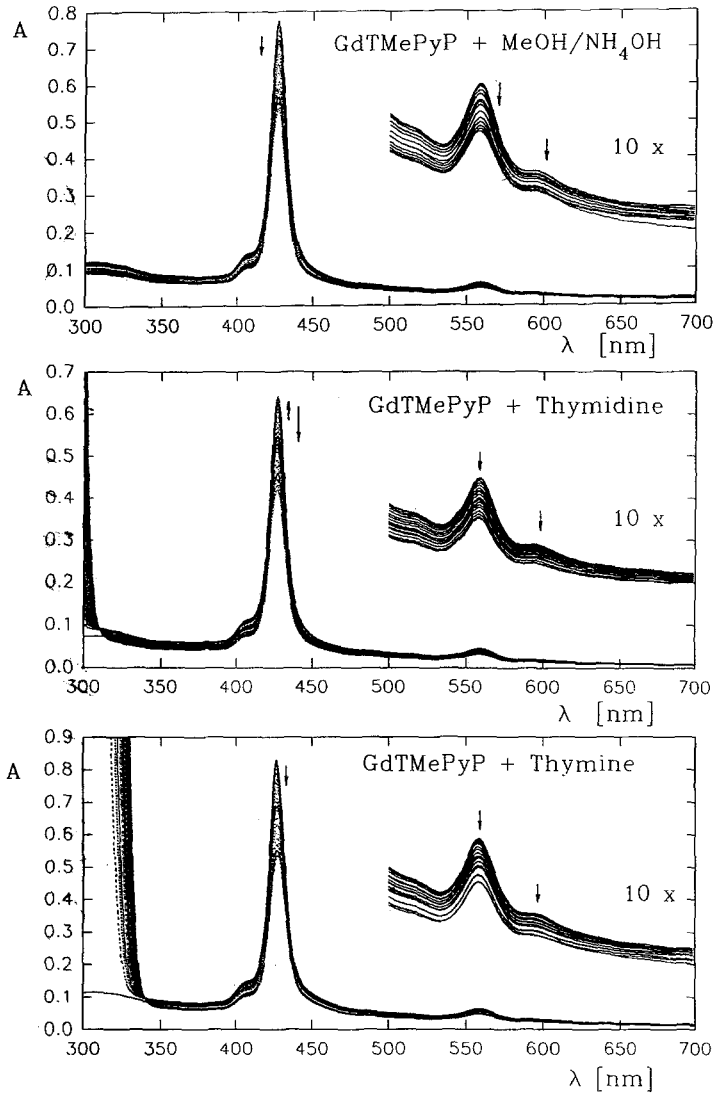


Fig. 2. Evolution of the absorption spectra occurring upon titration of: i) $1.5 \cdot 10^{-5}$ mol·dm^{-3} methanol-ammonia-water solution of Gd*TMePyP*(*acac*) with solvent, ii) $1.0 \cdot 10^{-5}$ mol·dm^{-3} methanol-ammonia-water solution of Gd*TMePyP*(*acac*) with 0.04 mol dm^{-3} thymidine in $MeOH/NH_4OH$, iii) $1.6 \cdot 10^{-5}$ mol·dm^{-3} methanol-ammonia-water solution of Gd*TMePyP*(*acac*) with 0.12 mol·dm^{-3} thymine in $MeOH/NH_4OH$

freshly prepared solutions. The process of monoanion formation is very slow (reaction is complete after two hours). This phenomenon can be at first approximation neglected in our consideration of complex formation between $H_2TMePyP$ and adenine or adenosine, especially since changes of the absorbance the exact wavelength of the *Soret* band has been taken into account for the association constant calculation. Additionally, during solvent titration there is no shift of the *Soret* band (422 nm) until the formation of the monoanion band about 450 nm. Such a shift can be observed for the $H_2TMePyP$ titration with adenosine and adenine (Fig. 1). The evolution of the spectra is different from that which occurs during

dilution of the porphyrin solution. The *Soret* band of the starting solutions are red-shifted from 424.4 to 426.8 nm (adenosine titration) and from 424.4 to 427.6 nm (adenine titration) before the monoanion band formation. For the adenine titration, we did not observe the monoanion band formation at 450 nm. Also, the isosbestic points are observed at different wavelengths with respect to solvent titration. Spectral changes upon $H_2TMePyP$ titration with nucleic bases or their nucleoside derivatives indicated that a process of molecular complex formation takes place; however, the interactions are rather weak, as formation of new bands was not observed.

The coordination chemistry of water soluble lanthanide porphyrins is a relatively unexplored area [25–28]. We report herein for the first time the absorption spectrum of Gd(III) *TMePyP(acac)*. The dilution tests for Gd*TMePyP(acac)* (Fig. 2) and Gd*TPP(acac)* obey *Beer-Lambert*'s law. This spectrum is similar to that known for the tetramethylpyridylporphyrin complexes of Pr and Sm [29, 30]. Figure 2 shows the absorption spectra of a Gd(III) *TMePyP* solution in $MeOH/NH_4OH$ upon titration with solvent, thymidine, and thymine. The evolution of the gadolinium porphyrin spectrum differs from that for the free base porphyrin. Neither shift or new band formation nor isosbestic points (excluding the one arising from increasing nucleoside concentration) has been observed. Only absorbance changes at the *Soret* band for the solvent and some nucleosides indicate a possible association between porphyrin and these nucleosides. In few cases, the absorbance increased at the beginning of the titration. Spectral changes during Gd(III) *TPP* titration with nucleic bases or their nucleosides are very similar to those obtained for Gd(III) *TMePyP*. Only changes in absorbance have been observed.

To decide if interactions between porphyrins and nucleic bases or nucleosides occur, the observed absorbance change at the *Soret* band during titration with nucleic bases or their nucleoside derivatives was plotted against the molar concentration of the porphyrins and compared with absorbances calculated using *Beer-Lambert*'s law. The calculated plot shows how absorbance would change with the assumption that interaction does not take place and only a dilution effect is observed. These plots were compared with identical plots for titrations with pure solvents. Examples are shown in Figs. 3a and 3b. The linearity of the plots was controlled using linear regression (data are presented in Table 1). In cases where no interactions take place, the slopes of the observed and calculated straight lines are almost identical, whereas those of interacting pairs of compounds are different. The significant difference between the calculated and the observed slope for the $H_2TMePyP$ solvent titration arises from monoanion formation. More significant for $H_2TMePyP$ is the comparison of the slope from solvent titration and the slope of ligand titration, rather than the comparison of observed and calculated slope. Also, observed linear regression coefficients (R^2) have lower values for interacting than for non-interacting pairs of compounds. The presented experimental results show that, as a first approximation, deviation from the linearity of *Beer-Lambert*'s law plots can be used as a measure of interaction between porphyrins and nucleosides.

For the porphyrin interacting with nucleic bases or their glycoside derivatives according to

$$P + L = PL \overset{L}{=} PL_2 \overset{L}{=} PL_n, \qquad 1$$

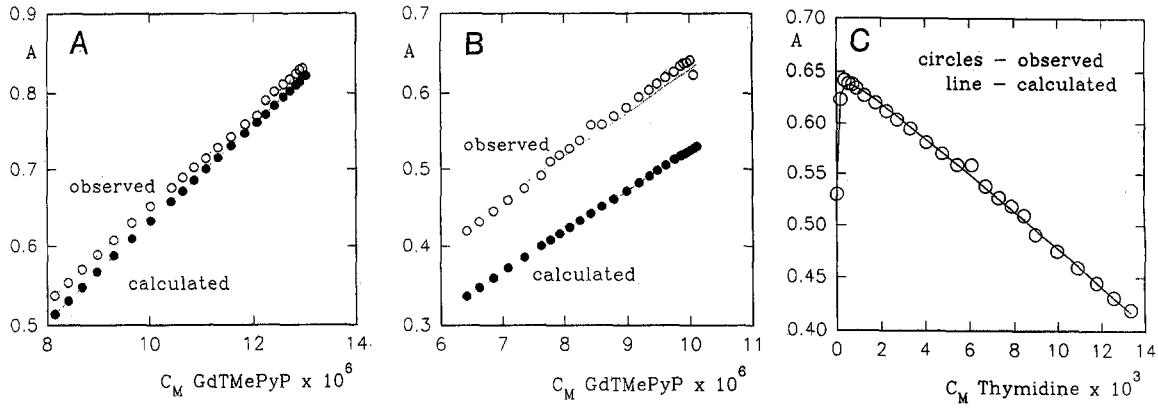


Fig. 3. a, b Plot of the absorbance change at the *Soret* band of Gd*TMePyP(acac)* upon titrations with thymine (A; no interaction) and with thymidine (B; complex formation) *vs.* c_M of porphyrin (○-observed points, ●-calculated from *Beer-Lambert*'s law); **c** plot of the absorbance change at the *Soret* band of Gd*TMePyP(acac)* upon titration with thymidine *vs.* c_M of thymidine; circles are experimental points; the theoretical curve is generated from equation 3

the equilibrium constants (K_n) can be written as

$$K_n = \frac{[PL_n]}{[PL_{n-1}]\cdot[L]} \qquad 2$$

To find out the stoichiometry of the reaction and to evaluate the magnitude of the nucleotide and porphyrin binding constants, the expression derived from the *Niels Bjerrun* complex formation function [31, 32] was used, where A is the absorbance ε_0 is the molecular absorbance coefficient for the starting porphyrin ε_1 and K_1, ε_2 and K_2,..., *etc.* are molecular absorbance coefficients and stability constants for complexes with the stoichiometry 1:1, 1:2,..., *etc.*, respectively and $[L]$ and $[P_0]$ are the analytical concentrations of nucleic bases or their glycoside derivatives and porphyrins (with the assumption that $[L] \gg [P_0]$).

$$A = \frac{\varepsilon_0 + \varepsilon_1\cdot K_1\cdot[L] + \varepsilon_2\cdot K_1\cdot K_2\cdot[L]^2 + \cdots + \varepsilon_n\cdot K_1\cdot K_2 \ldots K_n\cdot[L]^n}{1 + K_1\cdot[L] + K_1\cdot K_2\cdot[L]^2 + \cdots + K_1\cdot K_2\ldots\cdot K_n\cdot[L]^n}[P_0] \qquad 3$$

For the calculation of the stability constants, the experimental data were fitted to equation 3 using the non-linear fitting procedure based on the *Marquardt-Levenberg* algorithm [33]. The fitting was performed for complexes with stoichiometries 1:1 and 1:2, but only results for 1:1 complexes (except cytosine – Gd(III) *TPP*) have a good accordance between calculated curve and experimental points. An example of the fitting is shown in the Fig. 3C where experimental points cover very well the theoretical curve generated from equation 3 for the 1:1 complex between Gd*TMePyP* and thymidine. The values of the association constants K for the analyzed complexes are presented in Table 2. The calculated formation constants are in good agreement with data known from the literature for the same of similar pairs of interacting compounds, despite the different solvent. For H_2*TMePyP* – adenosine and H_2*TMePy* – uridine, *Pasternack, Gaudemer et al.* [8] have found values of 640 and 200, compared to our result of 554 and 318 $mol^{-1}\cdot dm^3$.

Table 1. Comparison of the deviation from linearity of observed and calculated absorbance plots *vs.* c_M of porphyrins

Compounds	Slope (observed)	R^2 (observed)	Slope (calculated)	R^2 (calculated)
$H_2TMePyP$				
+ MeOH/NH_4OH	0.2729	0.9815	0.1620	0.9999
+ Adenine	0.2748	0.9594	0.1693	0.9999
+ Adenosine	0.5124	0.9325	0.1622	1.0000
+ Thymine	0.2505	0.9793	0.1622	1.0000
+ Thymidine	0.2112	0.9753	0.1623	1.0000
+ Uracil	0.3050	0.9222	0.1624	0.9999
+ Uridine	0.3318	0.9570	0.1622	1.0000
+ Cytosine	0.1746	0.9961	0.1621	1.0000
+ Cytidine	0.1770	0.9953	0.1621	0.9999
Gd*TMePyP(acac)*				
+ MeOH/NH_4OH	0.05231	0.9999	0.05275	1.0000
+ Adenine	0.04945	0.9971	0.05246	1.0000
+ Adenosine	0.05118	0.9994	0.05245	0.9997
+ Thymine	0.05172	0.9994	0.05322	0.9998
+ Thymidine	0.05621	0.9828	0.05246	1.0000
+ Uracil	0.04670	0.9976	0.05245	1.0000
+ Uridine	0.04569	0.9992	0.05250	1.0000
+ Cytosine	0.05317	0.9900	0.05247	1.0000
+ Cytidine	0.05197	0.9881	0.05249	1.0000
Gd*TPP(acac)*				
+ MeOH/NH_4OH	0.6386	0.9989	0.6280	0.9997
+ Adenine	0.6585	0.9923	0.6323	0.9999
+ Adenosine	0.6516	0.9981	0.6313	1.0000
+ Thymine	0.6187	0.9989	0.6303	0.9994
+ Thymidine	0.5244	0.9802	0.6315	0.9996
+ Uracil	0.6394	0.9665	0.6311	1.0000
+ Uridine	0.5614	0.9966	0.6309	1.0000
+ Cytosine	0.3709	0.9980	0.6304	0.9999
+ Cytidine	0.3908	0.9915	0.6312	1.0000

Values of the association constants from Table 2 favour the conclusion that for H_2TMePy the interactions with nucleoside derivatives are stronger than with nucleic bases. This conclusion may be expanded for Gd*TMePyP* and Gd*TPP*; however, high values of K (comparable with published data for similar compounds with Zn porphyrins [10] for some complexes suggest a completely different mechanism of complex formation. A comparison of association constants with pK_a of the protonated ligand demonstrate some relation only for the interaction of particular nucleic bases or their nucleosides with particular porphyrins: the lower the value of pK_1, the higher the value of the association constant. On the other hand, it is difficult to expect a straight correlation between pK_a and K for such a diverse set of ligands.

Table 2. Association constants ($mol^{-1} \cdot dm^3$) between porphyrins and some nucleosides and their N-glycoside derivatives compared with their pK_a values

	$H_2TMePyP$	$GdTMePyP(acac)$	$GdTPP(acac)$	pK_{a1} [Ref.]	pK_{a2} [Ref.]
Adenine	253 ± 20	258 ± 13	a	4.2 [37]	9.8 [38]
Adenosine	554 ± 70	686 ± 35	3831 ± 150	3.5 [37]	1235 [38]
Thymine	107 ± 15	a	a	9.90 [39]	–
Thymidine	414 ± 73	19149 ± 2890	582300 ± 6700	9.79 [39]	12.85 [39]
Uracil	325 ± 38	250 ± 10	23 ± 2	9.46 [39]	–
Uridine	318 ± 74	323 ± 12	362400 ± 4600	9.30 [39]	12.59 [39]
Cytosine	160 ± 39	a	$K_1 = 142 \pm 18$		
			$K_2 = 3.9 \pm 2$	4.58 [39]	12.15 [39]
Cytidine	155 ± 7	155 ± 70	206058 ± 7500	4.08 [39]	12.24 [39]

[a] An appreciable absorption change is not observed

We have tried to isolate the complexes from the solutions at least for combinations with high K values) using a common procedure [34], but our attempts were unsuccessful. We observed the dication $H_4(TMePyP)^{2+}$ formation for the combinations with free-base porphyrin, or demetallation followed by dication formation for complexes with the gadolinium porphyrins.

It is not easy to answer the question about the nature of the analyzed set of the porphyrin-nucleoside complexes. The following phenomena must be taken into consideration:

(i) *Electrostatic interaction.* This mechanism is relatively well discussed in the literature for complexes with $H_2TMePyP$ [8, 10–12, 14]. However the participation of other interactions as charge transfer can not be neglected. Such a interaction is probably involved also in complex formation between $GdTMePyP$ and adenine, uracil, adenosine, uridine, or cytidine. Possible two-point fixation *via* coordination and hydrogen bonding must also be considered. For thymine and cytosine, an appreciable change in absorption spectra has not been observed. A surprisingly high value of K for the $GdTMePyP$-thymidine complex suggests that a ligand exchange mechanism may be also involved in complex formation.

(ii) *Ligand exchange.* $GdTPP(acac)$ forms very strong complexes with nucleosides, whereas it does not form complexes with nucleic bases (with the exception of cytosine). This can suggest that acetylacetonate, which plays the role of an axial ligand in the gadolinium complex, is substituted by the nucleoside. Such a mechanism is possible for tetraphenylporphyrin, but hindered by charged peripherals in the case of tetramethylpyridylporphyrin. This process is connected with an additional coordination of Gd(III). The existence of a coordination number higher than six is quite normal in the chemistry of lanthanide complexes. It means that the coordination sphere of gadolinium may be not entirely saturated by the tetradentate porphyrin ring and the bidentate acetylacetonate. This is confirmed by the formation of a 1:2 complex between $GdTPP(acac)$ and cytosine (and the magnitude of its K_1 and K_2), inasmuch as cytosine may be treated as unidentate ligand. It would be difficult to expect electron donation from nitrogen atoms under such conditions.

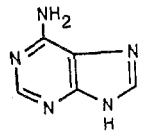
(iii) *Electron charge transfer adduct formation.* Although both nucleosides and porphyrins are considered to be electron donors rather then acceptors, some contribution of this effect to complex formation cannot be entirely neglected. A very low value of K for the Gd*TPP*(*acac*)–uracil adduct suggests that this mechanism may play a dominant role here.

As a conclusion, we can say that H_2*TMePyP* forms 1:1 complexes with nucleic bases and their nucleoside derivative. Gd(III)*TMePyP*(*acac*) and Gd(III)*TPP*(*acac*) form 1:1 complexes with all analyzed nucleosides, whereas such regularity was not observed for nucleic bases. Gd*TMePyP*(*acac*) does not form a complex with either thymine or cytosine. Gd*TPP*(*acac*) forms a very weak 1:1 compound with uracil and a 1:2 complex with cytosine. This is probably caused by a different mechanism of complex formation. The complexes formed between porphyrins and nucleic bases are weaker than complexes formed between porphyrins and nucleoside derivatives of these nucleic bases. Also, complexes of gadolinium porphyrins are stronger than complexes with free-base porphyrin. The last fact can be of advantage for the potential use of these compounds as a metal carriers to material of biological importance or as photosensitizers in photodynamic tumor therapy.

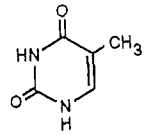
Experimental

Materials

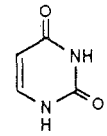
5,10,15,20-*Tetrakis*-(1-methyl-4-pyridyl)-21*H*,23*H*-porphin tetra-*p*-tosylate salt (H_2*TMePyP*), 5,10,15,20-tetraphenyl-21*H*,23*H*-porphyrin (H_2*TPP*), 6-aminopurine (adenine), cytosine, 2,4-dihydroxy-5-methyl-pyrimidine (thymine), 2,4(1*H*,3*H*)-pyrimidinedione (uracil), 9-(α-*D*-ribofuranosyl)-adenine (adenosine), cytidine, thymidine, uridine (Scheme 1): obtained from Aldrich, used without additional purification. Gadolinium(III) acetylacetonate hydrate (Strem Chemicals) and 1,2,4-trichlorobenzene (Merck) were also used without further purification. Neutral Al_2O_3 (activity 90, 70–230 mesh, Merck) was used for column chromatography. All solvents used were certificated as purex for analysis grade.



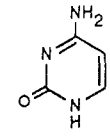
Adenine



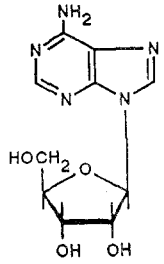
Thymine



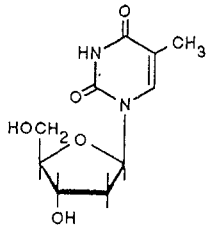
Uracil



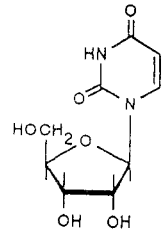
Cytosine



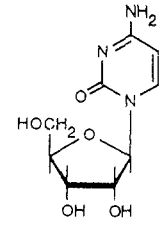
Adenosine



Thymidine



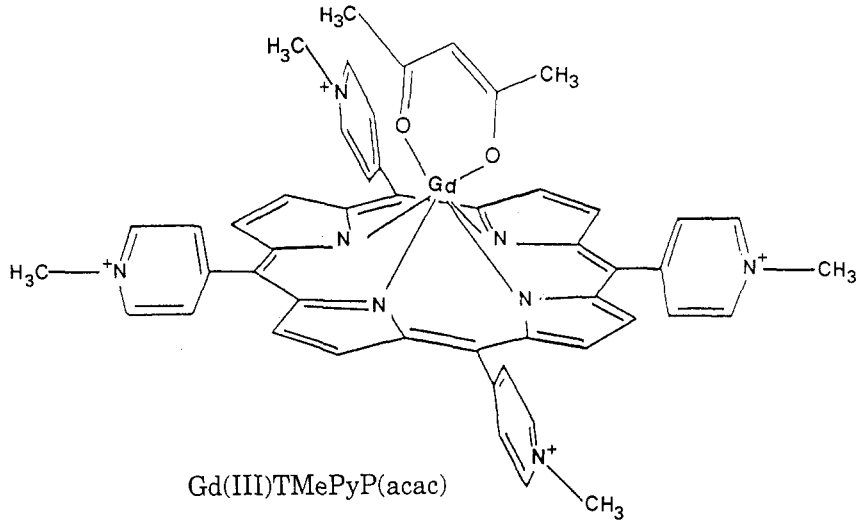
Uridine



Cytidine

Synthesis

Gd(III)tetraphenylporphyrine (Gd(III)*TPP(acac)*, H*acac* = acetylacetone) was prepared according to a procedure described earlier [35]. The tetramethylpyridylporphyrin complex of gadolinium (Gd(III)*TMePyP(acac)*, Scheme 2) was prepared by the method described originally by *Horrocks* and *Wong* [25, 26] and later modified by other authors [29, 36]. A mixture of hydrated Gd(*acac*)$_3$ (300 mg) and free-base porphyrin (100 mg) in 1,2,4-trichlorobenzene was heated at reflux under argon for 4 hours. After completion of the reaction, the 1,2,4-trichlorobenzene was removed by evaporation under reduced pressure. The solid residue was vacuum dried overnight, dissolved in MeOH/CH_2Cl_2, and applied to the top of an Al_2O_3 column. The unreacted free-base porphyrine was eluted first with pyridine and then with a mixture of toluene and MeOH (98.2, vol/vol). The pure Gd(III)*TMePyP(acac)* was eluted with *DMSO*. The solvent was removed by vacuum evaporation and the solid residue was washed with acetone. The final product, after vacuum drying overnight, was obtained as an amorphous powder. Calc. for Gd(III)*TMePyP(acac)*·$8H_2O$ ($GdC_{77}H_{87}N_8O_{22}S_4$): C, 52.49; H, 4.98; N, 6.36; found: C, 53.08; H, 4.81; N, 6.06%; UV/Vis (MeOH/NH_4OH, λ_{max} (logε)): 426.5 (4.72), 558.5 (3.82), 596.0 (3.58).



Gd(III)TMePyP(acac)

Measurements

Absorption spectra were taken with a Perkin Elmer Lambda 7 spectrophotometer using 1 cm quartz cells to record in the 300–700 nm region at a temperature of 21 ± 1 °C. Spectra were stored on disk under control of the Perkin Elmer program PECSS. The database program SigmaPlot was used for manipulation and plotting of the data [33].

Method

Control of complex formation, stoichiometry, and equilibrium constants for nucleic bases or nucleosides binding to gadolinium porphyrins were determined by a spectrophotometric procedure. A 1:1 mixture of methanol and 28% NH_3 in water was used as solvent. The nucleic base or nucleoside solutions were added in increments to 2 ml of nitrogen purged MeOH/NH_4OH solutions of porphyrins in a covered 10 mm spectrophotometric cell equipped with a magnetic stirrer using a Hamilton syringe until no further change in the spectrum (except dilution effects) could be observed. In parallel experiments, pure solvents were added in the same increments to solutions of porphyrins with the same concentrations.

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