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Review

Transient absorption and time-resolved vibrational studies of photophysical and photochemical processes in DNA-intercalating polypyridyl metal complexes or cationic porphyrins

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ABSTRACT

Recent advances in the use of transient absorption (TA) and time-resolved vibrational spectroscopies (TRIR and TR^3) to study both excited states and reaction intermediates in metal complexes and porphyrins which intercalate into DNA are reviewed. A particularly well-studied class of compounds, which nicely illustrates the comparative advantages of these techniques, is that of ruthenium dppz complexes where the complex might show light-switching or photo-oxidising behaviour depending on the nature of the ancillary ligand. Comparative data on Re- and Cr-dppz complexes are also considered. In the second part of this review transient studies of porphyrins, which are known to intercalate into DNA, are considered with particular emphasis on tetramethyl-pyridiniumporphyrins, where the photophysical behaviour of the metal-free and various metal derivatives are compared.

Contents

Abbreviations: 4,4′-bpy, 4,4′-bipyridyl; A, adenine; AMP, 5′- adenosine monophosphate; BAP, bis(arginyl)porphyrin; bpy, 2,2′-bipyridyl; C, cytosine; cpdppz$(CH_2)_nNH_2$, N-(12-cyano-12,13-dihydro-11H-cyclopenta[b]dipyrido[3,2-h:2′,3′-j]- phenazine-12-carbonyl)-1,4-diaminobutane; DNA, deoxyribonucleic acid; dppn, benzo[*i*]dipyrido[3,2-a:2′,3′-c]phenazine; dppp2, pyrido[2′,3′:5,6]pyrazino[2,3-*f*][1,10]phenanthroline; dppz, dipyrido[3,2-a:2′,3′-c]phenazine; dpq, dipyrido[3,2-*f*:2′,3′-*h*]-quinoxaline; dpqp, pyrazino[2′,3′:5,6]pyrazino[2,3-*f*][1,10]phenanthroline; ET, electron transfer; G, guanine; GMP, 5′-guanosine monophosphate; I, inosine; IL, intraligand; ILCT, intraligand charge transfer; MABAP, mono(acridyl)bis(arginyl)porphyrin; MLCT, metal to ligand charge transfer; NHE, normal hydrogen electrode; ODN, oligodeoxyribonucleotide; PDT, photodynamic therapy; phen, 1,10-phenanthroline; poly(dA-dT), poly(deoxyadenylic-thymidylic) acid; poly(dA).poly(dT), poly(deoxyadenylic acid). poly(thymidylic acid); poly(dC).poly(dG), poly(deoxycytidylic acid). poly(deoxyguanylic acid); Poly(dG-dC), poly(deoxyguanylic-deoxycytidylic) acid; py, pyridine; T, thymine; TA, transient absorption spectroscopy; TAP, 1,4,5,8-tetraazaphanthrene; TMP, 3,4,7,8-tetramethyl-1,10-phenanthroline; TMPyP4, 5,10,15,20-tetrakis(N-methylpyridinium-4-yl)porphyrin; Tpy, 2,2′:6′,2″-terpyridine; TR^3, time-resolved resonance Raman spectroscopy; TRIR, time-resolved infrared spectroscopy.

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1. Introduction

The area of metal complex photosensitised damage to biomolecules continues to grow apace driven in part by an increasing interest in the use of such complexes for photo-activated therapy, which could provide complementary alternatives to current approaches to photodynamic therapy [1–7]. One key target for such compounds is DNA and this has promoted a very substantial literature in the binding of metal complexes to this biomolecule. Most such publications involve the B-form of double-stranded DNA, where the bases of the two strands are base-paired by Watson-Crick H-bonding, although there are also examples of interaction with A-DNA [8], Z-DNA [9,10], triplex-DNA [11] and RNA [12], and quadruplex DNA [13,14]. Several modes for the binding of small molecules to B-DNA have been identified, including groove-binding, external stacking and partial or full intercalation [15,16]. In this review we will focus on metal complexes which have been shown to intercalate part of the molecule between the base-pairs, primarily octahedral metal complexes with the dipyrido[3,2-a:2′,3′-c]phenazine (dppz) groups, and cationic porphyrins bearing the *meso*-4-N-tetramethylpyridyl group (TMPyP). Our particular interest is to consider how the behaviour of transient species such as excited states or free radicals depends on the site (and perhaps the geometry) of intercalation.

Luminescence methods are, of course, invaluable for the study of most 'bright' excited states but generally do not provide information on other species. By contrast transient absorption/flash photolysis methods can, in principle, report on any short-lived species formed, with modern laser technology allowing such investigations down to the femtosecond time domain [17]. This type of pump–probe spectroscopy, which grew out of the flash photolysis methodology first reported by Norrish and Porter in 1949, was greatly aided by the development of pulsed lasers from the 1960s on. By determining the absorbance changes at wavelengths in the UV/visible/NIR at defined times after the initial laser excitation of the sample, a series of spectra are obtained. These spectra record the difference (ΔA) between the absorbance at each wavelength of the transient species present and that of the ground state. In general, therefore, it will have regions of positive absorbance change where the absorbance of the transient species dominates and areas of 'bleaching' where the extinction coefficient of the ground state is greater. The spectra are characteristic of the particular excited state, radical or other transient species and may be used to identify it, perhaps with the aid of DFT or similar calculations. In modern equipment signal-to-noise can be excellent (e.g. $\Delta A \geq 10^{-6}$), which makes this technique the one of choice for measuring rates of reaction. As lasers can be strongly focused, measurements can be performed on small volumes of solutions (e.g. $\geq$30 μl) or with heterogeneous samples such as biological cells, crystals etc.

Vibrational spectroscopy through the techniques of transient and time-resolved resonance Raman spectroscopy (TR^2 and TR^3) [18–21] and time-resolved infra-red [19,22–24] have been shown to provide insights into the nature and structure of transient species that are often inaccessible using only transient UV/visible methods. Although Raman scattering probabilities are inherently low, by tuning the excitation into allowed electronic transitions, the Raman signal may be enhanced up to a million times, so that resonance Raman methodology can be applied to weak solutions or to biological samples. In the specific case of metal complexes and DNA, pioneering TR^2/TR^3 studies were carried out by McGarvey et al. [25–30] and TR^3 studies have also proved invaluable in the study of DNA-bound porphyrins [31,32].

Even though the absorption coefficients of IR bands are generally lower than those observed for electronic transitions, modern TRIR instrumentation allows the monitoring of transient species with excellent signal-to-noise [22,24]. A notable caveat is that many solvents absorb strongly in the IR, and D_2O is preferred to H_2O when studying the main vibrations in DNA (ca. 1300–1800 cm^{-1}). Much of the early TRIR work on metal complexes examined carbonyl complexes, as the CO stretch vibrations at ca. 2000 cm^{-1} have relatively high absorption coefficients and are easy to monitor. These bands provide information on the symmetry of the species and on the nature of excited states (e.g. MLCT or IL(π–π^*)). TRIR also permits the probing of other vibrations of metal complexes, especially ones associated with the heteroaromatic rings. Since 2005, TRIR has been shown to be a powerful technique for studying the photophysics and transient spectroscopy of nucleic acids following direct UV excitation [33]. This work has allowed the detection of not only singlet excited states (including 'dark' ones [34,35]) but also vibrationally hot ground states [36] CT exciplexes [37,38], markers for one-electron guanine oxidation products [39–41], proton transfer [42–44] charge transfer in 8-oxoG [45], excited states in quadruplex [46] and i-motif structures [47], and thymine-thymine dimer formation [48]. For metal-complex – DNA systems, as will be discussed below, TRIR allows the simultaneous monitoring of both the metal complex and the DNA-based vibrations (the latter typically occurring between 1500 and 1720 cm^{-1}), a very useful feature for the study of these systems, especially if used in conjunction with transient absorption measurements [49].

The best characterised intercalating metal complexes are those containing the dipyrido[3,2-a:2′,3′-c]phenazine (dppz) ligand. The extended nature of this heteroaromatic ligand means that octahedral complexes of the type $[M(L–L)_2(dppz)]^{n+}$ can intercalate between the base-pairs of B-DNA. This is not the case for smaller ligands such as 1,10-phenanthroline, which can only semi-intercalate, causing a pronounced kinking of the duplex [50]. In the sections below, we review the reported work on metal-dppz starting with compounds $[Ru(L–L)_2(dppz)]^{2+}$, which are the most studied and which display light-switching or photo-oxidative behaviour depending on the nature of the ancillary ligand (L–L). Subsequently we consider other metal-dppz-type complexes, before turning our attention to another important class of DNA-intercalating compounds, namely cationic metalloporphyrins.

2. Light-switching complexes $[Ru(L–L)_2(dppz)]^{2+}$

It has been recognised for many years that the photophysical properties of complexes such as $[Ru(phen)_2(dppz)]^{2+}$ (Fig. 1) change dramatically when they bind to DNA [51–55]. The dominant type of binding of these complexes to double-stranded B-form of DNA is by intercalation, with the planar heteroaromatic dppz ligand being inserted between the Watson-Crick base-pairs.

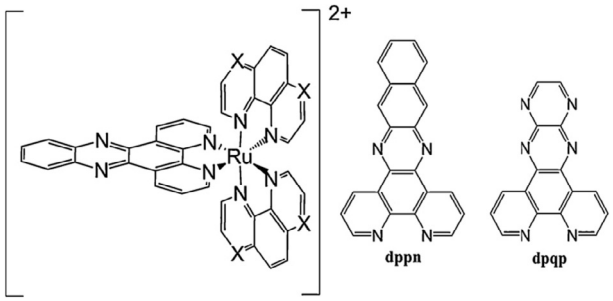

Fig. 1. Structures of Δ enantiomer of Ru(L–L)dppz complex; X = CH (phen); X = N (TAP), and modified ligands; benzo[*i*]dipyrido[3,2-a:2′,3′-c]phenazine (dppn) and pyrazino[2′,3′:5,6]pyrazino[2,3-*f*][1,10]phenanthroline (dpqp) [49]. Reproduced from Smith et al., Coord. Chem. Rev. 255 (2011) 2666–2675 with permission from Elsevier.