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Contrasting effect of guanidinium salts on kinetics of the Diels–Alder reaction

Anil Kumar,[1]* Usha D. Phalgune[2] and Sanjay S. Pawar[1]

[1]Physical Chemistry Division, National Chemical Laboratory, Pune 411 008, India
[2]Organic Chemistry (S) Division, National Chemical Laboratory, Pune 411 008, India

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ABSTRACT: Aqueous solutions of guanidinium perchlorate ($GnClO_4$), bromide (GnBr), chloride (GnCl) and acetate (CH_3COOGn) inhibit the reaction rates and *endo* products for the cyclopentadiene–methyl acrylate (CPMA) reaction, whereas that of guanidinium sulfate (Gn_2SO_4) accelerates them. These contrasting results obtained for the guanidinium salts are interpreted in terms of the salting-in and -out phenomena and by salting coefficients computed from the scaled particle theory. The contrasting effect of Gn_2SO_4 on the kinetic profiles of the Diels–Alder reactions reported for the first time can be attributed to the dominant role of $SO_4{}^{2-}$ over Gn^+ ion. It is also shown how the salting-out effect of NaCl can be neutralized by the salting-in effect of GnCl in the above reaction. This effect can also be explained in terms of mixing of hydrophilic with hydrophobic cationic species. The effects of the guanidinium salts are also supported by experimental data on solubility, surface tension, volume, compressibility and activation volume. The activation volume of the CPMA reaction calculated from the experimental volumetric data is shown to be salt dependent. Copyright © 2002 John Wiley & Sons, Ltd.

KEYWORDS: Diels–Alder reaction; salt effect; reaction rates; stereoselectivity

INTRODUCTION

Salt solutions prepared in aqueous and non-aqueous solvents have a pronounced effect on the reaction rates of Diels–Alder (DA) reactions, in spite of the fact that these reactions involve isopolar activated complexes (for a recent comprehensive review, see Ref. 1). For instance, LiCl enhances reaction rates of DA reactions, whereas $LiClO_4$ and guanidinium chloride (GnCl) inhibit them. During the course of our studies on the kinetics of these reactions, we noted some interesting features of several guanidinium salts on the cyclopentadiene–methyl acrylate (CPMA) reaction. In this work, we show that guanidinium sulfate, Gn_2SO_4, accelerates the reaction rates of CPMA reaction, in contrast to other guanidinium salts such as GnBr, CH_3COOGn and $GnClO_4$, which reduce them. This interesting effect of Gn_2SO_4 on the above reaction is supported by several properties of solutions, such as surface tension, solubility, salting behavior and volumes. We make use of our published information on the neutralization of water-ordering and -disordering characteristics obtained from thermodynamic properties of the mixing of Na^+ and Gn^+ species[2] and show how the mixture of hydrophilic and hydrophobic ions can alter the reaction kinetics. We also analyze the experimental rate data in terms of experimentally determined activation volume of this reaction. This work is a part of our continuing efforts to delineate the forces responsible for the effect of salts on kinetics of Diels–Alder reactions.[1,3]

EXPERIMENTAL

Commercially available AR-grade NaCl, GnCl and Gn_2SO_4 purchased from Aldrich Chemical were recrystallized from water and dried under vacuum. GnBr, CH_3COOGn and $GnClO_4$ were prepared as reported in the literature.[4] The salt solutions were prepared in deionized water.

Cyclopentadiene (CP) was freshly cracked from its dimer (Merck) just before its use. Methyl acrylate (MA) obtained from Merck was used after distillation.

In a typical run, 0.6 ml (7.26 mmol) of the freshly cracked CP was dissolved in 2 ml of the salt solution. Then, 0.6 ml (6.66 m mol) of MA was dissolved in 10 ml of the salt solution. The solution containing CP was added to the solution containing MA. The reaction mixture was magnetically stirred for about 5 h.

**Correspondence to:* A. Kumar, Physical Chemistry Division, National Chemical Laboratory, Pune 411 008, India.
E-mail: akumar@ems.ncl.res.in

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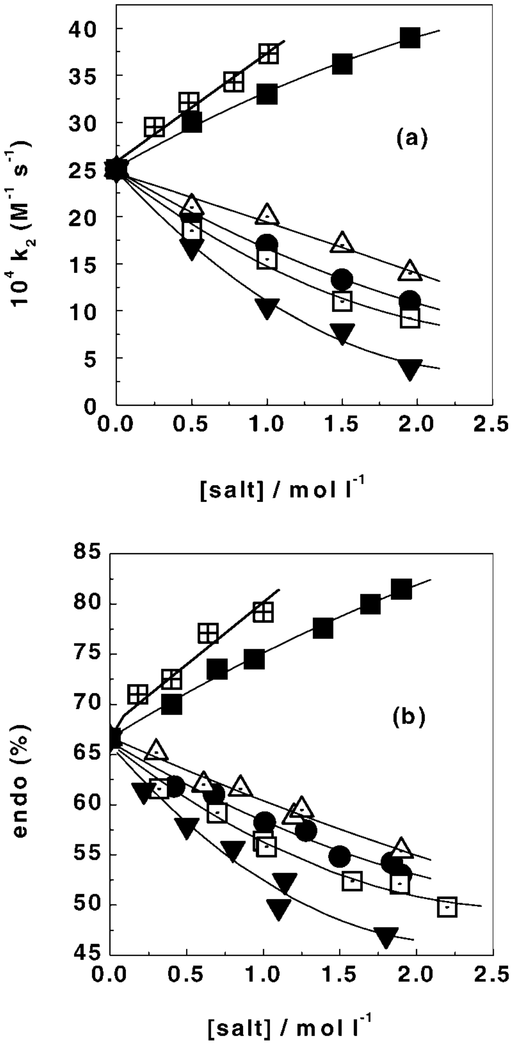

Figure 1. (a) Dependence of the rate constants, k_2 (l mol^{-1} s^{-1}), on the salt concentration for the CPMA reaction in Gn_2SO_4 (■), CH_3COOGn (△), GnCl (●), GnBr (⊡), $GnClO_4$ (▼) and Na_2SO_4 (⊞). (b) *Endo* (%) versus salt concentration for the CPMA reaction in the guanidinium salts; symbols as in (a)

The *endo* and *exo* products were determined using NMR as discussed in the literature.[5] Each reaction was carried out three times and the average was treated as the final reading.

The reaction rates were determined by a procedure outlined elsewhere.[6] This study was performed under pseudo-first-order conditions with 4 mmol of CP and 39.5 mmol of MA. The progress of the reaction was followed at 250 nm, in which the first-order disappearance of CP was observed over two half-lives. The pseudo-first-order rate constant was recorded to be first-order in MA, yielding a second-order rate constant $k_2 = 25 \times 10^{-4}$ l mol^{-1} s^{-1} in water. The rate constants were precise to within 1.6% as calculated from triplicate measurements.

The solubilities of MA were determined by measuring the optical densities of a solution saturated with MA in both pure water and salt solutions with a Lambda 15 UV spectrophotometer (Perkin-Elmer) at 196 nm.[7] The changes in the ionic concentrations produced negligible changes in the absorptivity of MA.

The entire experimental work was conducted at 298 K using a constant-temperature bath (Julabo) with an accuracy of ±0.01 K.

RESULTS AND DISCUSSION

The CPMA reaction was carried out at different concentrations of GnCl, GnBr, CH_3COOGn, $GnClO_4$ and Gn_2SO_4. The rate constants and *endo* products obtained are listed in Tables 1 and 2, respectively. In Fig. 1(a) we plot the concentration dependence of the rate constants, k_2, in different guanidinium salts. Similarly, the variation of *endo* products with the salt concentration is shown in Fig. 1(b). GnCl decreases both the reaction rates and *endo* products for this reaction throughout the concentration range studied. Examination of the plots of rate constants, k_2, versus salt concentration in Fig. 1(a) suggests a decrease in the rate constants with respect to the salt concentration of GnCl, GnBr, CH_3COOGn and $GnClO_4$. For example, CH_3COOGn, GnCl, GnBr, and $GnClO_4$ at 2 M salt concentration decrease the reaction rates by 44, 56, 63 and 84%, respectively. Thus, the order in which these guanidinium salts affect the progress of the reaction is $CH_3COOGn < GnCl < GnBr < GnClO_4$. This is also true for the *endo* products obtained for this reaction. For example, at a 1 M salt solution, the *endo* product is decreased by 7, 13, 16 and 21% in aqueous CH_3COOGn, GnCl, GnBr and $GnClO_4$, respectively, compared with that in water alone. The decrease in the *endo* products, at 1 M, for instance, is linearly related to

Table 1. Rate constants, k_2, for the CPMA reaction in different guanidinium salts (k_2 in pure water = 25×10^{-4} l mol^{-1} s^{-1})

Salt (mol l^{-1})	$k_2 \times 10^4$ (l mol^{-1} s^{-1}) GnCl	GnBr	CH_3COOGn	$GnClO_4$	Gn_2SO_4	Na_2SO_4 (mol l^{-1})	$k_2 \times 10^4$ (l mol^{-1} s^{-1})
0.5	20.0	18.5	21.0	16.8	30.0	0.25	29.5
1.03	17.0	15.5	20.1	10.5	33.1	0.48	32.1
1.51	13.3	11.0	17.0	7.8	36.2	0.78	34.3
1.95	11.0	9.2	14.1	4.1	39.3	1.01	37.3

Table 2. The *endo* (%) products of the CPMA reaction in aqueous solutions of different guanidinium salts (*endo* product in pure water = 66.6%)

GnCl		GnBr		$GnClO_4$		CH_3COOGn		Gn_2SO_4		Na_2SO_4	
Salt (mol l^{-1})	*Endo* (%)	Salt (mol l^{-1})	*Endo* (%)	Salt (mol l^{-1})	*Endo* (%)	Salt (mol l^{-1})	*Endo* (%)	Salt (mol l^{-1})	*Endo* (%)	Salt (mol l^{-1})	*Endo* (%)
0.42	61.8	0.32	61.6	0.22	61.4	0.3	65.2	0.4	70	0.18	71.0
0.68	61	0.7	59.2	0.5	57.9	0.61	62	0.7	73.5	0.4	72.5
1.01	58.2	1	56.4	0.8	55.6	0.85	61.6	0.94	74.5	0.64	77.1
1.28	57.4	1.02	55.8	1.1	49.8	1.2	58.8	1.39	77.6	1	79.2
1.5	54.8	1.58	52.4	1.14	52.4	1.25	59.5	1.7	80		
1.84	54.2	1.89	52.1	1.8	47	1.9	55.4	1.9	81.5		
1.9	53	2.2	49.8								

the anionic radii of the guanidinium salts (with correlation coefficient $r = 0.9857$), confirming that the effects of guanidinium salts in a DA reaction follow the Hofmeister series.[8] We noted that Gn_2SO_4 did not follow the Hofmeister series, possibly owing to ion-pair formation. This point is discussed later.

The most important point of this investigation is the effect of Gn_2SO_4, which is observed to enhance both the reaction rates and *endo* products. A 56% increase in the rate constant, k_2, at 2 M Gn_2SO_4 is noted with respect to that in pure water. Similarly, the *endo* products are enhanced to 81.5% at 2 M of Gn_2SO_4, compared with 66.6% obtained in pure water.

The behavior of the guanidinium salts with different anions seems very interesting, particularly as Gn_2SO_4 displays opposite effects to those shown by GnCl, GnBr, CH_3COOGn and $GnClO_4$. The associated anions of the guanidinium, i.e. Cl^-, Br^-, CH_3COO^- and ClO_4^-, are seen to offer higher *exo* products. However, Gn_2SO_4 reverses this trend by yielding higher *endo* products.

Since guanidinium is a common cation in all the salts, this effect is expected to emerge as being due to anions. The variations in the reaction rates and *endo* products can be attributed to the salting-out (S-O) and -in (S-I) phenomena.[6,9] It appears that GnCl, GnBr, CH_3COOGn and $GnClO_4$ act as S-I agents and Gn_2SO_4 as an S-O agent. The guanidinium salts with SCN^-, Cl^- and CH_3COO^- ions are known to be potential destabilizers of proteins.[9] On the other hand, Gn_2SO_4 was noted to enhance the transition temperature of the proteins, thus acting as a stabilizer, unlike other guanidinium salts.[10] It is suggested that although the effect of guanidinium cation is to decrease the transition temperature, the overall effect of the salt on the system depends on the constituent anion of the guanidinium salts.[10,11] The SO_4^{2-} ion in aqueous solution is known to be an S-O species.[12] In general, salts containing SO_4^{2-} anion act as S-O agents. The S-O nature of SO_4^{2-} is reasonably strong to influence the S-O or S-I nature of a cation to an appreciable extent. On the other hand, ClO_4^- is a strong S-I species. We have recently shown that an S-O ion converts into an S-I agent depending on the nature of solvent which is used to prepare a salt solution.[3a] Thus, a strong S-O anion, such as SO_4^{2-} will over-compensate the S-I tendency of guanidinium ion. The contrasting effect of Gn_2SO_4 was also observed during the investigation of efficacy of various protein denaturants (guanidinium salts) as hydrophobic bond breakers (in Ref. 13, the molecular basis of the relationship between the nature of ionic solutes and surface tension is described). It was observed that GnSCN showed a strong disruptive effect and increased the critical micelle concentration by several orders, of magnitude, whereas Gn_2SO_4 stabilized the micelles. On the other hand, S-I anions such as Cl^-, Br^-, SCN^-, ClO_4^-, etc. will further enhance the destabilizing behavior of their salts with guanidinium ion.

From the results on proteins and this study, it appears that these anions themselves increase the rate-retarding power of Gn^+ in the order $ClO_4^- > Br^- > Cl^- > CH_3COO^-$, as these anions act as S-I species, which further supports the S-I tendency of Gn^+. If S-I and S-O play effective roles in the reaction kinetics, it would be of

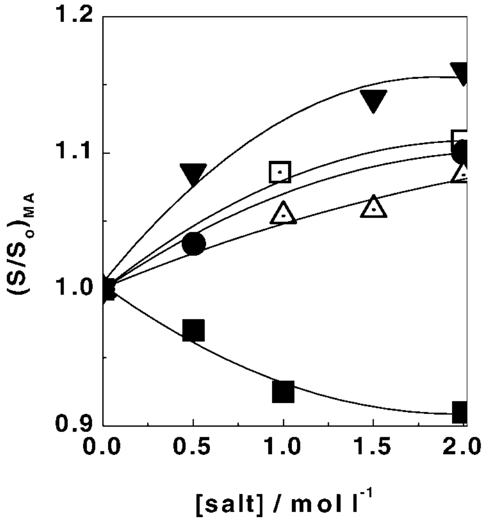

Figure 2. Relative solubilities of methyl acrylate, $(S/S_0)_{MA}$, in guanidinium salts; symbols as in Fig. 1

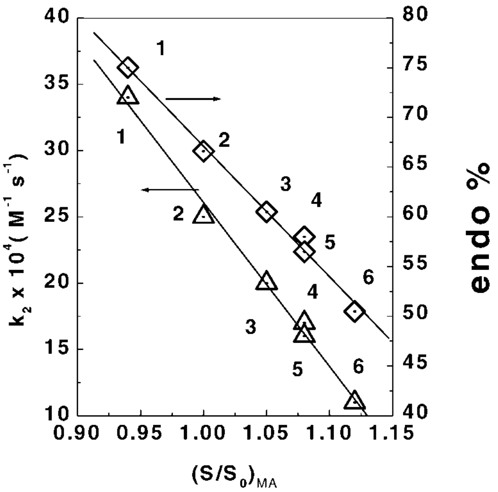

Figure 3. Plot of k_2 (l mol^{-1} s^{-1}) versus $(S/S_0)_{MA}$ (△) and plot of *endo* (%) versus $(S/S_0)_{MA}$ (◇) for the CPMA reaction in 1 M salt solution. 1 = Gn_2SO_4; 2 = H_2O; 3 = CH_3COOGn; 4 = GnCl; 5 = GnBr; 6 = $GnClO_4$

interest to investigate the solubilities of reactants in the aqueous guanidinium salts. In Fig. 2, we plot the relative solubilities of methyl acrylate $(S/S_0)_{MA}$ (S and S_0 are the solubilities of MA in the salt solution and water, respectively) in aqueous CH_3COOGn, GnCl, GnBr, $GnClO_4$ and Gn_2SO_4 solutions as solid symbols. It is noted from Fig. 2 that CH_3COOGn, GnCl, GnBr and $GnClO_4$ increase the solubility of MA up to 2 M salt solutions, indicating the S-I behavior of these salts. The $(S/S_0)_{MA}$ values are weakly altered by CH_3COOGn. The decrease in the solubility of MA in Gn_2SO_4 clearly indicates the S-O phenomena governing the rate acceleration. To elucidate the direct correlation of $(S_{MA}/S_0)_{MA}$ with the rate profiles, we have plotted in Fig. 3 the values of k_2 and *endo* products as a function of $(S/S_0)_{MA}$ at 1 M of each salt. The linear plots with steep slopes indicate the effective role of the increase or decrease in solubilities of the reactants on the kinetic progress of the DA reactions. Both the experimental solubility data and the calculations confirm that the S-I and S-O can be assigned as rate-controlling factors in the D-A reactions. $\log(S_0/S) = \log f$, where f is the molar activity coefficient, when calculated from the above solubility data correctly predicts the sign of the S-I and S-O coefficients.

Since the solubility of cyclopentadiene is very low in water, the reaction is likely to occur at the interface, hence a correlation of the rate profiles with the surface tension of aqueous guanidinium salts should be informative. These correlations for k_2 and *endo* products with respect to the change in surface tension of water upon addition of salts, $\Delta\sigma$ (data are from recently published work),[14] are given in Fig. 4(a) and (b), respectively. Both k_2 and *endo* products are linearly related with $\Delta\sigma$ in all the salt solutions. Although in the case of Gn_2SO_4 the k_2–$\Delta\sigma$ plot is slightly curved, it can be treated as linear considering the experimental errors in the determination of k_2. In Table 3 are listed the slopes of the plots obtained from the linear regression of the data plotted in Fig. 4(a) and (b). The values of slopes are positive for both k_2 and *endo* product in the case of Gn_2SO_4. The negative slopes and their magnitudes indicate the abilities of other guanidinium salts in retarding the rates of the reaction. These strong correlations also prove that the surface tension of the guanidinium salts can be an effective property in determining the progress of the reaction. In fact, the slope values for the guanidinium salts, except for Gn_2SO_4, vary linearly with the anionic radii.

Concerning the surface tension data, both the cavitation and solvation phenomena assume importance. Our published data[14] show that for $GnClO_4$ the increase in the surface tension of water is the least among the entire rate-retarding guanidinium salts. The slow increase in surface tension at a given concentration follows the order $GnClO_4 < GnBr < GnCl < CH_3COOGn$. This change in surface tension implies that the formation of cavities is not easy in these salt solutions. Hence the effect should originate from the solvation, i.e. the interaction of ions with the hydrocarbons of organic molecules. This argument is consistent with the S-I behavior of the rate-retarding guanidinium salts. Let us now examine the surface tension of aqueous Gn_2SO_4, which increases sharply with increase in salt concentration. This change is

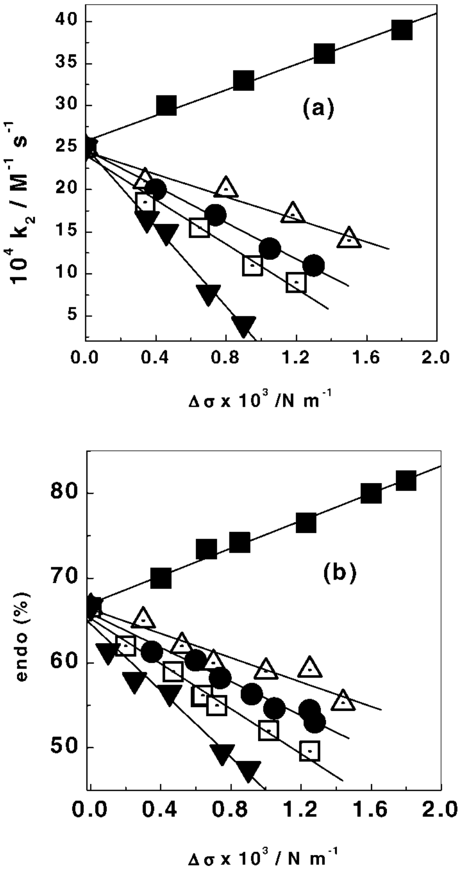

Figure 4. Plots of (a) k_2 (l mol^{-1} s^{-1}) and (b) *endo* (%) versus $\Delta\sigma$ (N m^{-1}) in guanidinium salts; symbols as in Fig. 1

Table 3. Values of $k_2/(\Delta\sigma)$ and *endo*/$(\Delta\sigma)$ in different guanidinium salts for the CPMA reaction

Salt	$k_2/(\Delta\sigma)$ $(\mathrm{l\,mol^{-1}\,s^{-1}\,N^{-1}\,m})$	*endo*/$(\Delta\sigma)$ $(\mathrm{N^{-1}\,m})$
GnCl	−0.11	−10600
GnBr	−0.14	−14600
CH_3COOGn	−0.07	−7667
$GnClO_4$	−0.19	−24333
Gn_2SO_4	0.0812	8375

similar to that observed with the rate-enhancing salts such as LiCl, NaCl, etc.,[15] where the rate enhancing effect is attributed to increased electrostriction[16] among other forces operating in the solutions.

Next, we examine the issue of the rate acceleration by Gn_2SO_4 in contrast to other guanidinium salts. The S-O effect of Gn_2SO_4, as discussed earlier, is the result of dominant S-O interactions due to SO_4^{2-} over the S-I interactions arising from Gn^+. It is possible to obtain information on the ion–water interactions from the volumetric measurements of the guanidinium salts. Ion–water interactions in a salt solution can be understood in terms of volume and its pressure dependence. In this connection, the partial molar volume, $\phi_V{}^o$, and compressibility $\phi_K{}^o$, yield valuable information. The $\phi_V{}^o$ values from our recent work[17] are 69.92, 79.84, 54.94, 92.33 and 18.66×10^{-6} $\mathrm{m^3\,mol^{-1}}$ for GnCl, GnBr, CH_3COOGn, $GnClO_4$ and Gn_2SO_4, respectively, and the $\phi_K{}^o$ values for GnCl, GnBr, CH_3COOGn, $GnClO_4$ and Gn_2SO_4 are −10.04, −9.09, −21.61, −1.51 and -38.23×10^{-15} $\mathrm{m^3\,mol^{-1}\,Pa^{-1}}$, respectively. The values of $\phi^o{}_V$ and $\phi^o{}_K$ for Gn_2SO_4 are the lowest among the guanidinium salts studied here. For instance, $\phi_V{}^o$ and $\phi_K{}^o$ for Gn_2SO_4, a rate- promoting salt, is about 5 and 25 times, respectively, lower than those of $GnClO_4$, a most effective rate-retarding salt. These low values of $\phi^o{}_V$ and $\phi^o{}_K$ for Gn_2SO_4 indicate the increased electrostriction compared with that in other guanidinium salts.[16c] The increased electrostriction or decreased volume around ionic species causes the reactants to squeeze out and then participate in the reaction, leading to the rate acceleration. $GnClO_4$, the most effective rate-retarding salt, is characterized by the highest $\phi_V{}^o$ $(18.66 \times 10^{-6}$ $\mathrm{m^3\,mol^{-1}})$ and $\phi_K{}^o$ $(-1.51 \times 10^{-15}$ $\mathrm{m^3\,mol^{-1}\,Pa^{-1}})$, indicating the least degree of electrostriction or the dominance of anti-electrostriction effects. Both $\phi_V{}^o$ and $\phi^o{}_K$ follow the order in which these guanidinium salts affect the reaction rates and *endo* products of the reaction.

The $\phi_V{}^o$ and $\phi^o{}_K$ data for other guanidinium salts show that both Gn^+ and its constituent anion together exert the S-I effect. Both $\phi_V{}^o$ and $\phi^o{}_K$ follow the order in which these guanidinium salts affect the reaction rates and *endo* products of the reaction. In fact, if we analyze the $\phi_V{}^o$ and $\phi^o{}_K$ data for Gn_2SO_4 in terms of principle of additivity for volumetric properties,[18] we note a large non-ideality in the case of Gn_2SO_4. Is this non-ideality in the thermodynamic properties due to the ion pairing by species $GnSO_4{}^-$? The conductance data (A. Kumar, unpublished data; the conductance data on aqueous Gn_2SO_4 give $\log K_A = 0.31$ indicating ion pairing in the solution) on aqueous Gn_2SO_4 solution confirm the presence of the ion pairs, but how these ion pairs affect the reaction rates is not yet clear to us. The aqueous Gn_2SO_4 possibly behaves like a mixture of free Gn^+, $SO_4{}^{2-}$ ions and $GnSO^-{}_4$ ion pairs, of which $SO_4{}^{2-}$ is the most effective. The rate enhancements with increasing Gn_2SO_4 concentration, however, indicate that free $SO_4{}^{2-}$ ions dominate over the solubilization of hydrocarbons by Gn^+ and ultimately accelerate the reaction. The $\phi_V{}^o$ and $\phi^o{}_K$ data for other guanidinium salts show that both Gn^+ and its constituent anion together exert the S-I effect. In terms of McDevitt and Long's theory[9c] of salting effects, the use of $\phi_K{}^o$ values together the molar volumes of CP and MA can yield the salting coefficients, κ_s, as positive for Gn_2SO_4 and negative for other guanidinium salts. This theory, however, fails to predict the salting coefficients due to simplified assumptions made during its development.

In order to confirm the role of $\phi_V{}^o$ and $\phi^o{}_K$ on the salting phenomena, we calculated the κ_s values for each salt by using the scaled particle theory,[19] as described by Shoor and Gubbins.[19a] According to this theory, the salting coefficient κ_s is calculated by combining the contributions due to the cavity formation, κ_a, and introduction of an organic molecule to the cavity, κ_b. The number density of solution species is given by κ_c. The input parameters for computing κ_a values for the guanidinium salts are the ionic radii and the diameter of water molecule taken from the compilation of Marcus.[20] The $\phi_V{}^o$ values required in the calculations are taken from our work[21] as noted above. The κ_s values can be estimated from the energy and polarizibility parameters of CP and MA molecules taken from earlier work.[20] The κ_c values are estimated from $\phi_V{}^o$ of the individual salts in water. The κ_s values for each salt listed in Table 4 indicate the expected trend in the salting coefficients. Negative κ_s values are obtained for all the rate-retarding guanidinium salts and a positive κ_s for the rate-promoting Gn_2SO_4. Further, a linear correlation exists between κ_s and $\phi_K{}^o$ of these salts with an intercept and slope of −0.446 and -0.0175×10^{15} $\mathrm{m^{-3}\,mol\,Pa}$, respectively. Both κ_a and κ_b for these salts follow the order in which the latter affect the rate constants and *endo* products. The effects arising due to κ_a and κ_b compete with each other to yield the total salting coefficient. In the case of CH_3COOGn, GnCl, GnBr and $GnClO_4$, higher negative values indicate strong solute–solvent interactions, i.e. solvation of hydrocarbons. The higher negative κ_b values out-compete the small positive κ_a values leading to the phenomenon of solvation of hydrocarbons by the rate-retarding salts. In contrast, a high positive κ_a value is obtained for Gn_2SO_4, suggesting the high cost of cavitation. The roles of the κ_a

Table 4. Components of the salting coefficients, κ_s, of GnCl, GnBr, CH_3COOGn, $GnClO_4$ and Gn_2SO_4 solutions as computed using scaled particle theory for the CPMA reaction ($\kappa_s = \kappa_a + \kappa_b + \kappa_c$)

Salt	κ_a	κ_b	κ_c	κ_s
GnCl	0.090	−0.323	−0.032	−0.265
GnBr	0.066	−0.350	−0.037	−0.321
CH_3COOGn	0.125	−0.215	−0.005	−0.095
$GnClO_4$	0.046	−0.373	−0.056	−0.383
Gn_2SO_4	0.258	−0.069	0.050	0.239

and κ_b terms in the reaction kinetics can be easily explained based on surface tension data.

In order to assess the effect of SO_4^{2-} on the kinetic progress of the reaction, we carried out a few reactions in Na_2SO_4. Addition of Na_2SO_4 in an aqueous environment is noted to increase both the rates and *endo* products. These results are within our expectation as both Na^+ and SO_4^{2-} are S-O species. The effect of Na_2SO_4 on the reaction rates and *endo* products is more pronounced than that of Gn_2SO_4, as the effect of SO_4^{2-} in Gn_2SO_4 is reduced by Gn^+, whereas in the case of Na_2SO_4, both Na^+ and SO_4^{2-} being S-O ions combine to enhance the reaction profiles. A comparison of two salts over the full concentration range is not possible, however, owing to low solubility of Na_2SO_4 in water. These results (from Tables 1 and 2) are plotted in Fig. 1(a) and (b).

If we argue that the decrease in the rates and *endo* products in the presence of GnCl results from the ion–water interactions, reactant solubilities and other salt-specific properties, more information can be extracted by carrying out the reactions in the ionic environment with contrasting ionic effects. We have recently demonstrated the mixing effects in the aqueous NaCl–GnCl system where the excess Gibbs free energy, $\Delta_m G^E$, volume, $\Delta_m V^E$, and compressibility, $\Delta_m K^E$, of mixing were computed from thermodynamic and volumetric data.[2] At a given ionic strength of this mixture, negative $\Delta_m G^E$ values in the GnCl-poor region indicate that water molecules are ordered in this concentration range. Above 20% GnCl, further addition of GnCl in the NaCl solution increases $\Delta_m G^E$ until it reaches nearly zero at about a 50% mixture of the salts. The $\Delta_m G^E$ values in the extremely GnCl-rich region are positive, suggesting a water-disorder zone. A neutralization of water-ordering and -disordering effects takes place in about 50% NaCl and GnCl mixtures. Other properties, $\Delta_m V^E$ and $\Delta_m K^E$, obtained from independent experimental density and sound rates also confirm this finding overall, it can be stated that appropriate mixing of a hydrophilic cation (Na^+) with a hydrophobic cation (Gn^+) can give rise to a reaction environment similar to that offered by water.

Guided by this experimental observation, we first set out to carry out the reaction in 1 M GnCl and then in a series of mixtures having different concentrations of NaCl. The concentration of GnCl was kept constant at 1 M throughout. The results of this study are plotted in Fig. 5 for the *endo* products and reaction rates. The k_2 value at 1 M GnCl (17×10^{-4} l mol^{-1} s^{-1}) increases on addition of NaCl and reaches the values recorded in pure water (i.e. 25×10^{-4} l mol^{-1} s^{-1}) at about 1 M NaCl. A similar trend is also observed in the case of the *endo* products. The *endo* product at 1 M GnCl, i.e. 58%, also increases on addition of NaCl and reaches the value obtained in pure water (66.6%) at about 0.9 M NaCl. The concentration of NaCl required in both the cases is almost same. Beyond ~1 M NaCl, k_2 and the *endo* product vary in the expected manner. The values of k_2 and *endo* product with a mixture of 1 M GnCl and ~1 M NaCl are identical with those obtained in pure water, suggesting that this mixture gives rise to an ionic environment which

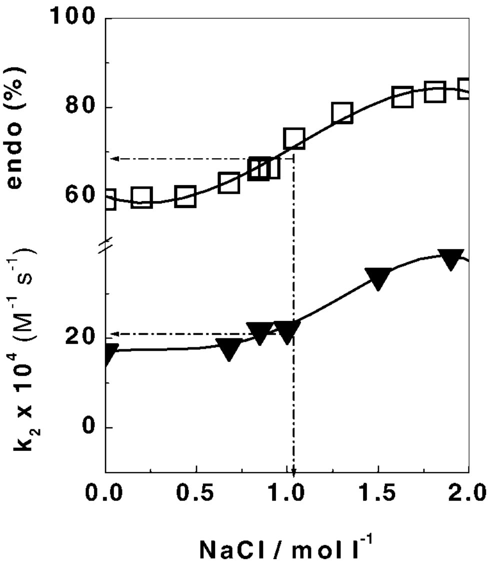

Figure 5. Variations in the reaction rates, k_2 (l mol^{-1} s^{-1}), and *endo* products for the CPMA reaction in mixtures of GnCl (1 M) and increasing NaCl concentrations

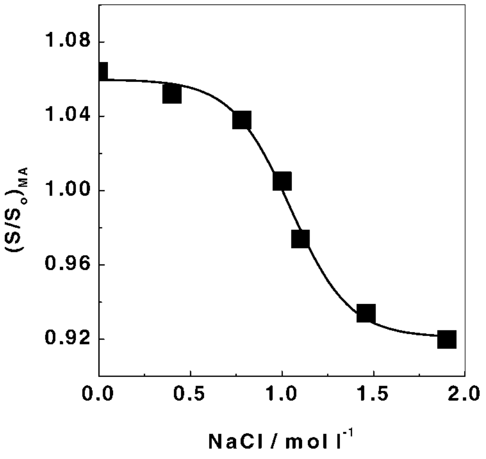

Figure 6. Variations in the relative solubilities of MA $(S/S_0)_{MA}$ in mixtures of GnCl (1 M) and increasing NaCl concentrations

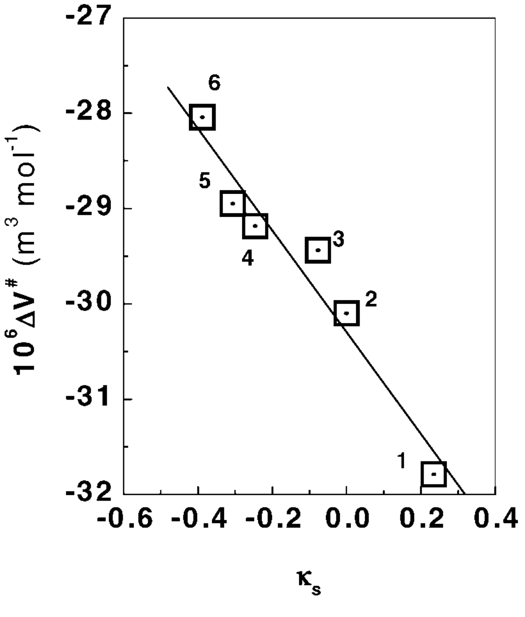

Figure 7. Calculated activation volume, $\Delta V^{\#}$ (m^3 mol^{-1}), of the CPMA reaction versus the salting coefficients, κ_s, of different guanidinium salts; numbering as in Fig. 3

is similar to pure water in terms of rate-influencing properties. This is an important point in the current investigation. In a broader sense, the S-I effect produced by 1 M GnCl is neutralized by the S-O effect of 1 M NaCl. This is possibly the reason why the use of an NaCl–GnCl mixture with definite composition yields reaction rates and *endo* products which are also obtained in pure water. The details of binary and ternary interactions are given elsewhere;[2] however their role in determining the kinetics of DA reactions is difficult to determine.

The reaction rates and *endo* products in the NaCl–GnCl mixture are further supported by the solubility measurements of MA in these mixtures in the form of a plot between $(S/S_0)_{MA}$ and the concentration of NaCl, as shown in Fig. 6. The enhanced $(S/S_0)_{MA}$ values in 1 M GnCl, i.e. the S-I effect, gradually decreases on the addition of NaCl and approach a zero salting effect at $(S/S_0)_{MA} \rightarrow 1$ at a concentration of about 1 M added NaCl.

The DA reactions are accompanied by negative activation volumes ($\Delta V^{\#}$).[22] The $\Delta V^{\#}$ value for a DA reaction is often suggested to be solvent independent. We calculated the $\Delta V^{\#}$ values of the CPMA reaction in guanidinium salts by measuring the densities and the method suggested by McCabe *et al.*[23] The components of the volumetric parameters, i.e. partial volumes of CP, MA and transition states, denoted by $\overline{V}_{CP}$, $\overline{V}_{MA}$ and $\overline{V}_{TS}$, respectively, in aqueous guanidinium salts are listed in Table 5. The volume of transition state, $\overline{V}_{TS}$, is the lowest in Gn_2SO_4 and the highest in $GnClO_4$ solutions. The order in which $\overline{V}_{TS}$ varies agrees well with the order in which these salts affect the reaction rates. The reported $\Delta V^{\#}$ value for this reaction is -30.1×10^{-6} m^3 mol^{-1} at the reaction temperature. The lowest $\Delta V^{\#}$ [i.e. more negative; $(-31.8 \pm 0.4) \times 10^{-6}$ m^3 mol^{-1}] value is observed in aqueous Gn_2SO_4 and the highest [i.e. less negative; $(-28 \pm 0.5) \times 10^{-6}$ m^3 mol^{-1}] in $GnClO_4$. As can be seen in Fig. 7, the $\Delta V^{\#}$ values obtained correlate linearly with the salting coefficients, κ_s, of the guanidinium salts with a correlation coefficient of 0.9818 for the CPMA reaction. The $\Delta V^{\#}$ profile of the reaction in these solutions further confirms that addition of Gn_2SO_4 will accelerate the reaction, in contrast to $GnClO_4$, GnCl, etc. The more compact transition state, i.e. with lowest $\Delta V^{\#}$, indicates the higher degree of hydrophobic packing of CP and MA in Gn_2SO_4 solution. Other guanidinium salts investigated here decrease the hydrophobic effects.

In recent work, Swiss and Firestone[24] suggested that $\Delta V^{\#}$ obtained from the pressure dependence of rate data was not truly an activation volume term. They incorporated a new term called the 'phantom activation volume' to account for the pressure-induced kinetic progress. Their thesis is significant but in view of complex ionic interactions in salt solutions, we are currently unable to extend this to our system. As the salt solutions employed in the above DA reaction are concentrated solutions, it is not easy to separate different ionic interaction terms and to incorporate them in the reaction kinetics. We have now begun to calculate these effects after the work of Swiss and Firestone.

CONCLUSION

We have shown the anomalous behavior of Gn_2SO_4 compared with other guanidinium salts on the kinetics of

Table 5. Volume components of CP, MA and transition states in different guanidinium salt solutions and the activation volumes obtained from the density measurements at 298.15 K

Medium	10^6V_{CP} (m^3 mol^{-1})	10^6V_{MA} (m^3 mol^{-1})	10^6V_{TS} (m^3 mol^{-1})	$10^6\Delta V^{\#}$ (m^3 mol^{-1})
Water	83.51	91.54	144.99	−30.06
Gn_2SO_4	87.20	86.22	142.00	−31.42
CH_3COOGn	85.60	89.68	145.5	−29.78
GnCl	85.80	90.16	146.60	−29.36
GnBr	85.00	91.70	147.50	−29.20
$GnClO_4$	84.00	92.90	148.10	−28.8

the reaction of cyclopentadiene with methyl acrylate. The variations in reaction rates and *endo* products can be understood in terms of the salting effects. The solubility, surface tension, volume, compressibility and activation volume data support the experimental findings reported above. It is possible to prepare a solvent medium comprised of species with opposing salting effects to exhibit a water-like influence on the kinetic data of the reaction.

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REFERENCES

1. Kumar A. *Chem. Rev.* 2001; **101**: 1.
2. Kumar A. *J. Phys. Chem. B* 2000; **104**: 9505.
3. (a) Kumar A, Phalgune UD, Pawar SS. *J. Phys. Org. Chem.* 2001; **14**: 577; (b) Kumar A, Phalgune UD, Pawar SS. *J. Phys. Org. Chem.* 2000; **13**: 555; (c) Kumar A. *Pure Appl. Chem.* 1998; **70**: 615; (d) Kumar A. *J. Phys. Org. Chem.* 1996; **9**: 287; (e) Kumar A. *J. Org. Chem.* 1994; **59**: 4612; (f) Kumar A. *J. Org. Chem.* 1994; **59**: 230.
4. Bonner OD. *J. Chem. Thermodyn.* 1976; **8**: 1167.
5. Nakagawa K, Ishii Y, Ogawa M. *Tetrahedron* 1976; **32**: 1427.
6. Rideout DC, Breslow R. *J. Am. Chem. Soc.* 1980; **102**: 7816.
7. Closson WD, Brady SF, Orenski PJ. *J. Org. Chem.* 1965; **30**: 4026.
8. (a) Hofmeister F. *Ach. Exp. Pathol. Pharmakol.* 1888; **24**: 247; (b) Collins KD, Washabaugh MW. *Q. Rev. Biophys.* 1985; **18**: 323; (c) Rizzo CA. *J. Org. Chem.* 1992; **57**: 6382; (d) Breslow R, Rizzo CA. *J. Am. Chem. Soc.* 1991; **113**: 4340.
9. (a) Debye P, McAulay J. *Phys. Z.* 1925; **26**: 22; (b) Long FA, McDevitt FW. *Chem. Rev.* 1952; **51**: 119; (c) McDevitt FW, Long FA. *J. Am. Chem. Soc.* 1952; **74**: 1773; (d) Pawar SS, Phalgune U, Kumar A. *J. Org. Chem.* 1999; **64**: 7055.
10. (a) von Hippel PH, Wong K-Y. *Science* 1964; **145**: 577; (b) von Hippel PH, Wong K-Y. *J. Biol. Chem.* 1965; **240**: 3909; (c) von Hippel PH, Schleich T. *Acc. Chem. Res.* 1969; **9**: 257; (d) Castellino FJ, Barker R. *Biochemistry* 1968; **7**: 4135; (e) Castellino FJ, Barker R. *Biochemistry* 1968; **7**: 3439.
11. Makhatadze GI. *J. Phys. Chem. B* 1999; **103**: 4781.
12. Gratzer WB, Beaven GH. *J. Phys. Chem.* 1969; **73**: 2270.
13. Breslow R, Guo T. *Proc. Natl. Acad. Sci. USA* 1990; **87**: 167.
14. Kumar A. *Fluid Phase Equil.* 2001; **180**: 185.
15. Horvath AL. *Handbook of Aqueous Electrolyte Solutions*. Wiley: Chichester, 1985.
16. (a) Kumar A. *Biochemistry* 1995; **34**: 12921; (b) Kauzmann W, Bodanszky A, Resper J. *J. Am. Chem. Soc.* 1962; **84**: 1777; (c) Millero FJ. *Chem. Rev.* 1971; **71**: 147.
17. Kumar A. *J. Solution Chem.* 2001; **30**: 281.
18. Millero FJ. In *Activity Coefficients in Electrolyte Solutions*, vol. II, Pytcowicz RM (ed). CRC Press: Boca Raton, FL, 1979.
19. (a) Shoor SK, Gubbins KE. *J. Phys. Chem.* 1969; **73**: 498; (b) Reiss H, Frisch HL, Lebowitz JL. *J. Chem. Phys.* 1959; **31**: 369; (c) Reiss H. *J. Phys. Chem.* 1992; **96**: 4736; (d) Pierotti RA. *Chem. Rev.* 1976; **76**: 717; (e) Kumar A. *J. Am. Chem. Soc.* 1993; **115**: 9243.
20. Marcus Y. *Ion Solvation*. Wiley: New York, 1986.
21. Cativiela C, Garcia JI, Royo AJ, Salvatella L, Assefeld Y, Urz-Lopez MF. *J. Phys. Org. Chem.* 1992; **5**: 230.
22. (a) Drljaca A, Hubbard CD, van Aldik R, Asono T, Basilevsk MV, Le Noble WJ. *Chem. Rev.* 1998; **98**: 2167; (b) van Eldik R, Asono T, Le Noble WJ. *Chem. Rev.* 1989; **89**: 549. (c) Le Noble WJ. *Progress in Physical-Organic Chemistry*, vol. 5. Interscience: New York, 1967; 207; (d) McCabe JR, Eckert CA. *Acc. Chem. Res.* 1974; **7**: 251.
23. McCabe JR, Grieger RA, Eckert CA. *Ind. Eng. Chem. Fundam.* 1970; **9**: 156.
24. (a) Swiss KA, Firestone RA. *J. Phys. Chem. A* 2000; **104**: 3057; (b) Firestone RA, Swiss KA. *J. Phys. Chem. A* 2001; **105**: 3430; (c) Swiss KA, Firestone RA. *J. Phys. Chem. A* 1999; **103**: 5369.