Enhancement of Ion Pairing of Sr(II) and Ba(II) Salts by a Tritopic Ion-Pair Receptor in Solution

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Tritopic ion-pair receptors can bind bivalent salts in solution; yet, these salts have a tendency to form ion-pairs even in the absence of receptors. The extent to which such receptors can enhance ion pairing has however remained elusive. Here, we study ion pairing of M\(^{2+}\) (Ba\(^{2+}\), Sr\(^{2+}\)) and X\(^{-}\) (I\(^{-}\), ClO\(_4\)^{−}) in acetonitrile with and without a dichlorooxacalix[2]arene[2]triazine-related receptor containing a pentaethylene-glycol moiety. We find marked ion association already in receptor-free solutions. When present, most of the MX\(^{+}\) ion-pairs are bound to the receptor and the overall degree of ion association is enhanced due to coordinative, hydrogen-bonding, and anion-π interactions. The receptor shows higher selectivity for iodides but also stabilizes perchlorates, despite the latter are often considered as weakly coordinating anions. Our results show that ion-pair binding is strongly correlated to ion pairing in these solutions, thereby highlighting the importance of taking ion association in organic solvents into account.

1. Introduction

Ion receptors have reached by now an elaborate design,[1–6] yet when coordinating a single ion, the corresponding counter-ion affects both binding strength and selectivity. To also control the binding of the counter-ion, ion-pair (IP) receptors, which have cation and anion recognition moieties in the same molecular scaffold, have become the focal point of recent ion sensing studies.[7–11] Since these receptors benefit from synergistic effects between the co-bound ions, such as electrostatic and allosteric interactions, they exhibit enhanced binding affinities. Additionally, the modification of the recognition sites allows for fine-tuning the selectivity, thus, a plethora of receptors has been designed for efficient binding of alkali metal (MX) and tetraalkylammonium salts (R\(_4\)NX).[7–39] As such, IP receptors have emerged as potential candidates for numerous applications, such as salt extraction,[7–37] transmembrane transport,[18–23] and catalysis.[24–25]

The ability to tailor cationic and anionic binding sites also enables the design of multitiopic receptors. In contrast to MX receptors, only a few structures that bind the cation and both anions of bivalent (MX\(_2\)) salts, have been reported to date.[39–42] Such MX\(_2\) receptors could improve the extraction of alkaline metal earth cations, like Sr\(^{2+}\) and Ba\(^{2+}\),[43–46] from aqueous solutions or the selective extraction of the hazardous \(^{90}\)Sr from calcium-containing radioactive wastes.[47–49]

The binding of MX\(_2\) salts to such receptors has been mostly derived from titration experiments. In such titrations typically the receptor is probed (NMR chemical shift or optical absorption/fluorescence), and thus interaction of individual ions with the receptor can be quantified given that ion binding results in salient variations of the receptor’s chemical environment. In turn, it is challenging to detect weak interactions of the anion or cation of an IP with the receptor, and it is impossible to account for the formation of bare IPs that are not directly bound to the organic molecule. The latter is in particular relevant to bivalent MX\(_2\) salts, as they have a high tendency to form IPs in solution – i.e. cations and anions form long-lived aggregates in solution – even in the absence of a guiding molecular scaffold.[49] Thus, one fundamental question about the function of IP receptors has remained elusive: can these receptors efficiently bind pairs of ions and thereby enhance the overall degree of ion association? That is, does the formation of receptor-IP complexes increase the overall concentration of associated ions (i.e. bare ion-pairs and receptor-bound ion-pairs)? Quantifying this receptor-induced enhancement of ion association can thus provide essential information about the function of such receptors in solution.

To address this question we focus in the present study on a tritopic IP receptor, for which cation binding can be rationally designed using appropriately sized pentaethylene glycol chains,[1–3,7–11] while anion coordination can be achieved by interaction of anions with electron-deficient aromatic triazine rings.[51–63] The bridging oxygen atoms conjugate with the triazines such that the aromatic trimeric fragment tends to form a pre-organized V-shaped pocket in which two triazines serve...
as homoditopic binding sites for anions.[58,61] Receptor 1[42] (Scheme 1) is based on a triazine-containing aromatic trimer fragment for anion recognition and a pentaethylene glycol chain for cation chelation. 1 has been reported to form stable complexes with Ca$^{2+}$ salts but shows low affinity to Mg$^{2+}$.[42]

Here we report on ion pairing of Sr(ClO$_4$)$_2$, Ba(ClO$_4$)$_2$, and Sr$_2$ dissolved in acetonitrile in the presence and absence of receptor 1. To explore to what extent 1 can induce ion pairing and the corresponding structures of the IPs formed, we use a combination of experiments. To quantify ion association in solution, we use dielectric relaxation spectroscopy (DRS), which is sensitive to the rotation of dipolar species and as such can detect both IPs bound by the molecular scaffold of the receptor and bare IPs. We compare these results to those obtained from $^1$H nuclear magnetic resonance spectroscopy ($^1$H NMR) titrations. To obtain information on the composition and structure of the formed complexes, we use electrospray ionization mass spectrometry (ESI-MS), single crystal X-ray diffraction (XRD), and density functional theory (DFT) calculations. We find that all salts have a marked tendency to form IPs in acetonitrile in the absence of 1. The addition of 1, which in solution adopts an open form favorable for ion binding, stabilizes IPs and thus results in the enhancement of ion association.

**Experimental Section**

**Sample Preparation**

Samples were prepared using HPLC grade acetonitrile (Fisher Scientific), deuterated acetonitrile, or HPLC-MS grade acetonitrile (VWR Chemicals) as solvents. Salts for DRS and ESI-MS experiments Sr$_2$ (Alfa Aesar, 99.99%); Sr(ClO$_4$)$_2$·3H$_2$O (Alfa Aesar, 98%); Ba$_2$ (Alfa Aesar, 99.99%); and Ba(ClO$_4$)$_2$ (Acros Organics, 99%) were used without further purification. To avoid the contribution of water to the dielectric spectra, Sr(ClO$_4$)$_2$·3H$_2$O was dried in vacuo at 160-170°C until constant weight was reached. For $^1$H nuclear magnetic resonance spectroscopic (NMR) titrations, all metal Sr(ClO$_4$)$_2$·6H$_2$O, Ba(ClO$_4$)$_2$·3H$_2$O, and tetrabutylammonium salts (Bu$_4$NCl, Bu$_4$NB, and Bu$_4$NI) were used as received. Receptor 1 was synthesized according to the procedure reported in Ref. [42].

**Dielectric Relaxation Spectroscopy (DRS)**

DRS probes the frequency-dependent macroscopic polarization of a sample in an external electric field$^{[46-50]}$ with field frequency $\nu$, which is generally expressed in terms of the complex permittivity, $\varepsilon(\nu)$:

$$\varepsilon(\nu) = \varepsilon'(\nu) - i\varepsilon''(\nu) = \frac{\varepsilon_0 + \varepsilon_1}{2}$$

with $\varepsilon'(\nu)$ and $\varepsilon''(\nu)$ being the frequency-dependent dielectric permittivity and loss, respectively; and $\varepsilon_0$ is the permittivity of free space. For conducting samples, the translational motion of mobile ions gives rise to Ohmic loss (last term of Eq. 1), which scales with the conductivity, $\kappa$, of the sample. We assume $\kappa$ to be real and independent of $\nu$ (i.e. the dc conductivity).

At microwave frequencies, polarization stems predominantly from rotation of species with an electrical dipole moment. Thus, besides its sensitivity to dipolar molecules, DRS is particularly sensitive to the formation of IPs in solution, as the oppositely charged ions of an IP are separated by a well-defined separation distance, yielding an intrinsically high dipole moment. As the dipole moment increases with increasing distance between cation and anion, DRS can distinguish between different IP species, like contact or solvent-separated ion-pairs.$^{[63,64]}$ For any dipolar relaxation (e.g. solvent or IPs), a dispersion in the real part, $\varepsilon'(\nu)$, and a peak in the imaginary part, $\varepsilon''(\nu)$, are observed.

The $\varepsilon(\nu)$ spectra were recorded at room temperature ((23 ± 2)°C), using an Anritsu Vector Network Analyzer (model MS4647 A). The frequency range at 0.2 ≤ $\nu$/GHz ≤ 50 was covered using a frequency-domain reflectometer, equipped with a coaxial open-ended probe based on 1.85 mm connectors. Spectra at 60 ≤ $\nu$/GHz ≤ 125 were recorded using an open-ended probe connected with 1 mm connectors to an external frequency converter module (Anritsu 3744 A mmW).[65] To calibrate the setup, air, conductive silver paint, and acetonitrile$^{[66]}$ were used as calibration standards.

To study solutions of the salts in acetonitrile using DRS, samples with $c_{\text{salt}}$ up to 0.14-0.16 M were prepared. To study the binding of salts to 1 in acetonitrile, two series of solutions were prepared. First, $c_1$ was varied from 0 to 0.11 M at a constant $c_{\text{salt}}$ (0.10 M), except for Ba$_2$, which is not sufficiently soluble in acetonitrile. Second, $c_{\text{salt}}$ was increased from 0 to 0.14 M at constant $c_1$ (0.05 M). All solution compositions are listed in Tables S1 and S2 in the Supporting Information (SI).

**$^1$H Nuclear Magnetic Resonance Spectroscopy (NMR) Spectroscopy**

To supplement the quantitative findings from the DR spectroscopic measurements, we performed $^1$H NMR titrations. The data evaluation was performed with the PSEQUAD$^{[70]}$ and Bindfit$^{[70]}$ software packages. More experimental details are given in the SI.
Single-Crystal X-ray Diffraction

Mixtures of 1 and M(ClO$_4$)$_2$ (M = Ba, Sr) were dissolved in CH$_3$OH/CHCl$_3$, and ethyl ether was allowed to slowly diffuse into the solution at 273 K to produce single crystals for X-ray analysis. Single crystal X-ray diffraction data were collected on a MM007HF Saturn724+ diffractometer using MoK$\alpha$ radiation ($\lambda = 0.71073$ Å) at a temperature of 173 K. The intensity data were collected by the omega scans technique, scaled, and reduced with the CrystalClear software.$^{[71]}$ X-rays were provided by a fine-focus sealed X-ray tube operated at 50 kV and 24 mA. Integrated reflection intensities were produced and the correction of the collected intensities for absorption was done using CrystalClear. The structures were solved by direct methods using SHELXT$^{[72]}$ and refined using full-matrix least-squares methods implemented in the SHELXL$^{[73]}$ program. All non-hydrogen atoms were refined anisotropically, and hydrogen atoms attached to carbon atoms were fixed at their ideal positions.

Electrospray Ionization Mass Spectrometry

To assess the composition of ionic/molecular complexes in solution, electrospray ionization (ESI) mass spectra were recorded using an Advion Expression-L Compact Mass Spectrometer equipped with a single quadrupole separator, providing an average resolution of 0.5 m/z units. Here, the range of 100 $\leq$ m/z $\leq$ 1200 was scanned in the positive-ion mode. Experiments were performed using samples with $c_{\text{Sr}} = c_1 = 0.01$ M (SrI$_2$, Sr(ClO$_4$)$_2$, BaI$_2$, Ba(ClO$_4$)$_2$ or $c_{\text{Sr}} = c_1 = 0.02$ M (SrI$_2$)).

Density Functional Theory (DFT) Calculations

The geometries of 1 and the ion-pair complexes at various configurations were optimized with the Gaussian 09$^{[74]}$ software using the B3LYP hybrid DFT functional$^{[75,76]}$ and the def2-TZVP or its def2-TZVPD variant including diffuse functions$^{[77]}$ to take non-covalent interactions into account. For all calculations, Grimme’s D3 empirical dispersion correction$^{[78]}$ was employed. Implicit solvent effects were taken into account applying the conductor-like polarizable continuum model (CPCM)$^{[79]}$ with acetonitrile as solvent.

2. Results and Discussion

2.1. Ion Pairing in the Absence of the Receptor

To explore ion pairing of the studied salts in the absence of the receptor molecules, we study the dielectric relaxation of solutions of Sr(ClO$_4$)$_2$ (Figure 1a), SrI$_2$, and Ba(ClO$_4$)$_2$ (Figures S1a and S2a, SI) in acetonitrile. For all samples we observe a relaxation at $\sim$50 GHz, evidenced by a peak in the dielectric loss and a dispersion in the dielectric permittivity spectra (Figure 1), due to the solvent acetonitrile.$^{[80]}$

As can be seen for Sr(ClO$_4$)$_2$ in Figure 1a (also for SrI$_2$ and Ba(ClO$_4$)$_2$, see Figures S1a and S2a in the SI), upon dissolution of salt a shoulder in the imaginary part at $\sim$1 GHz emerges with a shoulder in the real part, indicative of the formation of dipolar IPs.$^{[81,82]}$ Due to this low-frequency relaxation, which also goes along with a dispersion in $\varepsilon'(\nu)$, the static permittivity ($\varepsilon_0$, the low-frequency plateau of $\varepsilon'(\nu)$) exhibits an increase with increasing salt concentration. As such, the increase in sample polarization due to the formation of dipolar solute species, i.e. IPs, overcompensates its decrease due to the dilution of dipolar solvent molecules. This suggests that the studied iodide and perchlorate salts do not fully dissociate in acetonitrile due to its lower solvent permittivity and weaker solvation,$^{[83]}$ giving rise to the formation of dipolar IPs (i.e., Sr$^{1+}$, Sr(ClO$_4$)$_{2-}$, and Ba(ClO$_4$)$_{2-}$).

To analyze the spectra quantitatively, we fit a relaxation model to the data. For the present samples we find that a combination of two Debye-type relaxations$^{[84]}$ accounting for the solvent (AN) and the ion-pair (MX$^+$) relaxations, respectively, provides an excellent description of the experimental spectra with the least number of adjustable parameters:

$$\varepsilon(\nu) = \frac{S_{\text{AN}}}{1 + i2\pi \nu \tau_{\text{AN}}} + \frac{S_{\text{MX}}}{1 + i2\pi \nu \tau_{\text{MX}}} + \varepsilon_\infty - \frac{iK}{2\pi \nu \varepsilon_0} \quad (2)$$

where $S_{\text{AN}}$ and $S_{\text{MX}}$ are the MX$^+$ and the solvent relaxation amplitudes, respectively, while $\tau_{\text{AN}}$ and $\tau_{\text{MX}}$ represent the corresponding relaxation times. The infinite-frequency permittivity, $\varepsilon_\infty$, comprises all contributions at frequencies higher than covered in our experiment. Such decomposed dielectric loss spectra of the 0.14 M salt solutions are depicted in Figures 1b, 1c, and S2b (see SI).

To obtain quantitative information about the degree of ion pairing, we use the Cavell equation,$^{[85,64,80]}$ which relates $S_{\text{AN}}$ to the equilibrium concentration ([MX$^+$]) and effective dipole moment ($\mu_{\text{AN}}$) of the MX$^+$ ion-pairs:

$$S_{\text{AN}} = \frac{\varepsilon_\infty - \varepsilon_1}{\varepsilon_1} + A_{\text{MX}} \left( 1 - \frac{\varepsilon_1}{\varepsilon_1 + A_{\text{MX}} \frac{N_a}{3k_B T \varepsilon_0} \cdot \left[ \text{[MX$^+$]} \right] \cdot \mu_{\text{MX}}^2 \right) \quad (3)$$

where $A_{\text{MX}}$ is the so-called cavity-field factor (determined by the geometry of the rotating particle), $N_a$ is the Avogadro number, $k_B$ is the Boltzmann constant, and $T$ is the thermodynamic temperature.
In order to calculate [MX⁻] from \( S_{\text{MX}^{-}} \), the value of \( \mu_{\text{MX}^{-}} \), which predominantly depends on the spatial separation between cation and anion, needs to be known. In salt solutions, both contact (CIP, direct contact between the cation and anion) and solvent-shared (SIP, cation and anion are separated by one solvent molecule) IPs are conceivable species.\(^{50,56-58}\) Despite also the existence of triple IPs (consisting of one cation and two anions or one anion and two cations) it has been inferred from infrared spectra for Mg(ClO\(_4\))\(_2\) and Ca(ClO\(_4\))\(_2\) in acetonitrile, only one dipolar relaxation mode has been detected in the DRS spectra for these salts,\(^{68}\) in line with our present findings. Given the low salt concentrations of the present samples, at which triple-ion aggregates are minor species also for Mg(ClO\(_4\))\(_2\) and Ca(ClO\(_4\))\(_2\), we ascribe the low-frequency relaxation mode to CIPs or SIPs.

To determine which IP species prevails in solution, we consider the two limiting cases: exclusive formation of either CIPs or SIPs. Based on the geometric model described in detail in ref. [80], we calculate \( \mu_{\text{CIP}}, \mu_{\text{SIP}}, A_{\text{CIP}}, \) and \( A_{\text{SIP}} \) (Table S3, SI) using data for ionic radii, solvent radii, and polarizabilities from Refs. [81–83]. From these values, we obtain \( [\text{MX}^{-}] \) using Eq. 3. Assuming that \( [\text{MX}^{-}] = [\text{CIP}] \) or \( [\text{SIP}] \), we calculate the IP formation constants, \( K_{\text{CIP}} \) for the CIP \( (K_{\text{CIP}}) \) and SIP \( (K_{\text{SIP}}) \) species via Eq. 4:

\[
K_{\text{MX}} = \frac{[\text{MX}^{-}]^c}{[\text{M}^+]^c[\text{X}^-]^c} = \frac{[\text{MX}^{-}]^c}{[\text{M}^+]^c[\text{X}^-]^c} \left( \frac{c_{\text{ionic}} - [\text{MX}^{-}]}{2c_{\text{ionic}} - [\text{MX}^{-}]} \right)
\]

where \( [\text{M}^+] \) and \( [\text{X}^-] \) are the free cation and anion concentrations and \( c^a \) the standard molar concentration (1 M). As shown in Figure 2, the equilibrium constants for the two limiting cases (SIP and CIP) decrease with increasing salt concentration due to increased charge screening.\(^{59}\) Yet the curves are offset as a result of the different absolute values of \( \mu_{\text{MX}^{-}} \) for the CIP and SIP species. To elucidate which IP species predominates association equilibria, the formation constants have to be compared to literature data obtained from independent experimental techniques.

To exclude differences arising from different experimental sensitivities and ionic strengths, such comparison should be based on the standard thermodynamic association constant, \( K_{\text{MX}}^0 \) (i.e. the limiting value of \( K_{\text{MX}^{-}} \) at infinite dilution). To obtain \( K_{\text{MX}^{-}}^0 \), we extrapolate the values of \( K_{\text{MX}^{-}} \) to zero ionic strength using a Guggenheim-type equation:\(^{65,68}\)

\[
\log K_{\text{MX}^{-}} = \log K_{\text{MX}^{-}}^0 - \frac{2A_{\text{OH}}|\text{z}_+\text{z}_-|\sqrt{I}}{1 + B_{\text{OH}}d\sqrt{I}} + C + Dl^{1.5}
\]

where \( A_{\text{OH}} \) and \( B_{\text{OH}} \) are the Debye-Hückel constants at \( T = 23^\circ \text{C},\)\(^{69}\) \( d \) is the distance of charge separation, and \( C \) and \( D \) are adjustable parameters. We calculate the ionic strength, \( l \), from \( c_{\text{ionic}} \) by correcting for the IPs formed (that is, \( l = 3c_{\text{ionic}} - 2[MX^{-}] \)) and fit Eq. 5 to the data in Figure 3. Error bars (±\( \sigma \)) for \( K_{\text{MX}^{-}} \) were estimated assuming \( \sigma(S_{\text{MX}^{-}})=0.3. \) The fitted parameters of Eq. 5 for each IP are listed in Table S4, SI.

Figure 2 demonstrates that for SrClO\(_4\)\(^+\) (and also for SrI\(^+\) and BaClO\(_4\)\(^+\)), see Figures S3 and S4 in the SI), Eq. 5 describes the ionic strength dependence for both constants, \( K_{\text{CIP}} \) and \( K_{\text{SIP}}, \)

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Figure 2. Experimental ion-pair formation constants, \( \log K_{\text{SrClO}_4^+} \), assuming the formation of contact (CIP, red symbols) or solvent-separated (SIP, black symbols) SrClO\(_4\)\(^+\) ion-pairs as a function of ionic strength (\( I \)). Solid lines show fits using Eq. 5; error bars were calculated assuming \( \sigma(S_{\text{SrClO}_4^+})=0.3. \) Dashed lines indicate the thermodynamic formation constants (\( \log K_{\text{SrClO}_4^+}^0 \)) at infinite dilution, obtained in this work or reported in Ref. [84].

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Figure 3. Structures of the open (a) and twisted (b) conformers of receptor 1, optimized at the B3LYP-D3/def2-TZVP level. Implicit solvent effects were taken into account applying the CPCM approach. The calculated effective dipole moments are 8.3 D (a) and 1.6 D (b).
very well. This comparison shows that the extrapolated values
(marked as dashed lines in Figure 2) agree well with those
derived from previous conductometric experiments for the
same salts,\textsuperscript{84,85} if we assume the exclusive formation of CIPs (see
table A). Hence, this agreement provides evidence for CIP
being the dominant ion-pair species for the studied salts in
acetonitrile.

We note that this notion partially contrasts earlier findings
for solutions of Mg(ClO\textsubscript{4})\textsubscript{2} and Ca(ClO\textsubscript{4})\textsubscript{2} in acetonitrile, where –
despite CIPs also dominate – the formation of both CIP and SIP
at \(c_{\text{salt}} < 0.2\) M has been suggested.\textsuperscript{166} This apparent discrepancy
can be rationalized on the basis of different ionic radii: smaller
ionic radii give rise to higher ionic surface charge density and
thus to stronger solvation. As such, the interaction of
acetonitrile with the smaller Mg\textsuperscript{2+} / Ca\textsuperscript{2+} cations is stronger than
with the larger ions Sr\textsuperscript{2+} and Ba\textsuperscript{2+}. In turn, weaker solvation of
Sr\textsuperscript{2+} and Ba\textsuperscript{2+} relative to Mg\textsuperscript{2+} and Ca\textsuperscript{2+}, likely makes SIPs less
significant for the salts studied in this work.

Overall, our findings for these solutions imply that despite
perchlorate is often considered as weakly coordinating anion,
we find that both Sr(ClO\textsubscript{4})\textsubscript{2} and Ba(ClO\textsubscript{4})\textsubscript{2} tend to form IPs in
acetonitrile, in line with previous studies.\textsuperscript{166,84} The fraction of
ions that form IPs (\% [MX\textsuperscript{n-}]/c\textsubscript{salt} at \(c_{\text{salt}} = 0.1\) M, Table 1) exceeds
40% for the perchlorates, while for SrI\textsubscript{2} our results suggest that
more than 50% of all ions are bound in CIPs. In turn, only a
fraction of ions is present in solution as free ions. Upon addition
of IP receptors, which will be discussed below, binding of both,
free ions and ion-pairs to the receptor can occur.

### 2.2. The Structure of Receptor 1 in Acetonitrile

Before discussion of binding of salts to the receptor, we first
investigate the structure of receptor 1 in solution. Crystalllo-
graphic experiments have shown that 1 exists in two markedly
different conformations in the solid state,\textsuperscript{43} here referred to as
‘open’ and ‘twisted’ conformer (Figure 3). Given the different
symmetries of both conformers, studying the dielectric relaxa-
tion of 1 can provide information on the most stable
conformation in acetonitrile.

For solutions of 0.05 M of 1, we detect a small-amplitude
relaxation at ca. 1 GHz in the DR spectrum (amplitude \(S_{1} \approx 0.3,\)
relaxation time \(\tau_{1} \approx 130\) ps, see the decomposed loss spectrum
in Figure S5, SI). Based on Eq. 3, this relaxation amplitude
corresponds to a dipolar species with a dipole moment of \(\mu_{1} =
(8.3 \pm 0.8)\) D. We compare this value with the structures of the
open and twisted conformers (Figure 3), obtained from geometry
optimizations at the B3LYP-D3/def2-TZVP level of theory,
taking implicit solvent effects into account. These calculations
suggest that the calculated dipole moment of the open form is
\(\mu_{\text{calc}} = 8.3\) D, which is in excellent agreement with the experi-
mental value. Conversely, due to its high symmetry, the twisted
conformer has a much lower dipole moment (\(\mu_{\text{calc}} = 1.6\) D).
Thus, our results indicate that in solution the open conformer
prevails. In this geometry the ion binding sites are pre-
organized such that both cations and anions can readily access
the binding pockets, in contrast to the twisted form.

### 2.3. Ion Pairing in the Presence of the Receptor

#### 2.3.1. Qualitative Findings for the Binding of Salts Both in the
Solid and Solution Phases

Having established the relaxation dynamics of the binary
solutions, we now turn to ternary samples where both receptor
1 and salt are present. Through the diffusion of ethyl ether to a
mixture of receptor and alkali earth metal salts in CH\textsubscript{3}OH/CHCl\textsubscript{3},
we obtained single crystals of the \([\cdot \text{Sr(ClO\textsubscript{4})\textsubscript{2}]} \cdot \text{H\textsubscript{2}O} \cdot \text{CH\textsubscript{3}OH}\)
(Figure 4 and Table S5, SI) and \([\cdot \text{Ba(ClO\textsubscript{4})\textsubscript{2}]} \cdot 2\text{H\textsubscript{2}O}\) (Figure S6
and Table S6, SI) complexes. From the crystal structures, we find
the cation is coordinated equatorially by the oxygens of the
glycol chain, and are axially coordinated by the anion. The
respective coordination number (CN) is 9 for Sr\textsuperscript{2+} and 10 for

![Figure 4. Crystal structure of the [\cdot Sr(ClO\textsubscript{4})\textsubscript{2}] \cdot \text{H\textsubscript{2}O} \cdot \text{CH\textsubscript{3}OH} ion-pair complex. The anion-x distance is indicated by a dashed line between the O17 atom and the blue triazine plane (\(d_{\text{O17-Blue}} = 3.393\) Å). Also shown is the intra-
molecular H bond between the H\textsuperscript{+} aryl proton and O16 (\(d_{\text{O16-H\textsuperscript{+}}} = 2.486\) Å).](image-url)
Ba^{2+}; the higher CN of the latter reflects its higher ionic radius, providing room for more ligands.

In the structure of 1·Sr(ClO\textsubscript{4})\textsubscript{2} (Figure 4), one ClO\textsubscript{4}\textsuperscript{-} is located outside the receptor, interacting electrostatically with the cation. The second anion resides in the aromatic binding pocket, being stabilized by a triazine moiety through anion-\(\pi\) interaction, as indicated by the short distance between the aromatic ring and the O17 atom of the anion (3.393 Å). Moreover, an additional hydrogen bond between the O16 atom of ClO\textsubscript{4}\textsuperscript{-} and the H\textsuperscript{+} proton of the central aromatic ring is formed. Based on the distance (\(d_{\text{O16-H}} = 2.486\ \text{Å}\)), this hydrogen bond can be considered weak\textsuperscript{[85,86]}

The crystal structure of the 1·Ba(ClO\textsubscript{4})\textsubscript{2} IP complex shows similar binding motifs, with each Ba\textsuperscript{2+} coordinated by ten oxygens, four from the glycol chain, one from a water molecule and five from three ClO\textsubscript{4}\textsuperscript{-} anions (Figure S6, SI). The perchlorate are additionally coordinated by triazine rings, evidenced by the short distances between the O15, O16 atoms and the triazine planes (\(d_{\text{O-plane}} = 2.944\) and 3.063 Å). The perchlorates also act as bridge to link two IP complexes to form a dimer.

To obtain information on the binding of salts to 1 in the solution phase, we carried out ESI-MS measurements in solutions with \(c_{\text{sal}} = c_{1} = 0.01\) or 0.02 M. In the positive-ion mode, we observe peaks due to 1·Sr\textsuperscript{2+}, 1·Sr(ClO\textsubscript{4})\textsuperscript{-}, 1·Ba\textsuperscript{2+} and 1·Ba(ClO\textsubscript{4})\textsubscript{2} as well as to the bare and solvated 1·Sr\textsuperscript{2+} and 1·Ba\textsuperscript{2+} complexes (Figures S7–S11, SI). The perchlorates are additionally coordinated by triazine rings, evidenced by the short distances between the O15, O16 atoms and the triazine planes (\(d_{\text{O-plane}} = 2.944\) and 3.063 Å). The perchlorates also act as bridge to link two IP complexes to form a dimer.

To gain further insights into the structure of the receptor-bound IPs, we optimized the geometry of the 1·Sr(ClO\textsubscript{4})\textsubscript{2}, 1·Ba(ClO\textsubscript{4})\textsubscript{2}, 1·Sr\textsuperscript{2+} and 1·Ba\textsuperscript{2+} species at the B3LYP-D3/def2-TZVPD level of theory (Figure 5 as well as Figures S12–S14, SI), as these characteristics are common for weak C–H···I and the same aryl proton. The calculated distances (1·Sr\textsuperscript{2+}: 3.382 Å, 1·Ba\textsuperscript{2+}: 3.163 Å) indicate the formation of a strong C–H···I bond.\textsuperscript{[87]} From these findings we conclude that in addition to anion-\(\pi\) interaction, an intramolecular C–H···X hydrogen bond also contributes to the stabilization of the receptor-bound anion.

2.3.2. Quantifying Ion Pairing in the Presence of 1 by DRS

To study the formation of IPs in the presence of 1, we recorded dielectric spectra of the ternary samples. Upon addition of 1 to solutions of 0.10 M Sr(ClO\textsubscript{4})\textsubscript{2}, SrI\textsubscript{2} and Ba(ClO\textsubscript{4})\textsubscript{2}, we recorded the dispersion in \(\varepsilon'\) and the shoulder in \(\varepsilon''\) at ~1 GHz, to lower frequencies. The relaxation amplitude increases slightly upon addition of 1 (see also discussion below). The small variation of the IP amplitude directly implies that the spatial separation of the underlying dipolar species is only little affected by the presence of 1, given that the overall concentration of IPs does...

![Figure 5. Structure of the SrClO\textsubscript{4}\textsuperscript{2-} ion-pair bound to receptor 1, optimized at the B3LYP-D3/def2-TZVPD level of theory.](Image 526-724)

![Figure 6. (a) Relative permittivity (\(\varepsilon'\), triangles, left axis) and dielectric loss (\(\varepsilon''\), squares, right axis) spectra for a 0.10 M Sr(ClO\textsubscript{4})\textsubscript{2} solution with (red symbols) and without (black symbols) receptor 1. Solid lines are the results of fitting Eq. 2 to the data; dashed line shows the spectrum of pure acetonitrile, taken from Ref. [68]. The last term of Eq. 2 has been subtracted from \(\varepsilon''\) for visual clarity. (b) Ion-pair relaxation time in 0.10 M Sr(ClO\textsubscript{4})\textsubscript{2} as a function of receptor concentration.](Image 306-547)
not decrease in the presence of 1 (see Eq. 3). The decrease of the solvent relaxation amplitude is due to the reduced concentration of the solvent, but its peak position (~50 GHz = \(2\pi\tau_{\text{rel}}^{-1}\)) in the dielectric loss spectrum is hardly affected by the presence of the receptor.

Also for the ternary samples Eq. 2 describes the experimental spectra well; the contributions of both relaxations to the overall loss spectra for solutions \(c_{\text{salt}} = c_1 = 0.10\) M are plotted in Figures 15b–17b in the SI. The presence of only two discernible relaxations (solvent and ion-pairs) implies that we cannot resolve separate relaxations due to receptor-bound salts and due to bare IPs. Yet, the variation of the peak position of the solute mode – in contrast to the solvent peak – indicates the binding of MX salts (or IPs) to 1: we find the extracted values of the IP relaxation time, \(\tau_{\text{MX,IP}}\), to increase with increasing concentration of 1 (Figure 6b and S18, SI). For diffusive rotation, \(\tau_{\text{MX,IP}}\) is proportional to the hydrodynamic volume of the rotating species and to the viscosity of the sample.\(^{[66]}\) The low concentration of solutes and the insensitivity of \(\tau_{\text{SN}}\) to the addition of 1 renders increasing viscosity unlikely. Rather, the large increase of \(\tau_{\text{MX,IP}}\) provides evidence for the formation of receptor-bound complexes: the 1-MX\(^+\) species have a larger volume than the bare MX\(^+\) IPs. As such, the DRS relaxation times indicate that for all studied salts, 1-MX\(^+\) is the major IP species at high concentrations of 1, in line with the ESI-MS spectra. This notion is further supported by \(^1\)H NMR titration experiments, which indicate that 1-MX\(^+\) complexes are only significant for an excess of iodide (see discussion in the SI together with Figures S19–S24 and Table S7).

To relate the relaxation amplitudes, \(S_{\text{MX,IP}}\), to IP concentrations, the contribution of both MX\(^+\) and 1-MX\(^-\) species to \(S_{\text{MX,IP}}\) has to be taken into account. For quantitative analysis of ion pairing using Eq. 3, the dipole moment of 1-MX\(^-\), \(\mu_\text{1-MX}^-\), is required. Based on the direct contact between the cation and the anion in the crystal structure (Figures 4 and S6, SI), one might expect \(\mu_\text{1-MX}^- \approx \mu_{\text{MX,IP}}\), which is confirmed by DFT calculations that show the dipole moments of the receptor-bound and bare IPs to agree within less than 3 D (see Table S3, SI). Experiments on solutions of Ba\(_2\)+1 further support the similar dipole moments of 1-MX\(^-\) and MX\(^-\) (see the discussion together with Figures S25–S27 in the SI).

Thus, assuming \(\mu_\text{1-MX}^- \approx \mu_{\text{MX,IP}}\), the total IP concentration, \(c_{\text{MX,IP}}\approx [\text{MX}^-]+[1-\text{MX}^-]\), in the presence of the receptor can be extracted from \(S_{\text{MX,IP}}\) using Eq. 3. The thus obtained values for \(c_{\text{MX,IP}}\) (Figure 7) show an increase in [MX\(^-\)]+[1-MX\(^-\)] by ~10–25 %, upon addition of 0.1 M 1 to the 0.1 M salt solutions. Consequently, ion association is enhanced in the presence of 1. This increase in ion pairing is consistent with the 15–25 % decrease of the conductivities (Figure S28, SI) of the samples as 1-MX\(^-\) complexes hardly contribute to the overall conductivity due to their reduced mobility or charge/volume ratio.\(^{[65]}\) We note that similar conclusions can be obtained from the experiments where \(c_{\text{salt}}\) gradually increases (0.02–0.14 M) at \(c_1 = 0.05\) M: addition of 1 results in higher relaxation times, higher IP concentrations as well as lower conductivities (Figures S29–S34, SI).

Our results thus show that the presence of 1 enhances IP formation for all studied salts. For the overall degree of ion association \(([\text{MX}^-]+[1-\text{MX}^-])/c_{\text{salt}}\), we find 67 % for SrI\(_2\), 57 % for Sr(ClO\(_4\))\(_2\) and 50 % for Ba(ClO\(_4\))\(_2\) in the presence of 0.1 M 1 (see Table 1). Overall, the trend in the ion association strength is the same (SrI\(_2\) > Sr(ClO\(_4\))\(_2\) > Ba(ClO\(_4\))\(_2\)) with and without 1. Assuming that the formation of 1-MX\(^+\) prevails at \(c_1/c_{\text{salt}}\geq 1\) ratios (that is, \(c_{\text{MX,IP}}\approx c_1\)), we can estimate the cumulative stability constants of the 1-MX\(^+\) IP complexes for samples containing 0.10 M 1:

$$K_1\text{-MX}^+ = \frac{[1-\text{MX}^-] \cdot (c_1^2)}{[\text{MX}^-] \cdot [1-\text{MX}^-]}$$

$$= \left(\frac{1}{c_{\text{salt}} - [\text{MX}^-] - (2c_{\text{salt}} - [1-\text{MX}^-]) \cdot (c_1 - [1-\text{MX}^-])}\right) \cdot [1-\text{MX}^-]$$

The thus calculated constants are listed in Table 2. Accordingly, we find stronger association for Sr\(^{2+}\) salts as compared to Ba\(^{2+}\) showing that Sr\(^{2+}\) matches better the size of the polyethylene-glycol binding cavity. Also, this trend is consistent

![Figure 7. Concentrations of bare/receptor-bound MX\(^+\) ion-pairs for 0.10 M SrI\(_2\), Sr(ClO\(_4\))\(_2\) and Ba(ClO\(_4\))\(_2\) solutions as a function of concentration of 1. The values of \(c_{\text{MX,IP}}\) and their error bars were calculated via Eq. 3, assuming \(\alpha(S_{\text{MX,IP}}) = \pm 0.3\). The dashed lines are guide to the eye.](image-url)

| Table 2. Stability constants (log \(K\pm\alpha\), at (23 ± 2) °C) corresponding to the reactions in the first column, obtained in this work via DR spectroscopic measurements at \(I \approx 0.17–0.19\) M. |
|--------------------------------------------------------|----------------------|
| Reaction                                               | log \(K\)             |
| \(1 + \text{Sr}\(^{2+}\) + I\(^-\) \rightleftharpoons \text{SrI}^+\) | 2.66 ± 0.04          |
| \(1 + \text{SrI}^+ \rightleftharpoons \text{SrI}^+\)                               | 1.67 ± 0.04          |
| \(1 + \text{SrI}^+ + \text{ClO}_4^- \rightleftharpoons \text{SrClO}_4^+\)          | 2.35 ± 0.03          |
| \(1 + \text{SrClO}_4^- \rightleftharpoons \text{SrClO}_4^-\)                     | 1.52 ± 0.03          |
| \(1 + \text{Ba}\(^{2+}\) + \text{ClO}_4^- \rightleftharpoons \text{BaClO}_4^-\)    | 2.19 ± 0.03          |
| \(1 + \text{BaClO}_4^- \rightleftharpoons \text{BaClO}_4^-\)                     | 1.44 ± 0.03          |
with that of the cation-binding constants derived from 1H NMR titrations using perchlorate salts (i.e. \( K_{1 \cdot MX^+} > K_{1 \cdot Ba^{2+}} \), see Table S7 in the SI). These constants are however consistently higher than \( K_{1 \cdot LiClO_4^-} \) and \( K_{1 \cdot BaClO_4^-} \), obtained from DRS (Table 2). This discrepancy can be rationalized by the notion that DRS is sensitive only to the formation of dipolar 1-MX complex, while NMR detects all species that contain a cation (i.e. 1-MX\(^+\) + 1-MX\(^-\)). 1H NMR chemical shifts are primarily sensitive to the coordination of cations, while the binding of ClO\(^-\) does not alter the protons’ chemical environment. Consequently, NMR yields higher equilibrium concentrations and thus higher formation constants (for discussion, see the SI).

Overall, the ion association equilibria in the ternary systems studied in the present work consists of ion pairing and the binding of free ions as well as IPs by the receptor. Although the formation of 1-Sr\(^+\) species refers to thermodynamic equilibrium and therefore we cannot derive if such complexes are formed via the binding of free ions or IPs (or both), it is possible to compare the formation constants of these processes: we estimate the equilibrium constant for binding of IPs to 1 (\( K_{1 \cdot MX^+} \)) using the values of \( K_{1 \cdot MX} \) (referring to the binding of free ions, Eq. 6) and \( K_{MX^-} \) (referring to ion pairing, Eq. 4):

\[
K'_{1 \cdot MX^+} = \frac{[1 \cdot MX^+] \cdot c^d}{[1] \cdot [MX^-]} = \frac{K_{1 \cdot MX^+}}{K_{MX^-}}
\]

(7)

For this estimation we calculate the values of log \( K_{MX^-} \) at the same ionic strength at which we determined the log \( K'_{1 \cdot MX^+} \) constants (\( I \approx 0.16–0.19 \) M) using Eq. 5. The results (Table 2) suggest that 1 is also somewhat more efficient in binding Sr\(^+\) IPs as compared to SrClO\(^-\) and BaClO\(^-\). This difference can be explained by the stronger binding of Sr\(^+\) as compared to Ba\(^+\) as well as by the formation of strong hydrogen bonds to iodide as compared to perchlorate, as inferred from 1H NMR titrations and DFT geometries, respectively.

### 3. Conclusions

In the absence of 1, Sr\(^+\), SrClO\(^-\) as well as Ba(ClO\(^-\)), tend to form 1:1 contact ion-pairs (CIPs) in acetonitrile to a significant extent. The degree of ion pairing can be as high as ~50% for the I\(^-\) and ~40% for the ClO\(^-\) salts, already at low salt concentrations (<0.15 M). The neat receptor 1 exists predominantly in an open form in solution, to which a cation can bind without major structural reorganization.

In the presence of 1 we find simultaneous binding of cations and anions to the receptor. The ESI-MS results indicate that the receptor-bound CIP species, i.e. 1-Sr\(^+\), 1-SrClO\(^-\) and 1-BaClO\(^-\) prevail in solution over Sr\(^+\), SrClO\(^-\) and BaClO\(^-\) IPs. The formation of these receptor-bound IP complexes is confirmed by the increasing DRS relaxation times in the presence of 1. Quantitative analysis of the DRS results shows the overall degree of ion association to increase by approximately 10–25% in the presence of 1, relative to the receptor-free solutions. Despite the overall enhancement of ion pairing in solution by the receptor is only moderate, a large fraction of IPs is complexed by 1 in solution. Structural analysis of the complexes reveals that their higher stability (as compared to the bare IPs) can be traced to the formation of coordinative, anion-π as well as hydrogen bonding interactions.

We find that the overall degree of salt binding by 1 is higher for I\(^-\) salts than for ClO\(^-\) salts. The extent of ion association follows the order of 1-Sr\(^+\) > 1-SrClO\(^-\) > 1-Ba(ClO\(^-\)), which also resembles the ion association trends of the bare salt solutions. These parallelizing trends can be explained by that the cation-anion distance, i.e. the electrostatic interaction between the co-bound ions, remaining essentially unaffected upon binding to 1. This holds also for perchlorate salts, even though perchlorate is often considered as weakly coordinating anion. Generally, our study shows that ion-pair recognition is intimately related to ion pairing in solution, thereby highlighting the importance of taking the latter equilibrium into account when studying salt binding in organic solvents.

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### Conflict of Interest

The authors declare no conflict of interest.

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