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Non-covalent (iso)guanosine-based ionophores for alkali(ne earth) cations

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Dedicated to Professor Gerard van Koten.

Abstract

Different (iso)guanosine-based self-assembled ionophores give distinctly different results in extraction experiments with alkali(ne earth) cations. A lipophilic guanosine derivative gives good extraction results for K^+, Rb^+, Ca^{2+}, Sr^{2+}, and Ba^{2+} and in competition experiments it clearly favors the divalent Sr^{2+} (and Ba^{2+}) cations. 1,3-Alternate calix[4]arene tetraguanosine hardly shows any improvement in the extraction percentages compared to its reference compound 1,3-alternate calix[4]arene tetraamide. This indicates that one G-quartet does not provide efficient cation complexation under these conditions. In the case of the lipophilic isoguanosine derivative there is a cation size dependent affinity for the monovalent cations ($Cs^+ \gg Rb^+ \gg K^+$), but not for the divalent cations ($Ca^{2+} > Ba^{2+} > Sr^{2+} > Mg^{2+}$). In competition experiments the isoguanosine derivative, unlike guanosine, does not discriminate between monovalent and divalent cations, giving an almost equal extraction of Cs^+ and Ba^{2+}.

Keywords: (Iso)guanosine; Ionophores; Alkali metals; Alkaline earth metals; Self-assembly

1. Introduction

In general, ionophores for alkali(ne earth) cations are covalent compounds, such as, e.g., (calix[4])crown ethers [1]. In many cases, these covalent ionophores are based on the ''made to fit'' principle to introduce selectivity for one particular cation. This often requires a considerable synthetic effort. However, noncovalent synthesis has been shown to provide a useful alternative in the field of molecular recognition [2,3]. The preparation of ionophores via noncovalent synthesis is a logical step, as in Nature (iso)guanosine residues in nucleic acids form noncovalent tetraplex structures in the presence of a templating alkali(ne earth) metal ion [4,5]. Recently, synthetic (iso)guanosine derivatives have also shown to selectively bind group I and II cations via noncovalent self-assembly [6–8].

Three different lipophilic guanosine derivatives have been developed by the Davis group: lipophilic guanosine residues (Chart 1; G **1** [7]), guanosine residues attached to a calix[4]arene platform in the 1,3-alternate conformation (cG **2** [10]), and isoguanosine residues (isoG **3** [9]). During self-assembly, G **1** forms hexadecameric structures stabilized by lipophilic picrate anions [6], while cG **2** gives tetrameric guanosine assemblies, stabilized by water [10]. On the other hand, isoG **3** forms decamers, merely stabilized by cation complexation [9,11]. The complexation behavior of these assemblies has only been studied for a number of alkali(ne earth) cations [6,8]. In this paper, we present the results of a comprehensive binding study towards both alkaline

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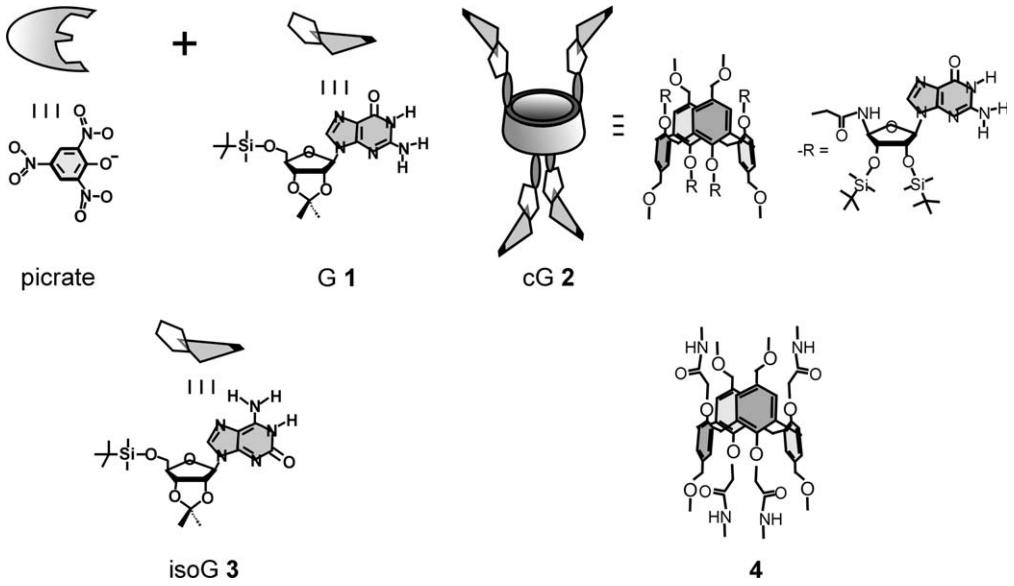

Chart 1.

and alkaline earth cations. The distinct difference in (iso)G-stacking of G **1**, cG **2**, and isoG **3** gives the unique opportunity to directly compare the cation binding affinity/selectivity of a single tetraplex (cG **2**), a G-quadruplex ((G **1**)$_8$), and a isoG-pentaplex ((isoG **3**)$_{10}$) [12].

2. Experimental

2.1. Materials

The preparation of G **1** [7], cG **2** [10], isoG **3** [6], and **4** [13] was according to the literature procedures. The acids (concentrated HCl and HNO_3) and CH_2Cl_2 were of p.a. grade and used as received. The nitrate salts of K^+ ($\geqslant$99.5%), Rb^+ (p.a.) were purchased from Fluka Chemie and Na^+ (p.a.), Cs^+ (99%), Mg^{2+}(p.a.), Ca^{2+} (p.a.), Sr^{2+} (p.a.), and Ba^{2+} (p.a.) were purchased from Acrôs Organics. ^{22}Na and $^{90}Sr^{2+}$ isotope solutions were purchased from Amersham, UK. $^{137}Cs^+$ and $^{133}Ba^{2+}$ isotope solutions were obtained from Isotope Products Europe Blaseg, GmbH.

2.2. Solutions

All basic experiments were performed using an aqueous phase with pH 8.9 (Tris–HNO_3 buffer) and an organic phase containing 10^{-4} M of ionophore, (G **1**)$_8$ and (cG **2**)$_2$ in CH_2Cl_2. The different nitrate salt concentrations were obtained by diluting 10^{-2} M stock solutions to the required concentration. From a carrier free stock solution of $^{22}Na^+$, a dilution of 2.0 kBq/g in 0.1 M $NaClO_4$ was prepared. From a CsCl carrier containing stock solution of $^{137}Cs^+$, a dilution of 9.8 kBq/g in 0.1 M HCl was made. From a carrier free stock solution of $^{90}Sr^{2+}$, a dilution of 2.5 MBq/g in 0.1 M HNO_3 was prepared. From a 10 μg Ba^{2+}/ml carrier containing stock solution of $^{133}Ba^{2+}$ in 0.1 M HCl, a dilution of 45.2 kBq/g in water was made.

2.3. General extraction procedures

Equal volumes (1.0 ml for the tracer experiments and 2 ml for the inductively coupled plasma mass spectroscopy, ICP-MS monitored experiments) of the organic and aqueous solutions were transferred into a screw cap vial with a volume of 4 ml. The samples were shaken (1500 rpm) at ambient temperatures (22–24 °C) for 1 h to ensure complete settling of the two-phase equilibration. After extraction, the solutions were disengaged by centrifugation (1600 rpm for 5 min) and aliquots (0.5 ml for the tracer experiments and 1 ml for the ICP-MS monitored experiments) of the organic and aqueous phases were pipetted out. Experiments were performed in duplicate; average values are reported, with an estimated error of 10–15%.

2.4. ICP-MS monitored extraction procedures

The solvent of the aliquot taken from the organic phase was evaporated and the residue destructed in 1 ml of concentrated HNO_3. The cation concentrations were measured on a Perkin Elmer Sciex Elan 6000 ICP-MS instrument, using a Cross flow nebulizer. The extraction percentage is defined as 100% times the ratio of cation concentration in the organic phase ([M_o]) and the added cation concentration ([M_{add}]) (Eq. (1)).

$$E\% = 100\%([M_o]/[M_{add}]) \quad (1)$$