

# Intramolecular charge transfer excitation of *meso*-tetrakis (1-pyrenyl) porphyrinato gold(III) acetate. Photosensitized oxidation of guanine

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## Abstract

The novel cationic gold porphyrin complex  $[(\text{TPYRP})\text{Au}^{\text{III}}]^+\text{CH}_3\text{COO}^-$  with TPYRP = dianion of 5,10,15,20-tetrakis(1-pyrenyl)porphyrin was prepared and characterized by optical spectroscopy and high-resolution electrospray mass spectrometry. In addition to metalloporphyrin intraligand transitions, the compound shows charge transfer (CT) absorptions in the visible spectral region that are sensitive to variations of the solvent polarity. The photoreactivity of an intramolecular charge separated state of the photosensitizer populated by CT excitation was investigated in the presence of dioxygen and an excess of the purine nucleobase guanine. A photocatalytic oxidative degradation of guanine with a quantum yield of  $0.03 \pm 0.01$  and an initial turnover frequency of 66 per hour was observed upon irradiation with monochromatic visible light at 298 K. The potential of the cationic metallointercalator complex  $[(\text{TPYRP})\text{Au}^{\text{III}}]^+$  to serve as a catalytic photonuclease for the sequence specific cleavage of DNA has been demonstrated. © 2001 Elsevier Science B.V. All rights reserved.

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Nucleobase modifications and irreversible DNA damage following the exposure of cells to free radicals and oxidative stress are considered as major factors in aging, inflammatory disease and cancerogenesis [1–5]. Unraveling the molecular mechanisms of these processes in vitro is attracting significant attention because of their key role for the rational design of specific chemotherapeutics, diagnostic agents and artificial restriction enzymes [6–9]. The heterocyclic bases are the most reactive moieties of nucleic acids, and it is generally accepted that the purine base guanine (G) is the site of lowest ionization potential in DNA [10–12]. Acting as a hole trap in long-range electron transfer reactions, guanine is oxidized to the intermediate radical cation  $\text{G}^+$ , which gives rise to permanent lesions that enable a sequence specific DNA strand scission [13–17]. Photoinduced formation of guanine radical cations [18–21] and the development of synthetic nucleic acid cleavage agents which can be controlled by light (photonucleases [22]) are therefore active areas of current research. In this

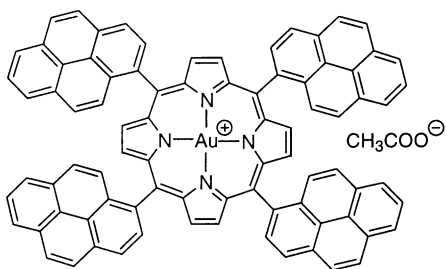
context, a novel metallointercalator complex has been designed as a potentially cytotoxic photosensitizer, which combines the high DNA binding affinities of cationic porphyrins [23–26] and polycyclic aromatic hydrocarbons [27–29] with the prodrug properties of gold-based chemotherapeutic agents [30–32].

The title compound tetrakis (1-pyrenyl) porphyrinato gold(III) acetate (Chart 1) was prepared by metallation of the atropisomeric mixture [33] of the novel free-base porphyrin ligand  $\text{H}_2(\text{TPYRP})$  with  $\text{AuCl}_4^-$  in glacial acetic acid according to the literature method reported for the gold(III) complex of tetraphenylporphyrin [34]. The nature of the counterion was confirmed by high-resolution electrospray mass spectrometry. <sup>1</sup>The optical spectrum (Fig. 1) of the ligand  $\text{H}_2(\text{TPYRP})$  in dichloromethane is characterized by an intense *B* (Soret) band at  $\lambda_{\text{max}} = 430 \text{ nm}$  ( $\epsilon = 4.14 \times 10^5 \text{ M}^{-1} \text{ cm}^{-1}$ ) and a pattern of four less intense *Q*-bands in the visible spectral region typical for nonmetallated *meso*-aryl substituted porphyrins. As expected for gold(III) porphyrin

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<sup>1</sup> ES-MS:  $[(\text{TPYRP})\text{Au}](\text{OAc})$ ,  $m/z$  1305.4 ( $\text{M}-\text{OAc}^-$ ), 70%, calc. 1305.32 ( $\text{C}_{84}\text{H}_{44}\text{N}_4\text{Au}$ );  $m/z$  1364.3 ( $\text{M}$ ), 100%, calc. 1364.36 ( $\text{C}_{86}\text{H}_{47}\text{N}_4\text{O}_2\text{Au}$ ).



[(TPYRP)Au](OAc)

Chart 1.

derivatives, which display *hypso*-type metalloporphyrin spectra [35] a considerably blue-shifted Soret band at  $\lambda_{\max} = 407$  nm ( $\epsilon = 2.82 \times 10^5$  M<sup>-1</sup> cm<sup>-1</sup>) and two blue-shifted *Q*-bands at  $\lambda_{\max} = 528$  nm and 593 nm are present in the electronic absorption spectrum of [(TPYRP)Au<sup>III</sup>](OAc) in dichloromethane.

The ultraviolet part of the spectra of both the free-base ligand and the gold(III) complex (Fig. 1) consists of an almost identical band pattern with a prominent vibronic structure that clearly corresponds to the strong dipole-allowed intraligand  $\pi\pi^*$  transitions localized at the pyrenyl moieties, which are orientated nearly perpendicular to the porphyrin plane [33]. In dichloromethane solution the absorption bands of [(TPYRP)Au<sup>III</sup>](OAc) are only very little perturbed with respect to a superposition of the spectra of the model components pyrene [36] and gold(III) tetraphenylporphyrin [34], indicating a negligible electronic coupling between the metalloporphyrin core and the attached *meso*-1-pyrenyl substituents.

The complex [(TPYRP)Au<sup>III</sup>](OAc) displays a conspicuous solvatochromic behavior suggesting the presence of charge transfer (CT) interactions. The maxima of the Soret band are shifted from  $\lambda_{\max} = 415$  nm in toluene to  $\lambda_{\max} = 403$  nm in acetonitrile solution. At the same time, in polar solvents a considerable broadening of the Soret band is observed, which is accompanied by

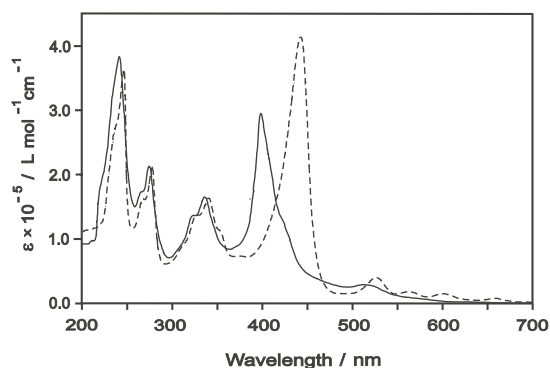


Fig. 1. Electronic absorption spectra of the free-base porphyrin ligand H<sub>2</sub>(TPYRP), (---), and the gold complex [(TPYRP)Au<sup>III</sup>](OAc), (—), in CH<sub>2</sub>Cl<sub>2</sub> solution at 298 K.

a relative increase in intensity of the poorly resolved shoulders in the visible region of the gold(III) porphyrin absorption spectrum (Fig. 1). The occurrence of a very weak  $\pi d^*$  ligand-to-metal charge transfer (LMCT) transition in water soluble gold porphyrin complexes has been reported previously [37].

Besides this weak LMCT band around 450 nm, which is covered by more intense absorptions and therefore could not be assigned unambiguously in the present case, the optical spectrum of [(TPYRP)Au<sup>III</sup>](OAc) shows an additional strong CT interaction, which is not occurring in the spectra of the reference compound gold(III) tetraphenylporphyrin and other gold porphyrin complexes. These additional spectral features are ascribed to the attachment of the pyrenyl subunits, which can act as electron donors in molecular assemblies containing metalloporphyrin compounds that are easily reduced to their corresponding radical anions [33,38]. The complex [(TPYRP)Au<sup>III</sup>](OAc) consists of weakly coupled oxidizing and reducing parts, giving rise to a typical intraligand charge transfer (ILCT) transition [39] from a pyrenyl substituent to the metalloporphyrin core. Upon long-wavelength irradiation in the region of this broad ILCT band, a charge separated state consisting of a pyrenyl radical cation Pyr<sup>+</sup> and a gold(III) porphyrin radical anion (P<sup>-</sup>)Au is formed as a consequence of the direct optical electron transfer process. The intermediate radical ion pair generated by intramolecular CT excitation of [(TPYRP)Au<sup>III</sup>](OAc) can undergo rapid charge recombination to the electronic ground state or participate in secondary redox processes in the presence of suitable substrates. A comparison with published electrochemical data shows that pyrene is oxidized to Pyr<sup>+</sup> at +1.48 V (vs NHE) in acetonitrile solution [40], while the nucleobase guanine (G) is oxidized to the radical cation G<sup>+</sup> at +1.29 V (vs NHE) [17], which enables an exergonic electron transfer from guanine bases to pyrenyl radicals. Since the ligand H<sub>2</sub>(TPYRP) was designed for the recognition of nucleic acids [33], the photosensitized formation of an intercalated pyrenyl radical substituent of the [(TPYRP)Au<sup>III</sup>](OAc) complex represents an attractive approach to induce oxidative damage to DNA with visible light. We explored this possibility and studied the photochemistry of the gold(III) porphyrin complex in the presence of the nucleobase guanine (Fig. 2). When a solution of [(TPYRP)Au<sup>III</sup>](OAc) and an excess amount of the purine base was irradiated with 436 nm light,<sup>2</sup> a rapid permanent bleaching of the

<sup>2</sup> Photolyses were carried out in stoppered 1 cm quartz spectrophotometer cells with a Hanovia Xe/Hg 977 B-1 (1 kW) lamp. Monochromatic light was obtained using a Schoeffel GM 250/1 high-intensity monochromator. Absorbed light intensities were determined by a Polytec pyroelectric radiometer which was calibrated by actinometry and equipped with a RkP-345 detector.

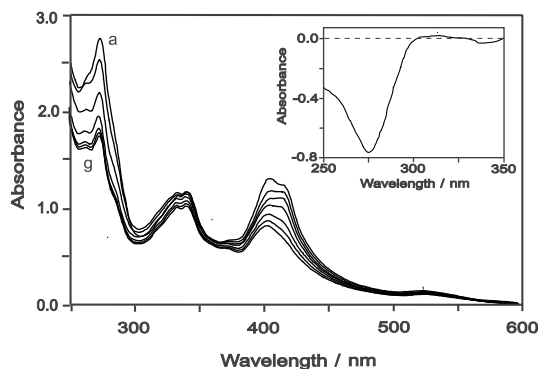


Fig. 2. Spectral variations during monochromatic photolysis of a mixture of 2.5 ml of  $1.1 \times 10^{-5}$  M [(TPYRP)Au<sup>III</sup>](OAc) in CH<sub>3</sub>CN, 0.4 ml H<sub>2</sub>O and 0.2 ml of  $2.0 \times 10^{-3}$  M guanine in 0.1 M aqueous NaOH. Subsequent curves were recorded at (a) 0, 2, 5, 10, 20, 30 and (g) 40 min of exposure to  $\lambda_{irr} = 436$  nm (298 K, 1-cm cell). The inset shows an absorbance difference spectrum for  $\Delta t = 10$  min of irradiation time.

guanine absorption at  $\lambda_{max} = 275$  nm ( $\epsilon = 8.09 \times 10^3$  M<sup>-1</sup> cm<sup>-1</sup>) was observed. Within the first 10 min of photolysis (Fig. 2) more than 75% of the initial amount of guanine disappeared with a quantum yield of  $0.03 \pm 0.01$  determined from the spectral changes under aerobic conditions. During steady state photolysis, a continuous bleaching of the [(TPYRP)Au<sup>III</sup>](OAc) complex occurred with a quantum yield of  $2 \times 10^{-4}$ , which is considerably lower than that of guanine oxidation and indicates a photocatalytic behavior of the system. Obviously, the gold(III) porphyrin radical anion resulting from reductive quenching of the photoexcited sensitizer with guanine is partially re-oxidized by O<sub>2</sub> as was observed before with other electrochemically generated (P<sup>-</sup>)Au species [37]. An initial turnover frequency of  $TOF(G^{+}) = 66$  per hour for guanine oxidation and a maximum number of possible catalytic cycles of approximately 700 for each [(TPYRP)Au<sup>III</sup>](OAc) molecule are estimated from the quantum yield data. Thus, in summary it has been demonstrated that this system has the potential to serve as a novel type of catalytic photonuclease for the long-wavelength sensitized cleavage of DNA and other guanine containing nucleic acids.

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