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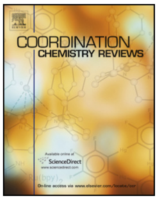

Review

Porphyrin tweezer receptors: Binding studies, conformational properties and applications

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ABSTRACT

Metallated porphyrins have been widely used as binding sites in covalently linked molecular tweezer receptors. This review describes selected examples of covalently linked porphyrin tweezer receptors extracted from the extensive literature generated in this area during the last 20 years. The binding processes of some porphyrin tweezer receptors with different substrates are discussed on the basis of the stoichiometry of the formed complexes, the magnitudes of their thermodynamic stabilities and the spectroscopic techniques used in the characterization. The physicochemical properties of the porphyrin units allow the use of a wide variety of techniques to probe the interaction of the tweezer receptors with different guests. The relationship that exists between the magnitude of the binding constant of 1:1 complexes involving ditopically bound ligands and the conformational features of the spacers is assessed in detail. The different strengths of the non-covalent forces, mainly metal–ligand coordination bonds and π–π interactions, involved in the formation of the host–guest complexes of the tweezers are also discussed and some of the relevant applications of molecular tweezers are also presented. In particular, the use of several porphyrin tweezers in the assignment of absolute configuration of chiral organic compounds using exciton-coupling circular dichroism spectroscopy is described. Finally, porphyrin tweezer receptors prepared through self-assembly processes are introduced and their binding properties emphasized.

1. Introduction

The term “molecular tweezers” was coined by Whitlock and Chen in the late 70s in reference to bifunctional caffeine derivatives (molecule **1** from Fig. 1) capable of producing 1:1 sandwich complexes with suitable planar aromatic guests. The 1:1 complexes displayed a supramolecular structure resembling a pincer holding an object. The object, in the particular case shown here, is a naphthalene carboxylic acid derivative **2**, which is sandwiched between two caffeine binding units covalently tethered through a 2,3-hexadiynil linker that form the pincer **1** (Fig. 1) [1,2]. The complexation studies were performed by phase partitioning tweezer receptor **1** between ethylene dichloride and an aqueous pH 7 phosphate buffer containing varying concentrations of the aromatic carboxylic acid **2**. The intermolecular forces holding together the components of the 1:1 sandwich-like complex $\mathbf{2}{\subset}\mathbf{1}$, are π–π stacking interactions and the hydrophobic effect. The mathematical analysis of the experimental extraction data (K_a^{app} vs [2]) was attempted using a theoretical binding model that considers the formation of two 1:1 complexes, the monotopic $\mathbf{2}{\cdot}\mathbf{1}$ (K_1) and the

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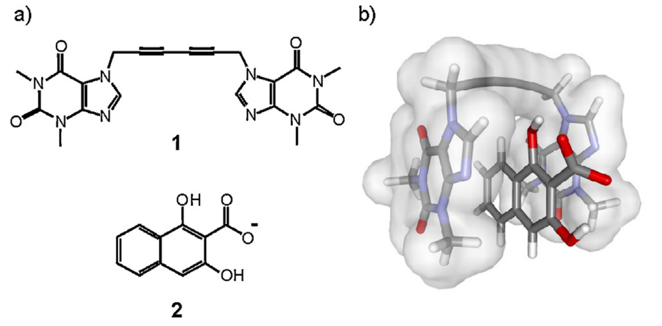
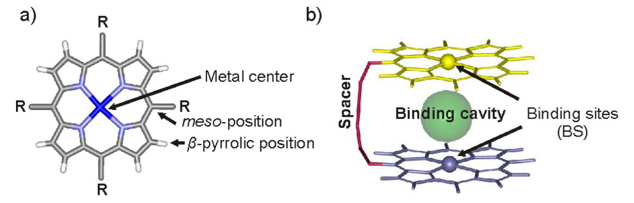


Fig. 1. (a) Structures of 1,3-dihydroxy-2-naphtoate **2** and the first "molecular tweezer" **1** described by Whitlock and Chen; (b) energy-minimized structure [2] of the corresponding 1:1 sandwich complex, $\mathbf{2}{\subset}\mathbf{1}$.



Scheme 1. (a) Metallated porphyrin scaffold indicating the main functionalization sites: *meso* and β-positions; (b) schematic representation of a porphyrin tweezer receptor highlighting the main components.

sandwiched $\mathbf{2}{\subset}\mathbf{1}$ (K_3), and one complex of 2:1 stoichiometry (K_2), $(\mathbf{2})_2{\cdot}\mathbf{1}$. A good fit to the experimental data returned a large stability constant for the 1:1 sandwich π-complex of $K_3 = 10^4\,\mathrm{M}^{-1}$. K_1 and K_2 could be fixed during the fitting procedure (~300 and $20\,\mathrm{M}^{-1}$, respectively) at values determined by model systems of a single caffeine binding unit. The fact that a large K_3 value is necessary to obtain a good fit of the experimental data was used as evidence for the formation of the tweezer-like 1:1 complex.

In general terms, "molecular tweezer" receptors consist of two binding sites (BS) separated by a more or less conformationally flexible spacer. When the two binding sites converge, they define a binding cavity opened at three sides, a molecular cleft. The molecular spacer serves to hold together the two binding units and constraints them within a certain proximity in space. When the spacer is conformationally locked at a fixed distance, a precise relative orientation of binding units is more or less achieved. The nature of the binding site plays a key role in substrate recognition. Many different types of binding sites have been used in the synthesis of molecular tweezers. These include for example anthracene, acridine, cyclohexyl rings or tetrathiofulvalene (TTF) moieties. Consequently, molecular tweezers can act as receptors for a wide variety of substrates ranging from carbon materials [3,4], anions [5,6], organic [7] and inorganic cations [8] and neutral organic guests [9]. The general use and applications of molecular tweezers in the complexation of a variety of substrates has been reviewed in several accounts [10–12]. A review covering molecular tweezers designed for fullerenes has also been published quite recently [3]. The present review focuses on molecular tweezers featuring metallated porphyrin units as binding sites (Scheme 1b).

Porphyrins comprise a relevant class of molecules found in many life processes. Porphyrins are highly colored, cyclic aromatic molecules formed by four modified pyrrole units held together by four sp^2 hybridized carbon bridges, referred to as *meso*-carbons (Scheme 1a). Porphyrins are useful building blocks in supramolecular chemistry. Thanks to the convergent electronic donor properties of the inner-ring periphery, porphyrins are easily functionalized by metallation, and a wide variety of metals have been incorporated into the porphyrin ring. Metallated porphyrins can be considered as acceptor building blocks having at least one axial binding site available for coordination with different ligands containing nitrogen or oxygen donor atoms [13]. The physico-chemical properties of porphyrins can also be tuned via functionalization at the *meso*- and β-pyrrolic positions (Scheme 1). Free-base and metallated porphyrins display a characteristic intense band (the *Soret* band) with a maximum between 380 and 420 nm in their UV–vis spectrum. This band corresponds to a π–π^* transition from the ground state to the second excited singlet state. The maximum of this absorption band is extremely sensitive to changes in the electronic environment of the porphyrin unit. Two or four additional bands (for metallated or free-base porphyrins, respectively) between 480 and 700 nm (*Q*-bands) can typically be observed in the electronic absorption spectra of porphyrins. They correspond to π–π^* transitions from the ground state to the first excited singlet state. In many cases, porphyrins also exhibit fluorescent properties. Fluorescence is only detected from the first exited state due to a rapid interconversion process. The fluorescence properties of the porphyrins can be used to detect binding events at very low concentration for diagnostic detection purposes [14]. Other relevant features of these relative electron-rich macrocycles are their redox properties. In this sense, porphyrins have been extensively exploited as molecular components in natural and synthetic light harvesting systems. The absorption of light by the porphyrin unit provokes its involvement in highly efficient photo-induced electron and energy transfer processes [15].

As mentioned above, the tetrapyrrole macrocyclic core of the porphyrin unit constitutes and ideal binding site for metals. During the metallation process, the porphyrin is doubly deprotonated by losing two protons of the pyrrole nitrogen atoms and behaves as a dianionic ligand. The two remaining nitrogen atoms coordinate to the inserted metal ion by their lone pairs. The use of free-base or metalloporphyrin units as binding sites of tweezer receptors has a strong impact on the type of guest that can be recognized. While host–guest chemistry of free-base porphyrins is mainly dominated by π–π interactions, the formation of coordination bonds between electron-rich atoms of the guests and the metal center in metalloporphyrins confers a strong driving force to the interaction. Free-base porphyrin and metalloporphyrin units are both ideal binding sites for many different guests ranging from neutral organic molecules [16] to carbon nanomaterials [17,18] (e.g. fullerene, carbon nanotubes CNTs) and many more besides [19–22]. In the interest of brevity, this review will concentrate on selected examples of porphyrin tweezer receptors containing metallated binding units. The type of metal inserted into the porphyrin core has an important role on the thermodynamic and kinetic binding properties of the tweezer complexes. Likewise, the inserted metal can be used to direct the selective coordination of different Lewis basic centers that are commonly present in mono- and ditopic ligands, i.e. N vs O or P complexation. Finally, the magnitude of the binding constant determined for bisporphyrin tweezer receptors is remarkably affected by the nature (polar or non-polar) of the solvent used for the titration experiments.

The kind of spacer used to hold together the two binding units of the tweezer receptors, and most importantly, its conformational flexibility are key factors in controlling the binding affinity. In this review, the porphyrin tweezer receptors with metallated binding units in question are classified on the basis of the conformational properties exhibited by the spacer component. Three different main distinctions of porphyrin tweezer receptors are considered: (a) receptors containing spacers that are conformationally highly flexible, (b) receptors with spacers that confer conformational restrictions and (c) receptors constructed with conformationally rigid spacers. In addition, a fourth group that includes porphyrin tweezers with non-covalent linkers such as supramolecular and metal coordination spacers are considered. While conformationally