

Ionic Interactions from the Mixing of NaCl with the Acetate, Nitrate, Perchlorate, and Sulfate Salts of Guanidinium in Water

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Ionic interactions have been investigated from the experimental isopiestic osmotic coefficient measurements on the mixing of NaCl with several guanidinium (Gn) salts, like CH_3COOGn , GnNO_3 , GnClO_4 , and Gn_2SO_4 , up to high ionic strengths. Analysis of osmotic coefficient data by the Pitzer theory offers valuable information on the mixing of ions of like and unlike charges of hydrophilic and hydrophobic nature. The mixing effects arising out of symmetrical and unsymmetrical mixing of ions are computed by the Pitzer theory in these systems. The excess Gibbs free energies of mixing, $\Delta_m G^E$ have been analyzed by the Friedman theory of cluster integral expansion. The $\Delta_m G^E$ values display very interesting features with respect to the ionic strength fraction of the acetate, nitrate, and perchlorate salts of guanidinium. The minima in the $\Delta_m G^E$ values are noted in the NaCl-rich mixtures, and the addition of these guanidinium salts slowly enhances $\Delta_m G^E$, passing through zero to positive values. The mixing of NaCl with Gn_2SO_4 offers negative $\Delta_m G^E$ throughout the mixture composition. Although binary interactions are nearly absent in the NaCl– CH_3COOGn mixtures, the ternary and quaternary interactions are noted to be important in the mixtures of NaCl with other guanidinium salts. The $\Delta_m G^E$ values of the mixture containing Na^+ , Gn^+ , Cl^- , and SO_4^{2-} ions (where binary interactions are important) can be estimated by Young's cross square rule (YCSR) with confidence. The YCSR is not obeyed when NaCl is mixed with CH_3COOGn , GnNO_3 and GnClO_4 , where ternary and quaternary interactions are dominant over the binary interactions.

Introduction

An accurate knowledge of ionic interactions is essential in delineating the influence of electrolytes on the physical and biological behavior of proteins and nucleic acids and on the kinetics of organic reactions. Recently, we have investigated the ionic interactions in the aqueous mixtures of guanidinium chloride (GnCl) with NaCl, KCl, MgCl_2 , CaCl_2 and tetrabutylammonium chloride (TBAC).^{1,2} GnCl being a potential denaturant of proteins and DNA duplex is also known to inhibit the reaction rates.³ We observed interesting changes in the excess free energies, volumes, and compressibilities of mixing in these cases, as Na^+ , Mg^{2+} , and Ca^{2+} are the hydrophilic cations and TBA^+ and Gn^+ the hydrophobic ones. We also showed the neutralization of opposing effects produced by the hydrophilic and hydrophobic nature of these ions. The mixing effects were discussed in terms of binary, ternary, and higher order interactions. Later, we employed this information to carry out the cycloaddition of cyclopentadiene with methyl acrylate in the aqueous mixtures of NaCl and GnCl .⁴ Several years ago, it was shown that the salts of guanidinium with Cl^- , Br^- , ClO_4^- , SCN^- , etc. destabilized the proteins, whereas Gn_2SO_4 , on the contrary, enhanced their stability.⁵ Later, we noted the similar behavior of these guanidinium salts on the cycloaddition reaction.⁶ To resolve the issue of anomalous behavior of Gn_2SO_4 , we measured vapor pressures and volumetric and transport properties of its aqueous solutions.^{7,8} The partial molar volumes and compressibilities of Gn_2SO_4 at infinite dilution were remarkably different from those of other guanidinium salts. The molality dependence of activity coefficients of Gn_2SO_4 showed resemblance with that of MgSO_4 .

Considering the importance of NaCl and the guanidinium salts as outlined above, we now aim to understand the thermodynamics of the aqueous mixtures of NaCl with CH_3COOGn (abbreviated henceforth GnAc , Ac being acetate ion), GnNO_3 , GnClO_4 and Gn_2SO_4 . To obtain deeper insights into the ionic interactions and their role in biological molecules and reactivities in organic systems, we in this investigation raise the following questions: (1) What are the types of interactions operating in the above ionic mixtures and how do they vary with the mixture compositions and ionic strengths? (2) In view of the opposite nature of Na^+ and Gn^+ species, how do these different types of interactions of Na^+ with Gn^+ containing Ac^- , NO_3^- , ClO_4^- and SO_4^{2-} species compete with each other to yield the total excess free energy of mixing? The orientations of water molecules by cations will be affected by anions of different types. And (3) though Young's cross square rule⁹ is applicable to simple electrolyte mixtures, e.g., NaCl–KBr and NaCl– MgSO_4 (systems with no common ions), does it also hold in the case of mixing of a hydrophilic cation with a strong hydrophobic cation? It is important to note that all the mixtures undertaken here do not include a common cation or anion.

Experimental Section

Commercially available AR grade NaCl, GnNO_3 , and Gn_2SO_4 purchased from Aldrich Chemical Co. were recrystallized from water and dried under a vacuum. GnAc and GnClO_4 were prepared as reported in the literature.¹⁰ All solutions were prepared by weight in deionized water and converted into mass. The purity and concentration of the aqueous guanidinium salts were estimated by the method of Nozaki.¹¹

The experimental method for measuring isopiestic osmotic coefficients is described in our previous work.^{1,2} Aqueous NaCl

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solution was used as a reference electrolyte for measuring isopiestic osmotic coefficients performed with an apparatus similar to that discussed by Rard et al.¹² The osmotic coefficients of aqueous NaCl (reference electrolyte) at 298.15 K were taken from Hamer and Wu¹³ after applying corrections for the nonideal vapor behavior.¹⁴ Isopiestic equilibrium was reached in 7 days for all the mixtures except those containing Gn_2SO_4 , which required 10 days for reaching equilibrium. Final isopiestic molality was calculated from an average of three samples with an agreement of 0.08%.

The temperature of a constant-temperature water bath (Julabo) was maintained to within 0.005 K. The molalities were accurate to 2×10^{-4} . Throughout the paper NaCl is denoted by 1 and GnAc, GnNO_3 , GnClO_4 , and Gn_2SO_4 are denoted by 2. The guanidinium salts, in general, are denoted by GnX , where X represents anion. The anions are Ac^- , NO_3^- , ClO_4^- , and SO_4^{2-} .

Results and Discussion

In Table 1 are listed the measured isopiestic osmotic coefficients, φ , as a function of the ionic strength fraction of the guanidinium salt, y_2 (with $y_1 = 1 - y_2$) in aqueous mixtures of NaCl with guanidinium salts at different ionic strengths. The quantity y_2 is given by I_2/I , where $I_2 = m_2$ for 1:1 electrolyte and $3m_2$ for 1:2 electrolyte. The symbol m stands for molality of a salt. I , the ionic strength of mixture is calculated as $0.5\sum m_i z_i^2$ with z being the ionic charge. Our experimental φ data for pure electrolytes are in excellent agreement with those reported in the literature (root-mean square deviation, rmsd ranging from 0.004 to 0.006).^{8,10,13}

Let us first examine how the φ values of NaCl vary on addition of guanidinium salts. Addition of GnAc sharply enhances the φ values of NaCl at all the ionic strengths. All the variations are nonlinear with respect to y_2 . However, if GnNO_3 and GnClO_4 are added to aqueous NaCl at constant ionic strengths, the φ values of NaCl are reduced quite sharply. There is, however, a crossover in the φ - y_2 curves in the NaCl-rich mixtures (about 80% of NaCl) of these two systems. In the case of NaCl- Gn_2SO_4 , where a monotonic reduction in the φ values of NaCl is seen on addition of Gn_2SO_4 , the crossover of the φ - y_2 curves at $I = 3, 4.5$, and 6 mol kg^{-1} is prominent near 60% of NaCl. A crossover in the curves was also noted in the case of aqueous NaCl-GnCl mixtures. It is thus clear that the addition of guanidinium salts such as above does not influence the φ values of NaCl in uniform manner. As Gn^+ is a common cation in these mixtures, this nonuniform effect should arise due to different anions that constitute guanidinium salts. Examples of the above type of behavior are shown in Figure 1 in the form of the φ - y_2 plots. In Figure 1a, for instance, we plot the dependence of φ on I at a constant $y_2 = 0.4$ for the mixtures of NaCl with GnAc, GnNO_3 , and GnClO_4 . Figure 1b shows the plots with crossover behavior for the mixtures of NaCl- Gn_2SO_4 at different ionic strengths.

We preferred to analyze the osmotic coefficients of these mixtures by using the virial coefficient approach of Pitzer.¹⁵ It should be pointed out here that Leifer and co-workers¹⁶ in the past, have successfully employed the Scatchard-Rush-Johnson equations¹⁷ to analyze the osmotic coefficients of the cluster forming electrolyte mixtures. The Scatchard-Rush-Johnson equations provide a more accurate description of thermodynamics of electrolytes at the expense of a large number of parameters.^{1,2,16,17} In the Pitzer theory, a combination of the Debye-Huckel and virial coefficient terms is used to describe the thermodynamic properties of electrolyte solutions. Earlier, we summarized the Pitzer equations applicable to the mixtures

TABLE 1: Experimental Isopiestic Osmotic Coefficients of the Aqueous Mixtures of NaCl with GnAc, GnNO_3 , GnClO_4 , and Gn_2SO_4 Mixtures at 298.15 K

$I/\text{mol kg}^{-1}$	y_2	φ	$I/\text{mol kg}^{-1}$	y_2	φ
NaCl-GnAc					
0.5012	0	0.912	2.0156	0	0.983
0.4889	0.1999	0.916	1.9985	0.2043	1.025
0.4993	0.4112	0.920	1.9900	0.4016	1.082
0.5014	0.5994	0.925	2.0332	0.5992	1.150
0.5043	0.7998	0.945	2.0104	0.8051	1.245
0.4902	1	0.970	1.9981	1	1.358
0.9894	0	0.936	2.4987	0	1.013
0.9990	0.2007	0.939	2.5013	0.2049	1.075
1.0016	0.4043	0.950	2.4986	0.3985	1.168
0.9956	0.5997	0.965	2.4976	0.5988	1.295
1.0093	0.7894	0.988	2.5025	0.8043	1.450
0.9957	1	1.017	2.4984	1	1.630
NaCl-GnNO ₃					
0.2001	0	0.925	0.9911	0	0.936
0.1998	0.2022	0.909	1.0110	0.1918	0.860
0.2081	0.4102	0.895	1.0346	0.4083	0.818
0.1898	0.5993	0.880	0.9932	0.6016	0.791
0.2046	0.8081	0.878	1.0104	0.8171	0.769
0.1997	1	0.875	0.9989	1	0.753
0.4912	0	0.921	1.3983	0	0.951
0.5072	0.2031	0.884	1.4009	0.2120	0.868
0.5111	0.4108	0.859	1.4110	0.4055	0.809
0.4961	0.6104	0.841	1.4026	0.6100	0.763
0.4902	0.8045	0.827	1.3987	0.7948	0.721
0.5031	1	0.818	1.4040	1	0.710
NaCl-GnClO ₄					
0.5005	0	0.921	2.0019	0	0.983
0.4998	0.2108	0.940	1.9987	0.2119	0.897
0.5022	0.3940	0.901	2.0104	0.3987	0.828
0.4887	0.5898	0.871	1.9986	0.6008	0.770
0.4926	0.8079	0.845	2.0191	0.8076	0.718
0.5044	1	0.823	1.9901	1	0.673
1.0108	0	0.936	2.6008	0	1.032
1.1121	0.2120	0.882	2.5995	0.2049	0.897
1.0007	0.3978	0.823	2.6164	0.4010	0.817
0.9998	0.6010	0.810	2.4996	0.6048	0.739
1.0009	0.8011	0.785	2.6019	0.8002	0.681
1.0013	1	0.764	2.5917	1	0.633
NaCl-Gn ₂ SO ₄					
0.7467	0	0.927	3.0054	0	1.045
0.7514	0.2071	0.881	2.9908	0.2107	0.937
0.7509	0.4041	0.843	2.9938	0.4039	0.840
0.7489	0.6108	0.824	3.0090	0.6013	0.749
0.7504	0.8077	0.811	3.0126	0.7973	0.671
0.7495	1	0.802	2.9869	1	0.603
1.5036	0	0.956	5.9682	0	1.271
1.5019	0.1934	0.885	5.9792	0.2014	1.025
1.4927	0.4102	0.827	6.0061	0.4096	0.851
1.5001	0.6055	0.781	6.0013	0.6106	0.699
1.4969	0.8012	0.737	5.9981	0.8079	0.592
1.5117	1	0.708	5.9907	1	0.522

of 1:1 electrolytes with a common ion. As the mixtures studied herein contain four uncommon ions, earlier simplified equations will not be applicable in the current situation. Moreover, we now have a case of unsymmetrical mixing i.e., the mixing of like charged ions with different charges on them (Cl^- , SO_4^{2-}). In Table S1 (Supporting Information) we tabulate a list of the working equations of Pitzer for the osmotic coefficient, φ , of the mixture (eq 1, Table S1) and activity coefficient, γ_{\pm} of an electrolyte in mixture (eq 2, Table S1). Analysis of these data by the Pitzer equations requires accurate estimates of the Pitzer coefficients of each pure electrolyte. The Pitzer coefficients, $\beta^{(0)}_{\text{MX}}$, $\beta^{(1)}_{\text{MX}}$, and C^{ϕ}_{MX} accounting for the interactions between cation and anion were obtained from the least-squares fitting of φ - m data by using the Pitzer equations for pure electrolytes.^{15a} These coefficients for 10 different pairs of cations and anions obtained by us and from the literature¹⁸ are recorded in Table S2 for ready reference and for the ease of computation. An additional term called $\beta^{(2)}_{\text{MX}}$ generally useful for 2:2 electrolytes

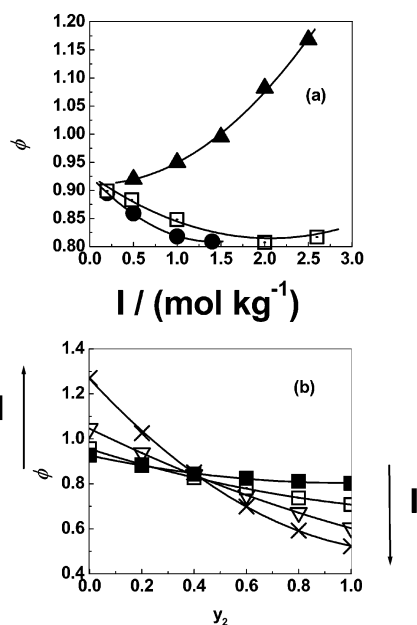


Figure 1. (a) Plots of ϕ - I at constant y_2 of 0.4 for the mixtures of NaCl with (▲) GnAc, (●) GnNO₃, and (□) GnClO₄. (b) Plots of ϕ - y_2 at different ionic strengths of the NaCl-Gn₂SO₄ mixtures: (■) $I = 0.75$, (□) $I = 1.5$, (▽) $I = 3$, (×) $I = 6$ mol kg⁻¹.

was not required in the present case. Besides accounting for the interactions between a cation and anion pair from pure electrolyte, the binary terms characterizing the interactions between two cations or two anions should be considered. Similarly, the ternary interactions among Na⁺, Gn⁺, and individual anions will assume significance in the present context. Thus, five binary terms will account for the pairs of θ_{NaGn} , θ_{ClAc} , θ_{ClNO_3} , θ_{ClClO_4} and θ_{ClSO_4} . As suggested by Pitzer, ionic interactions between two same ions, i.e., Na⁺-Na⁺, Gn⁺-Gn⁺, Cl⁻-Cl⁻, etc., are ignored in this approach, because Gn⁺ is a hydrophobic cation and its interaction with another Gn⁺ may indeed exist.¹⁹ There is, however, no way to that these interactions can be accounted for in the Pitzer theory. In addition, there will be another eight possible ternary interaction terms denoted by ψ_{NaGnCl} , ψ_{NaGnAc} , ψ_{NaGnNO_3} , ψ_{NaGnClO_4} , $\psi_{\text{Na}^+\text{Gn}^+\text{SO}_4^{2-}}$, ψ_{GnClAc} , ψ_{GnClNO_3} , and ψ_{GnClClO_4} . The role of these mixing terms in the Pitzer equations has been highlighted earlier in the literature.^{1,2,15} It should be mentioned here that at finite concentration, both ϕ and γ_{\pm} depend in a very complex way on short-range forces between ions both direct and as modified by water, in addition to the long-range electrostatic forces. If two ions of the same sign and charges are mixed, the effect is known as symmetrical mixing. The mixing of two ions of the same sign but with different charges yields to unsymmetrical mixing. In our study, both the cases are present. The interactions Na⁺-Gn⁺, Cl⁻-Ac⁻, Cl⁻-NO₃⁻, and Cl⁻-ClO₄⁻ are examples of symmetrical mixing whereas Cl⁻-SO₄²⁻ is of unsymmetrical mixing. We computed the values of $E\theta_{\text{Cl-SO}_4}$ and $E\theta'_{\text{Cl-SO}_4}$ for unsymmetrical mixing from eqs 15 and 16 of Table S1. These results are tabulated in Table 2 at constant ionic strengths. Values of the integrals employed for calculating $E\theta_{\text{Cl-SO}_4}$ and $E\theta'_{\text{Cl-SO}_4}$ were taken from Pitzer.¹⁵ The values of $E\theta_{\text{Cl-SO}_4}$ and $E\theta'_{\text{Cl-SO}_4}$ were inserted in eqs 12 to 14 (Table S1) to give the mixing terms, Φ_{ij} , Φ_{ij} , and Φ'_{ij} . The binary and ternary mixing terms evaluated by the procedure² are listed in Table 3. In an ionic mixture, the mixing parameters pertaining to binary and ternary interactions together with those arising out of symmetrical and unsymmetrical mixing occupy significant place. An example of their importance in the analysis of the

TABLE 2: High Order Electrostatic Functions at Constant Ionic Strengths for the Interaction between Cl⁻ and SO₄²⁻ in Water

$I/\text{mol kg}^{-1}$	$E\theta_{\text{Cl-SO}_4}$	$E\theta'_{\text{Cl-SO}_4}$
0.1	0.78785	-0.82145
0.2	0.44312	-0.39576
0.5	0.29577	-0.26531
1	0.19432	-0.19571
1.5	0.13378	-0.13587
2	0.09439	-0.11385
3	0.05124	-0.03478
4.5	0.01344	-0.01054
5	0.00787	-0.00943
6	0.00595	-0.00753

TABLE 3: Binary and Ternary Mixing Parameters for Different Ions in the Mixtures of NaCl with the Guanidinium Salts

mixing terms	values	mixing terms	values
$\theta_{\text{Na}^+\text{Gn}^+}$	0.019	$\psi_{\text{Na}^+\text{Gn}^+\text{SO}_4^{2-}}$	-0.059
$\theta_{\text{Cl}^-\text{Ac}^-}$	-0.003	ψ_{NaClAc}	0.002
$\theta_{\text{Cl}^-\text{NO}_3^-}$	-0.034	ψ_{NaClNO_3}	0.004
$\theta_{\text{Cl}^-\text{ClO}_4^-}$	-0.039	ψ_{NaClClO_4}	0.005
ψ_{NaGnCl}	-0.005	ψ_{GnClAc}	-0.011
ψ_{NaGnAc}	-0.011	ψ_{GnClNO_3}	-0.019
ψ_{NaGnNO_3}	-0.023	ψ_{GnClClO_4}	-0.005
ψ_{NaGnClO_4}	-0.029		

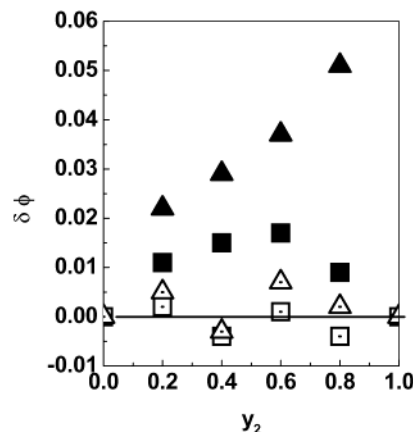


Figure 2. Deviations ($\delta\phi$) calculated from the experimental and calculated ϕ values by the Pitzer equations for NaCl-GnAc at $I = 2.5$ mol kg⁻¹ without (■) and with (□) mixing terms and for NaCl-Gn₂SO₄ at $I = 6$ mol kg⁻¹ without (▲) and with (△) mixing terms.

mixture data on ϕ is demonstrated in Figure 2, where we have plotted the deviations, $\delta\phi$ ($\phi_{\text{expt}} - \phi_{\text{calc}}$, ϕ_{calc} is computed without and with mixing terms listed in Tables 2 and 3) for NaCl-GnAc and NaCl-Gn₂SO₄ at $I = 2.5$ and 6 mol kg⁻¹, respectively. These two systems are chosen because the former is a representative of symmetrical mixing and the latter of unsymmetrical. In the case of the NaCl-GnAc system, the systematic deviation in ϕ disappears on including the mixing parameters. The deviations in the case of NaCl-Gn₂SO₄ are large and systematic, which become random if the mixing parameters are included in the calculations. In a nutshell, the osmotic coefficients of the mixtures of NaCl with GnAc, GnNO₃, GnClO₄, and Gn₂SO₄ can be analyzed with the Pitzer equations, including various mixing effects with average rmsd of 0.004, 0.005, 0.003, and 0.007, respectively, in the ionic strength range studied.

The activity coefficients of an electrolyte in a mixture can be calculated from eq 2 of Table S1 together with the mixing terms given in Tables 2 and 3. In Figure 3a is shown the variation of $\ln \gamma_{\pm}$ of NaCl with respect to y_2 in different guanidinium salts at the highest ionic strengths studied herein.

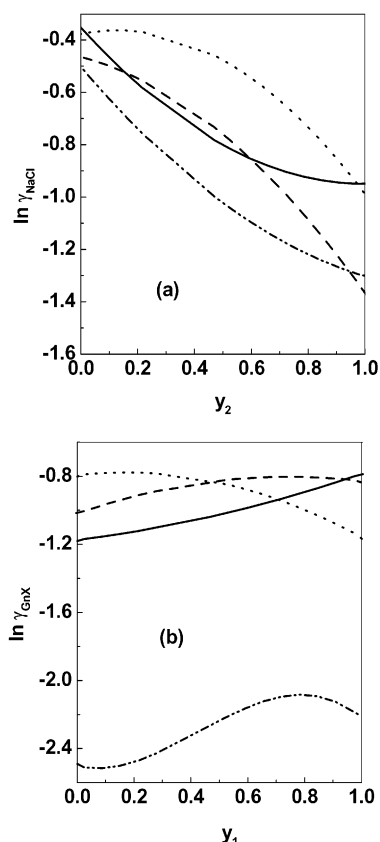


Figure 3. (a) Variation of $\ln \gamma_{\pm\text{NaCl}}$ with y_2 in (···) GnAc at $I = 2.5$ mol kg^{-1} , (—) GnClO_4 at $I = 2.6$ mol kg^{-1} , and (---) GnNO_3 at 1.4 mol kg^{-1} , and (---) Gn_2SO_4 at 6 mol kg^{-1} . (b) Plots of $\ln \gamma_{\pm\text{GnX}}$ versus y_1 in the NaCl mixtures: (···) GnAc at $I = 2.5$ mol kg^{-1} ; (---) GnNO_3 at 1.4 mol kg^{-1} ; (—) GnClO_4 at $I = 2.6$ mol kg^{-1} ; (---) Gn_2SO_4 at 6 mol kg^{-1} .

In Figure 3b are presented similar plots for $\ln \gamma_{\pm}$ of different guanidinium salts as a function of y_1 in the mixtures. The activity coefficients of NaCl vary nonlinearly with y_2 in the guanidinium salts at all the ionic strengths. In the NaCl-rich mixtures with GnAc; the activity coefficients of NaCl are not affected. However, a noticeable decrease in the activity coefficients of NaCl is seen above 40% of GnAc. GnNO_3 displays similar behavior. A monotonic decrease in the activity coefficient values of NaCl is witnessed on addition of up to 40% of GnClO_4 . Further addition of GnClO_4 brings about very mild change in the activity coefficients of NaCl. The influence of Gn_2SO_4 on the activity coefficients of NaCl is the maximum among the guanidinium salts studied. The changes in the activity coefficients of NaCl in GnAc and GnNO_3 are very similar to those produced by GnCl .¹ In general, the activity coefficient of NaCl at $y_2 \approx 0.5$ decreases in the order $\text{GnCl} < \text{GnAc} < \text{GnNO}_3 \approx \text{GnClO}_4 < \text{Gn}_2\text{SO}_4$. Addition of NaCl into GnAc substantially reduces the activity coefficients of GnAc. A mild increase in the activity coefficients of GnNO_3 is witnessed up to 40% NaCl, which then levels off in the NaCl-rich mixtures. A steady increase in the activity coefficients of GnClO_4 is noted with the increasing NaCl concentration. NaCl slowly (above 20% NaCl) enhances the activity coefficients of Gn_2SO_4 , reaching a maximum at about 80% NaCl composition. It then lowers the activity coefficients of Gn_2SO_4 in the mixtures containing more than 80% NaCl. In $\ln \gamma_{\pm\text{GnNO}_3}$ and $\ln \gamma_{\pm\text{GnClO}_4}$ vary with y_1 in the manner $\ln \gamma_{\pm\text{GnCl}}$ varies at high ionic strengths of the mixtures. However, the effect of GnAc is opposite to that seen in the case of GnCl .¹ The degree of nonlinearity of the $\ln \gamma_{\pm\text{NaCl}}$ versus

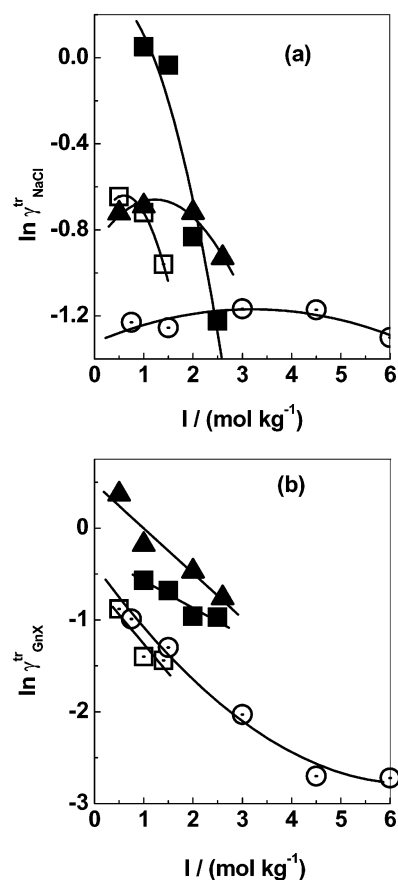


Figure 4. (a) Dependence of $\ln \gamma_{\pm\text{NaCl}}$ on I of the mixtures of NaCl with GnAc (■), GnNO_3 (□), GnClO_4 (▲), and Gn_2SO_4 (○). (b) Dependence of $\ln \gamma_{\pm\text{GnX}}$ on I of the mixtures of NaCl with GnAc (■), GnNO_3 (□), GnClO_4 (▲), and Gn_2SO_4 (○).

y_2 or the $\ln \gamma_{\pm\text{GnX}}$ versus y_1 plots decreases at lower ionic strengths, and these plots tend to become linear.

Dependence of $\ln \gamma_{\pm}$ of an electrolyte on y_1 or y_2 at constant ionic strength can be described by the Harned-type equations²⁰

$$\ln \gamma_{\pm\text{NaCl}} = \ln \gamma_{\pm\text{NaCl}}^0 - \alpha_{11}y_2 - \alpha_{12}y_2^2 - \alpha_{13}y_2^3 \quad (1)$$

and

$$\ln \gamma_{\pm\text{GnX}} = \ln \gamma_{\pm\text{GnX}}^0 - \alpha_{21}y_1 - \alpha_{22}y_1^2 - \alpha_{23}y_1^3 \quad (2)$$

with $\alpha_{11}...$ and $\alpha_{21}...$ being the Harned coefficients. $\ln \gamma_{\pm}^0$ is the activity coefficient of the pure electrolyte at the ionic strength of the mixture. The activity coefficients of either electrolyte in the present study do not obey the Harned rule, as can be seen from the $\ln \gamma_{\pm}$ - y curvatures depicted in Figure 3. This is also evident from the Harned coefficients obtained from the least-squares analysis of activity coefficient data using eqs 1 and 2 and listed in Table S3 as Supporting Information.

The trace activity coefficients, $\ln \gamma_{\pm}^{\text{tr}}$, of either NaCl or guanidinium salts computed using standard procedure²⁰ are shown in Figure 4. In Figure 4a, we first show the ionic strength dependence of $\ln \gamma_{\pm}^{\text{trNaCl}}$ in different guanidinium salts. The $\gamma_{\pm}^{\text{trNaCl}}$ values are significantly lowered with increasing ionic strength in the case of GnAc followed by GnNO_3 . A poor decrease in $\gamma_{\pm}^{\text{trNaCl}}$ with ionic strength is seen in the mixture of NaCl with GnClO_4 . Gn_2SO_4 fails to display any noticeable influence on $\gamma_{\pm}^{\text{trNaCl}}$ throughout the ionic strength. The general trend in which the guanidinium salts affect $\gamma_{\pm}^{\text{trNaCl}}$, for example, at $I = 1$ mol kg^{-1} follows the order $\text{GnAc} > \text{GnNO}_3 \approx \text{GnClO}_4$

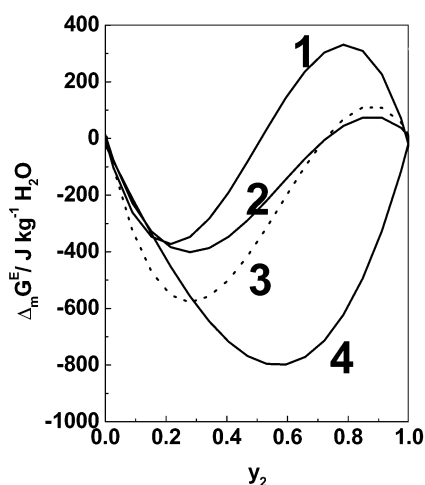


Figure 5. Plots of $\Delta_m G^E - y_2$ for the mixture of NaCl with (1) GnAc $I = 2.5 \text{ mol kg}^{-1}$, (2) GnNO₃ $I = 1.4 \text{ mol kg}^{-1}$, (3) GnClO₄ $I = 2.6 \text{ mol kg}^{-1}$, and (4) Gn₂SO₄ $I = 6 \text{ mol kg}^{-1}$.

> Gn₂SO₄. The $\gamma_{\pm}^{\text{GnAc}}$ is lowered with increasing ionic strength with a similar behavior shown by the trace activity coefficients of GnClO₄ and GnNO₃. The order in which the trace activity coefficients of the guanidinium salts are affected was noted to be GnClO₄ > GnAc > Gn₂SO₄ > GnNO₃.

The excess Gibbs free energies of mixing, $\Delta_m G^E$, for these mixtures were calculated by the following equation:

$$\Delta_m G^E = Q_1 [\ln(\gamma_1/\gamma_1^0) + (\varphi_1 - \varphi)] + Q_2 [\ln(\gamma_2/\gamma_2^0) + (\varphi_2 - \varphi)] \quad (3)$$

where $Q_1 = \nu_1 y_1 m_1 RT$; ν_1 is stoichiometry of an electrolyte with an identical definition for Q_2 . R and T have usual significance. The $\Delta_m G^E - y_2$ curves are plotted in Figure 5 for different mixtures. These plots belong to the highest ionic strengths studied for each mixture. The mixtures of NaCl with GnAc, GnNO₃, and GnClO₄ show a very interesting trend with respect to y_2 . These curves go to minima in the NaCl-rich mixtures. For instance, the minima occur at $y_2 \approx 0.2-0.25$. The $\Delta_m G^E$ values at these minima are -380 , -400 , and $-575 \text{ J kg}^{-1} \text{ H}_2\text{O}$ in the NaCl mixtures of GnAc, GnNO₃, and GnClO₄, respectively. Further addition of the guanidinium salt into NaCl at a constant ionic strength increases $\Delta_m G^E$, reaching to zero at $y_2 \approx 0.5$ in the case of GnAc and ≈ 0.72 for GnNO₃ and GnClO₄. In the NaCl-poor region, positive $\Delta_m G^E$ are seen with maxima of 300 (at $y_2 \approx 0.8$), 100 (at $y_2 \approx 0.9$), and $70 \text{ J kg}^{-1} \text{ H}_2\text{O}$ (at $y_2 \approx 0.9$) in the mixtures of NaCl with GnAc, GnNO₃, and GnClO₄, respectively. The mixing of NaCl with GnAc, GnNO₃, and GnClO₄ accompanying the negative $\Delta_m G^E$ at $y_2 \approx 0.2-0.25$ indicates that the water molecules are ordered in this region and the structure-breaking effect of the guanidinium salts when mixed in low concentrations does not seem to influence that ordering. It shows that the nature of the anion affects the ordering of the water molecules. The magnitudes of $\Delta_m G^E$ are greatly affected in the NaCl-rich region. This ordering changes gradually into disordering on addition of the guanidinium salts. As discussed earlier, NaCl is a hydrophilic salt, whereas GnAc, GnNO₃, and GnClO₄ are the hydrophobic ones. The resultant zero $\Delta_m G^E$ at $y_2 \approx 0.5$ for GnNO₃ and GnClO₄ systems indicates neutralization of hydrophobic and hydrophilic forces at 72% of NaCl. In the case of GnAc, this neutralization takes place in its 50% mixture with NaCl. This disordering effect in these three mixtures also suggests that ternary interactions are enhanced in the NaCl-poor region of the mixtures. Ternary interactions

are more important in the mixtures of NaCl with GnNO₃ and GnClO₄ than with GnAc. The presence of the ternary interactions is also evidenced from the asymmetry of the $\Delta_m G^E - y_2$ plots. The size of anions seems to be playing an important role in determining ternary interactions in the GnAc-rich mixtures. Ternary interactions are enhanced in the GnAc-rich mixtures with NaCl followed by GnNO₃ and GnClO₄. The binary interactions in the case of NaCl-GnAc are very weak as compared to the ternary ones. We noted the similar situation for the mixtures of GnCl with NaCl, CaCl₂, and MgCl₂.²

Both NaCl and Gn₂SO₄ are the structure makers, as evidenced by the viscosity data.^{4,6-8} Gn₂SO₄, due to the strong structure making ability of SO₄²⁻, not only neutralizes the structure breaking effect of Gn⁺ but also acts as a structure maker. The mixing of these two electrolytes yields negative $\Delta_m G^E$ through the composition range with a minimum of $\approx -800 \text{ J kg}^{-1} \text{ H}_2\text{O}$ at $y_2 \approx 0.6$. Addition of Gn₂SO₄ into NaCl up to $y_2 \approx 0.5$ enhances binary interactions. In the Gn₂SO₄-rich mixtures, ternary interactions become important. The water molecules are ordered in this system.

The cluster integral expansion theory of Friedman²¹ can be used to analyze the $\Delta_m G^E$ data for these systems by

$$\Delta_m G^E = RT y_2 (1 - y_2) I^2 [g^0 + g^1 (1 - 2y_2) + g^2 (1 - 2y_2)^2] \quad (4)$$

where g^0 , g^1 , and g^2 are the Friedman interaction parameters. As suggested by Leifer and Wigent,^{16b} the binary interactions were found to enter only into the g^0 term, whereas the effect of ternary interactions was found to contribute to both g^0 and g^1 .

The values of g^0 , g^1 , and g^2 for these systems are listed in Table S4 as Supporting Information. The sign of Friedman interaction parameters indicates the importance of binary, ternary, and quaternary interactions. Negative and positive signs characterize the favorable and unfavorable interactions, respectively. The ionic strength dependence of g^0 and g^1 for these systems is demonstrated in Figure 6. The Friedman parameter, g^0 , is very small for NaCl-GnAc throughout the ionic strength (Figure 6a), suggesting weak binary interactions in this system, as stated above. At lower ionic strengths, g^1 becomes important, decreasing slowly at high ionic strengths showing the presence of strong ternary interactions in the acetate system. Both the g^0 and g^1 parameters are very significant throughout the ionic strength in the mixtures of NaCl with GnNO₃. The slopes of these parameters with ionic strength show that the binary and ternary interactions are more prominent in the NaCl mixtures with GnNO₃ than with GnAc. The Friedman parameters for NaCl-GnClO₄ display similar ionic strength dependence (Figure 6b). The above mixtures of NaCl with 1-1 guanidinium salts are examples of symmetrical mixing. Friedman showed that for 1-1 symmetrical mixing g^0 should be linear with respect to ionic strength and it should have a finite value when I approaches zero. In this case, both the binary and ternary interactions contribute to g^0 . Our results are in good agreement (Figure 6a) with the cluster integral expansion theory of Friedman.²¹ The mixing of Gn⁺ with Na⁺ in the Cl⁻ ion environment also showed similar behavior.¹ The g^0 and g^1 parameters due to mixing of NaCl with Gn₂SO₄ vary strongly up to $I = 1.5 \text{ mol kg}^{-1}$ and then become independent of ionic strength (Figure 6b). The curvature of g^0 and g^1 parameters in low ionic strengths with their limiting values approaching infinity is a case of unsymmetrical mixing between Cl⁻ and SO₄²⁻ species. The magnitude and sign of g^2 also points toward the contribution made by quadruples. Figure 6c displays comparative behavior of quadruples in terms of g^2 for all the mixtures studied herein.

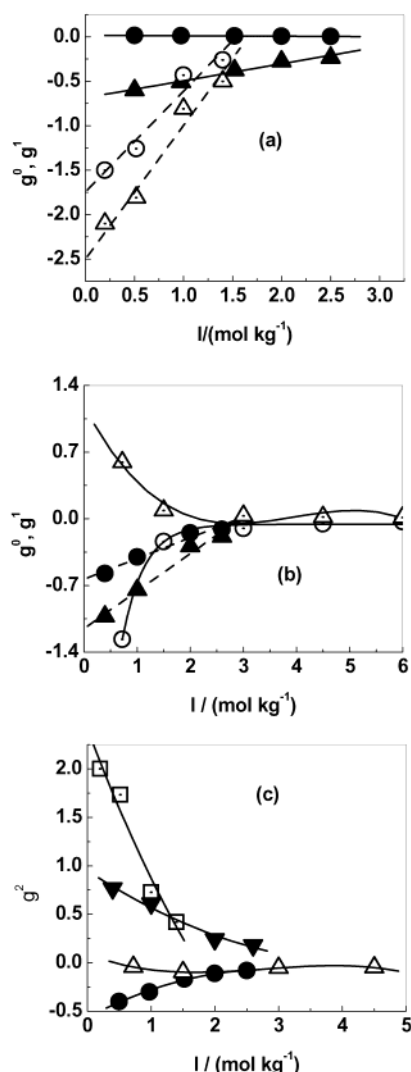


Figure 6. Ionic strength dependence of Friedman interaction parameters for the mixtures of NaCl with (a) GnAc (●) g^0 , (▲) g^1 ; GnNO₃ (○) g^0 , (△) g^1 ; (b) GnClO₄ (●) g^0 , (▲) g^1 ; Gn₂SO₄ (△) g^0 , (○) g^1 ; (c) g^2 (●) GnAc, (□) GnNO₃, (▼) GnNO₃, (△) Gn₂SO₄.

The binary interactions are independent of the ionic strength of mixtures except for the Gn₂SO₄-containing system, where the binary interactions increase with increasing ionic strength at the cost of ternary interactions. The mixtures of Gn₂SO₄ with NaCl at lower ionic strengths, e.g., 0.75 mol kg⁻¹, are enriched with binary interactions, and these interactions reduce at higher ionic strengths. A mild enhancement in ternary interactions can be seen with increasing ionic strength. In general, binary interactions account for about 5, 50, and 74% at $y_2 = 0.3$ of the NaCl mixtures with GnAc, GnNO₃, GnClO₄, and Gn₂SO₄, respectively.

An inspection of $\Delta_m G^E$ values, for example, at $y_2 = 0.5$ and at $I = 3$ mol kg⁻¹ shows that the interactions for the mixing of Cl⁻ and SO₄²⁻ in the presence of Na⁺ and Gn⁺ are strongest in the mixtures studied here. The mixing of Cl⁻ with NO₃⁻ and with ClO₄⁻ are of the same order and slightly weaker than those noted for the mixing of Cl⁻ and SO₄²⁻. The binary interactions between Cl⁻ and Ac⁻ are not favorable.

The above-mentioned interactions contribute toward the total $\Delta_m G^E$ of the mixtures. In the GnAc-containing mixtures, ternary interactions contribute to $\Delta_m G^E$ in the NaCl-rich region, whereas quaternary interactions (though 20%) remain present throughout the mixture compositions. In the case of the GnNO₃ mixtures,

the $\Delta_m G^E$ values originate from the binary interactions throughout the mixture composition. The ternary interactions also contribute in the GnNO₃-poor mixtures with NaCl. The quaternary interactions do not contribute to $\Delta_m G^E$ in these mixtures. The contribution by the ternary interactions remains important in the GnClO₄-poor mixtures with NaCl. The binary interactions also contribute to total $\Delta_m G^E$. In the NaCl-rich mixtures of Gn₂SO₄, binary and quaternary interactions play a major role. In the Gn₂SO₄-rich mixtures, even ternary interactions are important.

$\Delta_m G^E$ summarizes the effect of the mixing process on the relative chemical potentials of the electrolytes and water. Certain regularities, known collectively as Young's rule have been observed in the variation of $\Delta_m G^E$ with mixture composition. Young's rule, an important tool to understand thermodynamics of multicomponent electrolytes such as seawater, assumes that the properties of the mixture can be approximated by some suitable weighting of the properties of the component single electrolyte solutions. Young's cross square rule (YCSR) suggests that the sum of the $\Delta_m G^E$ values for the four 2-electrolyte mixtures with a common ion prepared from M, N, X, and Y (M, N = cations; X, Y = anions). For a mixture having no common ion, for example, a MX–NY mixture, four mixtures of two electrolytes each with a common ion are possible. These are MY–NY, MY–MX, MX–NX, and NX–NY. Two more pairs, namely, MX–NY and MY–NX, are possible, which have no common ions. The YCSR suggests that the sum of the $\Delta_m G^E$ values for the four 2-electrolyte mixtures with a common ion prepared from M, N, X, and Y equals to the sum of $\Delta_m G^E$ of those two pairs having no common ions. Thus, at a constant ionic strength and a fixed composition, YCSR can be written as

$$\Delta_m G^E(\text{MX} - \text{MY}) + \Delta_m G^E(\text{MY} - \text{NY}) + \Delta_m G^E(\text{NX} - \text{NY}) + \Delta_m G^E(\text{MX} - \text{NX}) = \Delta_m G^E(\text{MX} - \text{NY}) + \Delta_m G^E(\text{MY} - \text{NX}) \quad (5)$$

In the current situation, we therefore have

(a) NaCl–GnAc, pairs with a common ion, NaCl–NaAc, NaCl–GnCl, NaAc–GnAc, and GnCl–GnAc, and pairs with uncommon ions, NaCl–GnAc and GnCl–NaAc;

(b) NaCl–GnNO₃, pairs with a common ion, NaCl–NaNO₃, NaCl–GnCl, NaNO₃–GnNO₃, and GnCl–GnNO₃, and pairs with uncommon ions, NaCl–GnNO₃ and GnCl–NaNO₃;

(c) NaCl–GnClO₄, pairs with a common ion, NaCl–NaClO₄, NaCl–GnCl, NaClO₄–GnClO₄, and GnCl–GnClO₄, and pairs with uncommon ions, NaCl–GnClO₄ and GnCl–NaClO₄;

(d) NaCl–Gn₂SO₄, pairs with a common ion, NaCl–Na₂SO₄, NaCl–GnCl, Na₂SO₄–Gn₂SO₄, and GnCl–Gn₂SO₄, and pairs with uncommon ions, NaCl–Gn₂SO₄ and GnCl–Na₂SO₄.

Application of the YCSR to our systems is demonstrated in Table 4, where we list the $\Delta_m G^E$ values for different pairs. Experimental osmotic coefficient data required to calculate $\Delta_m G^E$ at required y_2 and ionic strengths are compiled in Table S5 as Supporting Information. Let us first take the case of NaCl–Gn₂SO₄. The sum of the $\Delta_m G^E$ values for the NaCl–Na₂SO₄, NaCl–GnCl, Na₂SO₄–Gn₂SO₄, and GnCl–Gn₂SO₄ pairs at $I = 3$ mol kg⁻¹ is -1155 J kg⁻¹ H₂O, which is very near (3%) the sum of the $\Delta_m G^E$ values of NaCl–Gn₂SO₄ and GnCl–Na₂SO₄, i.e., -1186 J kg⁻¹ H₂O. The YCSR was also noted to obey in the case of Na⁺–Mg²⁺–Cl⁻–SO₄²⁻ and Na⁺–K⁺–Cl⁻–Br⁻ systems.²² The calculations show that the YCSR is obeyed by the above system containing SO₄²⁻ ions in the environment of Na⁺ and Gn⁺ ionic species with opposite

TABLE 4: Testing the YCMR for $\Delta_m G^E$ of the Mixtures of NaCl with the Guanidinium Salts ($y_2 = 0.5$)

mixtures with a common ion	$\Delta_m G^E/J$ $kg^{-1} H_2O$	mixtures with uncommon ions	$\Delta_m G^E/J$ $kg^{-1} H_2O$
$I = 1 \text{ mol } kg^{-1}$			
NaCl–NaAc	3	NaCl–GnAc	7
NaCl–GnCl	4	GnCl–NaAc	20
NaAc–GnAc	3		
GnCl–GnAc	5		
total	15		27
$I = 1 \text{ mol } kg^{-1}$			
NaCl–NaNO ₃	–185	NaCl–GnNO ₃	–267
NaCl–GnCl	4	GnCl–NaNO ₃	–200
NaNO ₃ –GnNO ₃	6		
GnCl–GnNO ₃	–141		
total	–316		–467
$I = 1 \text{ mol } kg^{-1}$			
NaCl–NaClO ₄	–222	NaCl–GnClO ₄	–247
NaCl–GnCl	4	GnCl–NaClO ₄	–273
NaClO ₄ –GnClO ₄	9		
GnCl–GnClO ₄	–185		
total	–394		–520
$I = 3 \text{ mol } kg^{-1}$			
NaCl–Na ₂ SO ₄	–590	NaCl–Gn ₂ SO ₄	–576
NaCl–GnCl	17	GnCl–Na ₂ SO ₄	–610
Na ₂ SO ₄ –Gn ₂ SO ₄	23		
GnCl–Gn ₂ SO ₄	–605		
total	–1150		–1186

tendencies to alter the arrangement of water molecules around them. This is probably due to the moderating effect of SO_4^{2-} (structure maker) on Gn^+ (structure breaker). There are, however, violations of YCSR in the mixtures of NaCl with GnAc, GnNO₃, and GnClO₄, as shown in Table 4. As seen above, the GnAc mixtures with NaCl do not show the presence of binary interactions and these mixtures are populated with ternary and quaternary interactions. In the past, it has been shown that the YCSR is obeyed in those systems, where binary interactions are dominant.²³ Similarly, the GnNO₃ and GnClO₄ systems with NaCl also fail to obey YCSR owing to the presence of strong ternary and quadruples. The deviations between the $\Delta_m G^E$ values obtained as a sum of pairs with common ion and those with uncommon ions is about 80, 48, and 32% for the GnAc, GnNO₃, and GnClO₄ systems, respectively. Unlike SO_4^{2-} , Ac^- , NO_3^- , and ClO_4^- are the structure breaker ions, further adding to the structure-breaking character of the Gn^+ ion. In the case of the nitrate systems, large deviations from the YCSR have been earlier noted in the Mg^{2+} – Ca^{2+} – Cl^- – NO_3^- and Na^+ – K^+ – Cl^- – NO_3^- systems owing to the formation of ion pairs in these systems.²⁴ The activity coefficient data do not indicate any ion pairing in the pure guanidinium salts.^{8,10} It therefore seems that such large deviations are due to higher types of interactions in these mixtures.

The above results show that the YCSR cannot be employed to reasonably estimate the excess free energy of mixing of the electrolyte mixtures, where ternary and quaternary interactions are dominant over the binary interactions. Thus, YCSR is unable to provide empirical guidance to create a mechanistic model to describe the excess free energy of mixing of guanidinium-containing non-sulfate mixtures.

Conclusion

From the above, answers to our questions raised in the Introduction follow.

We have delineated ionic interactions in the mixture of NaCl with several guanidinium salts by analyzing the excess Gibbs free energy of mixing by using Friedman's cluster integral expansion theory.

Young's square mixing rule is not obeyed by those mixtures where ternary and quaternary interactions are dominant over binary ones.

It is hoped that the above information will be of great use to several biophysical chemists and physical-organic chemists who are investigating the role of ionic interactions in such types of systems in biological and organic systems.

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Supporting Information Available: Useful and operating forms of the Pitzer equations are compiled in Table S1. Table S2 lists the Pitzer coefficients. The Harned coefficients are collected in Table S3. The Friedman parameters are given in Table S4. Experimental osmotic coefficient data required to validate Young's cross rule are listed in Table S5. The material is available free of charge via the Internet at <http://pubs.acs.org>.

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