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Review

Anion recognition using dimetallic coordination complexes

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Contents

Abstract

This article describes advances made over the past 3 years in anion recognition using coordination complexes, with a specific focus on dimetallic architectures that utilize a bridging mechanism. The formation of coordination complexes is a relatively straightforward method of constructing fluorescent and colorimetric chemosensors and imaging agents, and a particularly effective way to develop indicator displacement assays that operate in water. These assays are likely to find increased application in various aspects of analytical and environmental chemistry, as well as biomedical imaging and drug discovery. Significant progress in phosphoesterase mimics has been made, and concomitant with the increased mechanistic insight, is the discovery of a catalyst that cleaves phosphodiesters with poor *O*-alkyl leaving groups. Also discussed is a macrocyclic coordination complex whose shape and supramolecular function is pH-dependent.

Keywords: Anion coordination; Metal coordination; Fluorescence sensing; Indicator displacement assay; Macrocycle; Zinc; Copper; Dipicolylamine; Nucleotides; Phospholipids; Dyes

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1. Introduction

Anion recognition continues to be a major research goal for many supramolecular chemistry groups around the world [1]. As the field matures there is an increasing emphasis on synthetic receptors that operate in aqueous solution [2]. This is because most of the important biomolecular targets such as peptides, nucleotides, phospholipids, and carbohydrates are anionic compounds. However, anion recognition in water is an extremely challenging task for a number of reasons. For a start, anions are strongly hydrated and any complexation process that involves anion dehydration will likely have to pay a large energetic penalty [3]. It is particularly difficult to develop anion recognition systems that form hydrogen bonded complexes in aqueous solvent, for the obvious reason that the water competes strongly for the hydrogen bonding sites. Compared to cations, anions are larger and they come in wide range of different geometries such as spherical, linear, trigonal, tetrahedral, octahedral, etc. This means that synthetic anion receptors are likely to be larger than cation receptors and they should also have complementary shapes. From a supramolecular chemistry perspective, it is not surprising that there are so few low-molecular-weight natural

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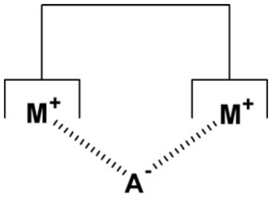
products with anion binding ability. The structures of several anion binding proteins are known; indeed there are examples of phosphate and sulfate binding proteins that only utilize hydrogen bonding [4]. However, in these cases, the anion binding sites are typically buried deep inside the protein structures. Thus, it seems that uncharged, hydrogen bonding synthetic receptors for anions must be designed with structural features that protect the binding sites from the aqueous environment. Although, a few successful examples have been reported, most notably by the group of Kubik et al. [2,5], a potential limitation with this approach is the requirement for relatively large molecules with sophisticated architectures and potentially time-consuming syntheses. Because of these drawbacks, there is a need to boost affinity by incorporating additional bonding interactions that are more competitive in aqueous environments. One common approach is to combine hydrogen bonding with electrostatic attraction. The group of Schmuck and Geiger has been particularly active on this topic in recent years, and they have developed a series of effective carboxylate receptors that operate in water [6]. An alternative bonding interaction is direct coordination of the anion to a cationic metal center that in turn is simultaneously coordinated to an organic scaffold [7]. This recognition strategy takes advantage of the fact that water is a strong hydrogen bonding agent but a relatively poor Lewis base. Thus, water interferes less with anion recognition systems that are based on anion coordination to Lewis acidic metal cations. Since the enthalpy of a single coordination bond is usually quite high, it is relatively easy to construct structurally simple coordination complexes that have sub-millimolar affinities for anions. In many cases, these affinities are good enough for practical use, e.g., in indicator displacement assays. Structurally more complicated versions of these recognition systems can often be constructed in a modular fashion using readily accessible building blocks.

The current field of anion recognition using metal coordination complexes has roots in classical coordination chemistry [8]. A large number of metal complexes are known to form coordination bonds in water, and in many cases the bonding is so strong that the interactions are essentially irreversible. However, irreversible bonding is not useful in most types of supramolecular devices; rather the need is for metal complexes with vacant coordination sites that can form reversible bonds to anions with dissociation constants in the millimolar to nanomolar range. Typically, the rates of association and dissociation need to be fast on the laboratory scale, with half-lives that are less than one second. In terms of receptor design, a common approach is the chelating strategy illustrated in Scheme 1, where an organic scaffold with coordinating atoms (typically nitrogens) holds two metal centers at a specific distance, so they can be bridged by a target anion. When the scaffold is a macrocycle, the bridged structure is sometimes referred to as a cascade complex [9,10]. In terms of the recognition mechanism, there are two limiting cases to consider. In one case, the scaffold binds the metal cations so strongly that the complex can be considered as a single molecular unit with two Lewis acidic sites whose separation is controlled by the length and rigidity of the scaffold. The alterative mechanism is when the scaffold has an inherently weak affinity for one or both of the metal cations. However, the presence of a suitable bridging anion induces a three-component assembly to occur that brings together the scaffold, metal cations, and bridging anion. While the difference between these two association mechanisms is subtle, it has important implications for the successful operation of certain types of molecular devices. An example that will be discussed below is fluorescent sensing, where the anion-induced binding of both metal cations to the scaffold is the event that triggers an increase in fluorescence emission. This type of signal switch would not work if both metal cations were irreversibly coordinated to the scaffold.

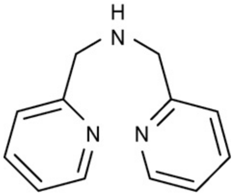


Scheme 1. Anion recognition by a dimetallic coordination complex. The organic scaffold may also be a macrocycle.

The purpose of this article is to describe advances made over the past 3 years in anion recognition using coordination complexes. Moreover, the specific focus is on dimetallic architectures that utilize the bridging mechanism that is shown in Scheme 1. Readers who are looking for a more extensive description of receptors with Lewis acid centers are directed to other articles in this special issue [1], and a recent comprehensive review on molecular recognition of anions in aqueous solution [2].

2. Dimetallic coordination complexes

The dipicolylamine (DPA) ligand, was first reported by Kabzinska [11]. The ligand in known to form stable complexes with numerous metal cations but Zn^{2+}-DPA complexes are popular for molecular recognition. Zinc(II) is a particularly attractive metal cation for chemosensing because unlike other metal cations, it does not quench the fluorescence of an attached dye and it is not redox active. The three nitrogens of a DPA ligand can coordinate strongly to a Zn^{2+} cation, with an association constant around $10^7\ M^{-1}$ in water, leaving one or perhaps two vacant coordination sites for an anionic guest. Furthermore, it is synthetically straightforward to incorporate multiple DPA units into a single organic scaffold.



DPA

2.1. Chemosensors and imaging agents

In recent years, the group of Hamachi and coworkers has developed a number of effective recognition systems using