Osmotic Coefficients and Activity Coefficients of Guanidinium Chloride in Concentrated Aqueous Solutions at 25 °C

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Isopiestic vapor pressure measurements of aqueous solutions of guanidinium chloride of molalities from 0.1 to 12 mol kg^{-1} have been made at 25 °C by equilibration with standard solutions of sodium chloride. The osmotic coefficients and activity coefficients are lower than those of the alkali chlorides at high concentrations. There is evidence of ion pairing in these solutions.

Guanidine (iminourea, $(NH_2)_2C{=}NH$) is a moderately strong base with $pK_a = 13.6$ at 25 °C (*4*). Its salts are of particular biochemical interest as denaturation agents for proteins. Guanidinium chloride (GuCl) is freely soluble in water, yet the thermodynamic properties of its solutions have been little studied. Isopiestic vapor pressure measurements have now been made and are reported here.

Experimental Section

Sodium chloride was recrystallized twice from water and dried at 300 °C. Stock solutions were prepared by weighing the solid. Guanidinium chloride was the "water-soluble" product supplied by Sigma Chemical Co.; it was recrystallized from methanol/water and dried under vacuum at 80 °C. A portion of this solid showed no further loss in weight on drying at 120 °C and, on gravimetric analysis for chloride, assayed as 99.98 ± 0.05% pure. A stock solution was prepared and standardized by gravimetric analysis.

Results

Solutions of sodium chloride and guanidinium chloride were equilibrated isopiestically in an apparatus described elsewhere (*6*). The molalities (mol kg^{-1} of water) of the isopiestic solutions are recorded in Table I. Osmotic coefficients of GuCl were calculated from these data by means of the relation

$$m_{NaCl}\phi_{NaCl} = m_{GuCl}\phi_{GuCl} \qquad (1)$$

using values of ϕ_{NaCl} available in the literature (*8*). The osmotic coefficients of GuCl were then fitted to the equation (*5*)

$$\phi = 1 - (S/A^3I)[(1 + AI^{1/2}) - (1 + AI^{1/2})^{-1} - 2\ln(1 + AI^{1/2})] + BI + CI^2 + DI^3 + EI^4 \qquad (2)$$

using the value 1.172 02 for the Debye–Hückel constant S; I is the ionic strength. The method of least squares gave $A = 1.1834$, $B = -0.096\,93$, $C = 0.016\,339$, $D = -0.001\,301\,6$, and $E = 3.9156 \times 10^{-5}$ with a standard deviation of 0.0012 in ϕ over the molality range 0.1–12 m. The corresponding equation for the activity coefficient is

$$\ln\gamma = -(SI^{1/2}/(1 + AI^{1/2})) + 2BI + 3/2CI^2 + 4/3DI^3 + 5/4EI^4 \qquad (3)$$

Values of ϕ and γ calculated by eq 2 and 3 at round values of the molality m of GuCl are given in Table II.

Table I. Molalities of Isopiestic Solutions of Sodium Chloride and Guanidinium Chloride at 25 °C

NaCl	GuCl	NaCl	GuCl
0.1112	0.1139	2.1595	3.0325
0.1137	0.1160	2.5889	3.8279
0.3312	0.3503	2.6615	3.9429
0.6273	0.7026	2.9782	4.5568
0.6291	0.7049	3.0097	4.6185
0.7832	0.8980	3.3533	5.3278
0.9258	1.0840	3.6257	5.9180
1.0583	1.2718	4.1287	7.0095
1.1301	1.3610	4.3742	7.5800
1.2691	1.5662	4.6926	8.3108
1.5123	1.9325	5.2303	9.6717
1.6755	2.2032	5.6222	10.646
1.9865	2.7359	6.1330	11.993
2.1304	2.9884	6.1411[a]	12.011

[a] Saturated solution.

Table II. Osmotic Coefficients and Activity Coefficients of Guanidinium Chloride at 25 °C

m	ϕ	γ
0.1	0.914	0.749
0.2	0.890	0.684
0.3	0.873	0.641
0.4	0.859	0.608
0.5	0.848	0.582
0.6	0.837	0.559
0.7	0.827	0.540
0.8	0.819	0.522
0.9	0.810	0.507
1.0	0.802	0.493
1.2	0.788	0.468
1.4	0.776	0.447
1.6	0.764	0.428
1.8	0.754	0.412
2.0	0.744	0.397
2.5	0.724	0.367
3.0	0.708	0.343
3.5	0.696	0.324
4.0	0.687	0.308
4.5	0.680	0.295
5.0	0.675	0.283
5.5	0.671	0.273
6	0.668	0.265
7	0.663	0.251
8	0.660	0.239
9	0.657	0.229
10	0.654	0.220
11	0.653	0.212
12	0.656	0.207

Discussion

Figure 1 shows the concentration dependence of the osmotic coefficient for GuCl compared with that for some other uni-univalent salts. Among the latter, cesium chloride is an example of a salt both of whose ions are either unhydrated or only slightly hydrated. The ionic radius of the Cs^+ ion is 1.69 Å while that of the Cl^- ion is 1.81 Å. The sum of the ionic radii is therefore 3.5 Å, or only slightly less than the critical Bjerrum distance (3.58 Å at 25 °C) at which ion-pair formation can occur. The other alkali metal chlorides have higher osmotic coefficients; these salts are completely dissociated, with hydration increasing in the order Rb < K < Na < Li. By contrast, the osmotic coefficient of GuCl is much lower; it is lower than that of $NaNO_3$ but higher

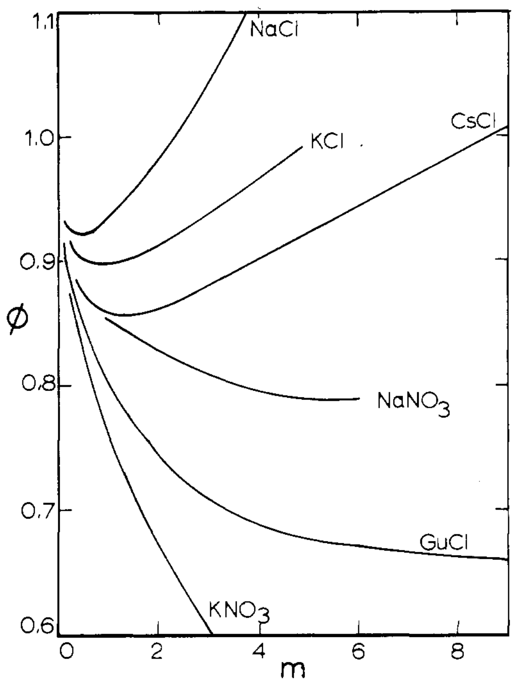

Figure 1. Osmotic coefficients of guanidinium chloride and five other uni-univalent electrolytes as a function of molality at 25 °C.

than that of KNO$_3$. Both of these nitrates exhibit ion pairing (*3*), KNO$_3$ more so than NaNO$_3$. Ion-pair formation is thought to be possible because the nitrate ion is planar and there are two directions from which the cation can approach comparatively closely to the anion. Furthermore, the hydrated K$^+$ ion is smaller and can therefore approach the NO$_3^-$ ion more closely than can the larger and more hydrated Na$^+$ ion. Hence, KNO$_3$ is more ion paired than is NaNO$_3$. Figure 1 suggests that GuCl also exhibits ion pairing, perhaps for the same reason, namely the planar configuration of the guanidinium ion. By this reasoning, guanidinium nitrate would be expected to have an osmotic coefficient even lower than that of GuCl. This prediction is borne out by experiment (*7*).

During the course of this work, two publications reporting data on GuCl solutions appeared. The first, that of Mihajima et al. (*7*), reports isopiestic data for GuCl solutions using NaCl as the reference electrolyte. Values of ϕ(GuCl), given at rounded molalities, do not agree with those from the present study listed in Table II. For example, ϕ = 0.920 (0.911) at 0.1 *m*, ϕ = 0.835 (0.802) at 1 *m*, and ϕ = 0.732 (0.668) at 6 *m*, the first figure being the value from their work and the one enclosed in parentheses being that from the present study. For the nine solutions of GuCl studied by Mihajima et al. (molalities from 0.4 to 5.32 mol kg^{-1}), the experimental osmotic coefficients are not consistent with their smoothed values, the latter being higher than the experimental results by as much as 2.5%. This discrepancy between experimental and smoothed results is curious, but the difference between our results and their experimental data is still serious. It has prompted us to make a second series of measurements with solutions prepared from a different sample of GuCl. The results so obtained were in good agreement with the first series; Table I, in fact, contains the results of both sets of measurements.

That our results are the more nearly correct is suggested by the recent work of Barone et al. (*1*), who report isopiestic data for 12 solutions of GuCl (molalities from 0.7 to 4.57 mol kg^{-1}) using KCl as the reference salt. Their values of ϕ(GuCl) are in acceptable agreement with those reported here. There is an average difference of 0.005 in ϕ, excluding their most concentrated solution (4.57 *m*), for which their value of ϕ is 0.712 as compared to our value (interpolated in Table II) of 0.679. We believe this single point to be in error, since it indicates that ϕ(GuCl) has begun to increase with increasing molality. On the contrary, our results indicate that such an increase does not begin until the molality exceeds about 12 mol kg^{-1}.

Since this paper was submitted for publication, two further reports of iospiestic measurements on guanidinium chloride have appeared. The work of Bonner (*2*) covers the molality range 0.3–8 mol kg^{-1} and that of Schrier and Schrier (*9*) the range 0.75–11 mol kg^{-1}. Our results for the osmotic coefficient of guanidinium chloride are in excellent agreement with the results of both of these investigations, confirming our opinion that other recent results (*7*) are in error.

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