Supramolecular assembling of the cationic complex (2,2′:6′,2″-terpyridine)methylplatinum(II) ion on α-helical poly(L-glutamic acid)

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The cationic organometallic platinum(II) complex ion [Pt(terpy)Me]$^+$ aggregates on α-helical poly(L-glutamic acid) through a multistep process leading to highly organised supramolecular assemblies.

Planar dyes, such as porphyrins and acridines, bind to helical biopolymers leading to adducts which exhibit induced circular dichroism (ICD) in the wavelength region where the bound molecules absorb light.[1–3] The biological matrix acts as a template support for the formation of short- or long-range organised assemblies of chromophores, stabilised by an interplay of electrostatic, hydrogen bonding and dispersive forces. Different types of biopolymers have been reported to behave as template systems including double-stranded DNA,[3] single-stranded DNA and RNA[4] and polypeptides.[5,6] The kinetics of the supramolecular aggregation are in general multiphasic[7] and the use of simple matrices offers a way of reducing the difficulty in assessing the mechanism of interaction. In this respect, poly(glutamic acid) is an interesting biopolymer, because the only interaction modes are electrostatic and hydrogen bonding. Furthermore, it undergoes a transition from α-helix to random-coil above pH 5[8] so that it is possible to control the structure and the nature of the resulting adduct by modulating the pH and the ionic strength.

In a previous study,[9] we reported on the strong tendency for self-aggregation of the complex ion [Pt(terpy)Me]$^+$ **1** in contrast with the well studied [Pt(terpy)(het)]$^+$ (het = 2-hydroxyethanethiolate).[10] The addition of low concentrations of nucleic acids, such as DNA[9] or single-stranded poly(rA),[11] leads to a distribution of complex **1** between its free self-aggregated form in solution and on the backbone of the DNA. The very weak ICD and resonance light-scattering (RLS)[12] signals of these adducts indicate that the aggregation on these matrices is not well structured over extended lengths.

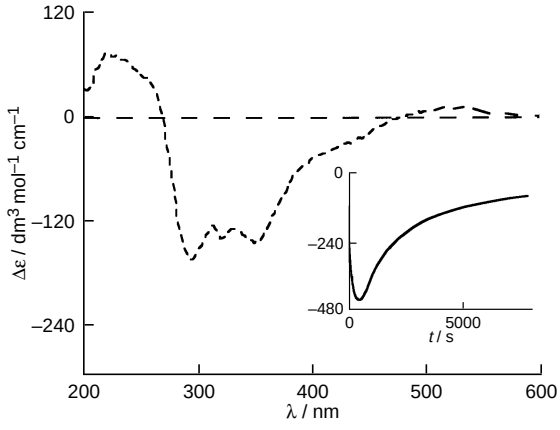
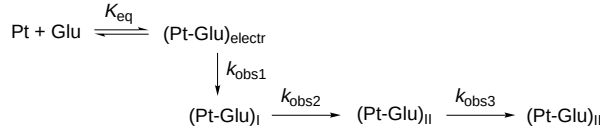


Fig. 1 CD spectrum of the final adduct between the complex [Pt(terpy)-Me]Cl and poly(L-glutamate). The inset shows the kinetic trace recorded at 280 nm. Experimental conditions: [Pt] = 2.5×10^{-5} M, [Glu] = 5×10^{-5} M, pH 4.5 in 5 mM acetate buffer, T = 298 K. (k_{obs1} = 0.25 ± 0.03 s^{-1}, k_{obs2} = 0.016 ± 0.002 s^{-1}, k_{obs3} = 0.0008 ± 0.0001 s^{-1}, as derived from the best fitting analysis of the overall kinetic trace, see text).

Here we report a preliminary kinetic investigation of the interaction between **1** and the poly(L-glutamic acid) in the α-helical conformation. To the best of our knowledge this is the first example of a supramolecular aggregate formed by an organometallic platinum(II) complex.

On adding a solution of complex to a prethermostated solution of poly(L-glutamic acid) at pH 4.5,† the absorption spectrum shows an instantaneous and small bathochromic shift (< 2 nm) associated with a slight hypochromicity of the 313 and 331 nm bands of the complex. The spectral changes are rapidly masked by an increase in Rayleigh scattering. The time behaviour of the scattered intensity can be monitored by conventional light-scattering techniques and shows an initial rapid increase followed by slower steps. The time evolution of the process can be monitored more conveniently by CD spectroscopy (Fig. 1). On addition of the polymer, the sequence of CD spectra reveals a multiphasic process which involves the formation of at least four different species (Scheme 1), characterised by large values of $\Delta\varepsilon$ (*ca.* −180 dm^3 mol^{-1} cm^{-1} at 300 nm for the final adduct). Kinetic runs were performed at 280 nm (inset in Fig. 1) and were analysed as three coupled consecutive first-order steps. The initial CD spectral change is faster than the mixing time.



Scheme 1

The observed rate constants (k_{obs1}, k_{obs2}, k_{obs3}) exhibit a bell-shaped dependence on the concentration of the polymer (Fig. 2). The k_{obs} values increase to reach a maximum corresponding to a ratio r_f = 0.5 (r_f = [Pt]$_o$/[poly(Glu)]$_o$). Therefore, when the concentration of the matrix is below a threshold, an increase of its concentration determines an acceleration of the rates, as a result of the increased availability of binding sites. A further increase of the concentration provokes a dispersion of the complex on the matrix and leads to a decrease in the rate. A similar concentration dependence is shown by the intensity of the ellipticity corresponding to the final adduct. In order to establish the importance of the α-helical conformation of the polymer, the dependence of the kinetic rate constants and ellipticity intensities on the pH was investigated. It has been found that these parameters exhibit, also in this case, a bell-shaped profile with the maximum centred at pH 4.5 and 4.8 for the rate and the ellipticity, respectively. An experiment performed at pH 7.0, well above the helix to coil transition, showed that the ICD spectrum is very weak and it is reversed in phase with respect to lower pH.[13]

According to the experimental findings, the following mechanism can be suggested (see Scheme 1). The first step

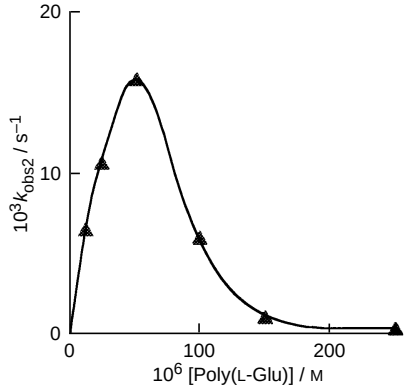


Fig. 2 Dependence of the observed first-order rate constant (k_{obs2}/s^{-1}) for the second stage of the assembling on the concentration of poly(L-glutamate) (in molar glutamate residues). Experimental conditions: [Pt] = 2.5×10^{-5} M, pH 4.5 in 5 mM acetate buffer, 298 K.

involves a fast electrostatic pre-equilibrium between oppositely charged species leading to a low-ordered adduct. The fairly high initial value of the ellipticity suggests the formation of dimers or higher aggregates (nucleation step). These small aggregates serve as promoters for the subsequent growth of the assembly. The following steps can be ascribed to conformational re-arrangements owing to changes in the relative orientation of the chromophores with respect to the matrix backbone or to a conformational change of the matrix itself caused by the aggregation.[14]

The reaction intermediate $(Pt–Glu)_{II}$ and the final adduct are characterised by large values of ellipticity. The value of $|\Delta\varepsilon/\varepsilon| \approx 2.3\%$ for the final adduct and resonance light scattering measurements[12] indicate the presence of extended arrays of strongly coupled chromophores forming a highly organised assembly in which the biopolymer acts as a template matrix.[5] A structural model for the supramolecular assembling can be inferred from the presence of maxima in the rate and ellipticity profiles, as shown by the glutamate concentration and pH dependences. At pH 4.5 the negative charges on the side chains are half-neutralised and, given the observed maxima at $r_f = 0.5$, a stoichiometric ratio of 1 : 1 (cationic complex to unprotonated glutamate residues) is indicated. Taking into account the translational rise of 1.5 Å for a residue in the α-helix,[15] it is possible to assume the presence of a negative charge every 3 Å. This distance is that expected for π–π stacking interactions between two terpyridine moieties.[16] Therefore, we are inclined to think that the polypeptide acts as template support to form an α-helix of chromophores, which is stabilised by electrostatic interactions with the polymer and by π–π stacking interactions between the aromatic region of the complexes.

The remarkable tendency to give supramolecular assemblies is peculiar to $[Pt(terpy)Me]^+$, as demonstrated by the fact that the closely related cation $[Pt(terpy)Cl]^+$, under the same experimental conditions, does not lead to any organised adduct. The higher hydrophobicity together with the higher extent of electron density on the metal center, in the case of the organometallic species, could be responsible for this behaviour.

The possibility of tuning the electronic and steric properties of the chromophore‡ and of the supporting biopolymer opens the way to control the molecular recognition between the interacting species.

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Footnotes

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† Poly(L-glutamic acid) was obtained from Sigma as its sodium salt ($M_W \approx 13\,600$; polydispersity = 1.2). The pH of the reaction mixtures was adjusted to the desired value using 5 mM acetate buffer.

‡ The organometallic compound [Pt(Phterpy)Me]Cl (Phterpy = 4′-phenyl-2,2′ : 6′,2″-terpyridine), under the same experimental conditions, leads to ICD spectra four times less intense than those of complex **1**, as a consequence of the steric congestion brought about by the phenyl substituent on the terpyridine ring. Steric effects are crucial in determining the behaviour of the complexes [Pt(terpy)Ph]Cl and [Pt(Phterpy)Ph]Cl, where the phenyl ring is directly bound to the metal center and out of the coordination plane. These latter compounds show no detectable interaction with the polypeptide.

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