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Rate Enhancement in Dilute Salt Solutions of Aqueous Ethanol: The Diels−Alder Reaction[1]

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Enhancement in the rate of Diels−Alder reactions can be achieved in dilute aqueous ethanol solutions of inorganic and organic salts. Both NaH_2PO_4 and KH_2PO_4 induce up to a 40% rate enhancement in a Diels−Alder reaction. Many different salts give modest rate enhancements of 30−50%, relative to the same reaction without added salt. There is a concentration dependence on the alkene/diene partners, and the rate enhancement quickly disappears on either side of a concentration maximum.

Enhancement in the rate of Diels−Alder reactions using aqueous media has assumed an increasingly important role in organic chemistry since the pioneering work of Berson,[3] Breslow,[4] and Grieco.[5] The earliest report of this effect probably dates to Hopff and Rautenstrauch,[6] in a 1939 patent, who observed enhancement in the rate of Diels−Alder reactions when done in aqueous solutions of detergents. The rate enhancement is generally attributed to aggregation effects or micelle effects caused by the basic insolubility of the organic substrates in the aqueous medium. More recently, Breslow and also Grieco have observed that rate enhancement is possible if rather concentrated solutions of salts (between 4 and 5 M) such as lithium perchlorate or lithium chloride are added. Grieco employed a 4−5 M solution of $LiClO_4$ in ether,[4a] but Breslow found that a 4.86 M solution of LiCl in water led to significant rate enhancement of the Diels−Alder reaction.[7] Aqueous solutions of $LiClO_4$ also gave a modest rate enhancement,[7] but smaller than that observed with LiCl. Although the rate of a Diels−Alder reaction in $LiClO_4$ solution is slower when compared to the rate of the reaction in water alone, it is faster than in organic solvents. Berson suggested that these salts increase the "salting out" effect, which increases aggregation and thereby the rate of the Diels−Alder reaction. Both Dailey[8] and Righetti[9] have suggested that the rate acceleration with lithium perchlorate in ether is due to a specific lithium cation effect. It is also important to note that the rate enhancement of lithium perchlorate is relative to water alone and that the Diels−Alder reaction of anthracene-9-carbinol and *N*-ethylmaleimide is retarded upon addition of lithium perchlorate[7,10] Addition of lithium perchlorate was also shown to slow the rate of the benzoin condensation, which is a hydrophobic reaction.[11] What is clear is that lithium perchlorate has opposite effects under the two solvent conditions and acts by a dramatically different mechanism.[12]

In at least one report, as the concentration of salt was diminished, the rate enhancement also diminished.[7] Breslow categorized these salt effects as chaotropic and antichaotropic.[7] A chaotropic agent decreases the tendency of the substrates to stay self-associated and away from water and generally decreases the rate relative to aqueous media without an additive. These are the "salting in" agents. An antichaotropic agent, which includes most salts, decreases the solubility of hydrocarbons in water and generally increases the rate relative to aqueous media without an additive. These are the "salting out" agents. It is noted that Breslow has recently changed the terminology of chaotropic and antichaotropic effects, encouraging the use of the terms hydrophobic effects and antihydrophobic effects.[13] In this work, Breslow also described the binding constants of antihydrophobic reagents in aqueous ethanol.[10] Breslow studied the effects of additives in "water-like" solvents (ethylene glycol, formamide, etc.),[4a] and our results with phosphate buffers in ethanol may parallel those in such solvents.

While studying the possibility of preparing a "designer chiral auxiliary", we discovered that the rate of Diels−Alder reactions can be enhanced when done in aqueous ethanol where the aqueous phase is actually a dilute solution of a pH 7 buffer.[14] The rate enhancements observed in this preliminary study were lower than those reported in more concentrated salt solutions, but their occurrence in dilute solution sparked further interest. This paper describes our further studies into this phenomenon. We have discovered that (1) rate enhancements occur in dilute salt solutions of aqueous ethanol, (2) several salts, particularly those with the $H_2PO_4^-$ anion, will induce a modest rate enhancement, and (3) there is a marked concentration dependence on the alkene-diene substrates.

In Berson's work, a clear relationship was shown between the rate as well as the endo:exo product ratio and solvent polarity in the Diels−Alder reaction of cyclopentadiene and acrylates.[3] In general, the rate

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increased with increasing solvent polarity.[3] In 1980, Breslow showed that there was a rate acceleration in the Diels–Alder reaction between cyclopentadiene with methyl vinyl ketone.[4b] This was attributed to the relative insolubility of the acrylate and cyclopentadiene, leading to an associative effect that diminished the water–hydrocarbon interfacial area and brought the reactive partners into close proximity, increasing the rate of reaction. Any additive that increases this hydrophobic effect would lead to an increase in the rate by "salting out" the organic substrates.[7] Addition of salts such as lithium chloride increases the hydrophobic effect and the rate, but guanidinium chloride decreased hydrophobic interactions and decreased the rate of reaction.[7] The observation that the addition of guanidinium perchlorate to a Diels–Alder reaction slowed the reaction and that LiCl and $LiClO_4$ solutions increase the rate was taken as evidence of the special ability of water to enhance the rate of the Diels–Alder reaction due to a hydrophobic effect.[15] Holt examined the reaction of cyclopentadiene and methyl acrylate in the "interphase environment of detergentless micro-emulsions" and also with the addition of surfactants.[16] Using a toluene/1-propanol/water ternary system, more endo product was observed in water-in-oil microemulsions and in small aggregates. Addition of the surfactant did not influence this ratio in these two systems. In a normal ternary system, addition of the detergent increased the amount of endo product, presumably by increasing the polar environment of the reactants.[15] Rizzo[10] reported that the salt effects on a hydrophobically accelerated Diels–Alder reaction followed the Hofmeister series (the effect of salts on the magnitude of the melting temperature of biopolymers).[17] These effects roughly correlate to the size of the anion.[16,18] Rizzo used published rate data for a Diels–Alder reaction in 2 M guanidinium X^- (X = chloride, bromide, tetrafluoroborate, thiocyanate, perchlorate), which decreased with increasing size of the anion, although the solubility increased with increasing size of the anion. It was speculated that this effect on the hydrophobic effect was due to some surface contact between the electrolyte and the organic solute.[16] Such increases in rate upon addition of salts have also been attributed to an increase in internal pressure,[19] an idea examined and not generally favored by Breslow.[20] This explanation was later discredited[8,9] in reactions done in 5 M $LiClO_4$ in ether.

In other work connected with this phenomenon, Grieco showed that iminium salts formed by reaction of an amine and formaldehyde reacted with cyclopentadiene in aqueous media to give a near quantitative yield of the Diels–Alder adduct.[5] This approach has been used in several synthetically important Diels–Alder reactions.[21] Ammonium salts also enhance the rate of Diels–Alder reactions.[15,22]

It is believed that the hydrophobic effect described above generates an environment where "reactants orient themselves within a micelle, thereby increasing their effective molarity and, consequently, the rate".[23] Liotta, however, pointed out that reaction of substrates essentially insoluble in water gave virtually no rate enhancement. The conclusion was that rate enhancement in aqueous media requires at least partial solubility of the diene and/or dienophile. Liotta showed that ethylene glycol was particularly effective for enhancing molecular aggregation while maintaining the solubility of the reactants. Liotta explained this effect in terms of a model where the reactants were ordered within a micelle, either in a π-stacked arrangement, which has a smaller volume and is probably preferred, or in an "end-on" arrangement with a larger micelle volume and a higher energy.

Engberts also studied the Diels–Alder reaction of cyclopentadiene with various electron deficient alkenes in aqueous solutions of 1-propanol and other monohydric alcohols.[24] Their studies showed that the "free energies of activation decreased gradually and almost linearly with the mole fraction of added water".[24a] The activation parameters for the Diels–Alder reaction showed significantly different behavior in highly aqueous media (0.95 H_2O and greater). The rate constants correlated in a linear manner with the molality of the added cosolvent. They explained the rate accelerations in water and aqueous binary solvent mixtures by "enforced hydrophobic interactions", which was different from the hydrophobic bonding of diene and dienophile during the activation process.[24a] They concluded that changes in hydrophobicities of the reactants induced only moderate rate effects and that rate enhancement in water arises by destabilization of the transition state aggregate arising from reaction of diene and dienophile.[24b] Blake and Jorgensen recently presented an ab initio study of the Diels–Alder transition state in water[25] and found enhanced hydrogen bonding[26] for the transition state, augmented by a relatively constant hydrophobic contribution. In the absence of hydrogen-bonding sites, modest rate acceleration was predicted from the hydrophobic term. They concluded that the largest solvent effects are to be found in hydrogen-bonding solvent. In our study, we are probing the effects of added salts that enhance the rate of reaction above that observed in aqueous ethanol without added salt. A discussion of the effects of added salts on the effects described by Engberts or Blake and Jorgensen has not appeared in our literature searches, and it is not clear how our study will influence this particular discussion.

The effect of lithium chloride and other salts on the rate of Diels–Alder reactions was apparent only when that salt was present in relatively high concentrations. Breslow reported that the Diels–Alder reaction of *N*-ethyl maleimide and anthracene-9-carbinol in 4.86 M solutions of aqueous lithium chloride showed an increased rate of reaction, relative to the same reaction in water, by a factor of 2.5.[7] This contrasted with the same reaction in 1 M aqueous lithium chloride, which showed only a 15% increase in the rate of reaction.[4,7] Breslow also showed that addition of sodium dodecyl sulfate or cetyltrimethylammonium bromide had little effect on the endo:exo ratio or on the yield in reactions of cyclopentadiene and various dienophiles, at 0.15 M.[15] Interestingly,

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at 0.02 M sodium dodecyl sulfate concentrations, a 15% increase in the rate was observed,[15] in general agreement with the effects seen in our study. The effects of such salting in denaturants was described by Breslow,[27] who listed five key effects. (1) Salting in agents increase the surface tension of water, and this phenomenon does not reflect easier cavity formation in water. (2) Salting in agents probably directly contribute to the solvation in water of a solute such as benzene by direct interaction. (3) Surface tension effects do not overbalance the solvation effects. (4) The salting in agent tetrabutylammonium chloride lowers the surface tension of water, probably contributing to easier cavity formation and to direct solvation of the substrate. (5) The relative polarities of solvents and additives can explain why salting in agents switch to salting out agents in polar solvents, except for tetrabutylammonium chloride.[27]

In view of the known effects in aqueous media, our results remain interesting since the pH 7 buffer used in our study consisted of sodium monohydrogen phosphate and potassium dihydrogen phosphate, salts not previously reported to give rate enhancement. Our reactions occurred at concentrations of about 0.007 M in the salts. The effects of these salts appeared analogous to the effect of detergents and salting in agents described by Breslow. The descriptions of micelle effects by Liotta also seemed appropriate. If a formal micelle did not form in the dilute salt solution, a microemulsion or even a microaggregate might give similar effects. These effects might allow the salt to increase the solubility of both alkene and diene in the aqueous media. We examined the reaction of 2,3-dimethyl-1,3-butadiene (**1**) with ethyl acrylate to give **2** using a 1:1 aqueous ethanol solution in which pure water was replaced with an aqueous solution of the pH 7 buffer. We were interested in several parameters of this buffered reaction: the influence of the concentration of alkene and diene, the influence of the concentration of the salt, and the pH of the medium. In our first study, we varied the concentration of the alkene/diene partners using a fixed concentration of the aqueous buffer. In Figure 1, we report on the enhancement in rate (comparing second order rate constants) relative to the same reaction done in aqueous ethanol with no buffer. At concentrations of alkene/diene higher than 0.7 M, solubility problems led to unreliable rate data, so we are unable to confirm if the rate value at 0.65 M is a true minimum as suggested by Figure 1. The maximum rate enhancement was only 35–40%, but this maximum occurred at about 0.5 M in alkene/diene with a buffer concentration of 0.007 M. Surprisingly, the rate enhancement in this dilute solution diminished at both higher and lower concentrations of reactants. At concentrations of reactants lower than 0.5 M, rate enhancement was greatly diminished (i.e., the rate of reaction with the salt additive is the same as the rate in aqueous ethanol without an additive). To our knowledge, this type of concentration dependence is unprecedented in aqueous Diels–Alder reactions. We have done this reaction in refluxing toluene and did not observe this 0.5 M concentration dependence.

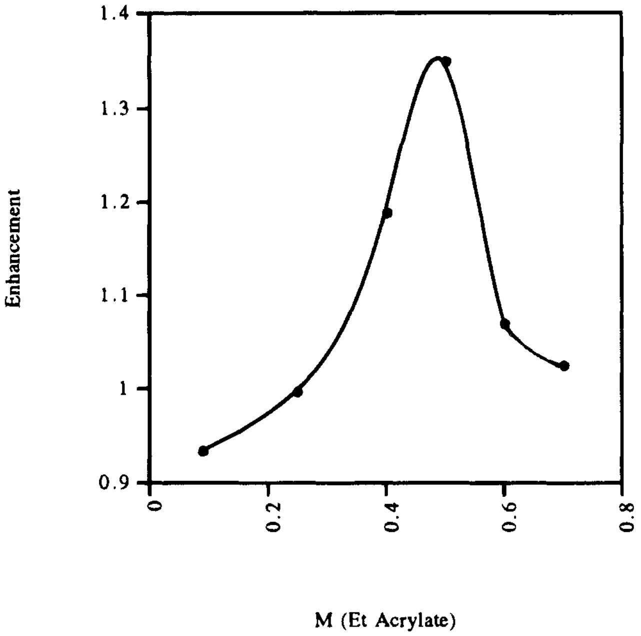

Figure 1. Rate enhancement in the reaction of 2,3-dimethyl-1,3-butadiene and ethyl acrylate as a function of alkene/diene concentration at 7 × 10^{-3} M aqueous pH 7 buffer concentrations.

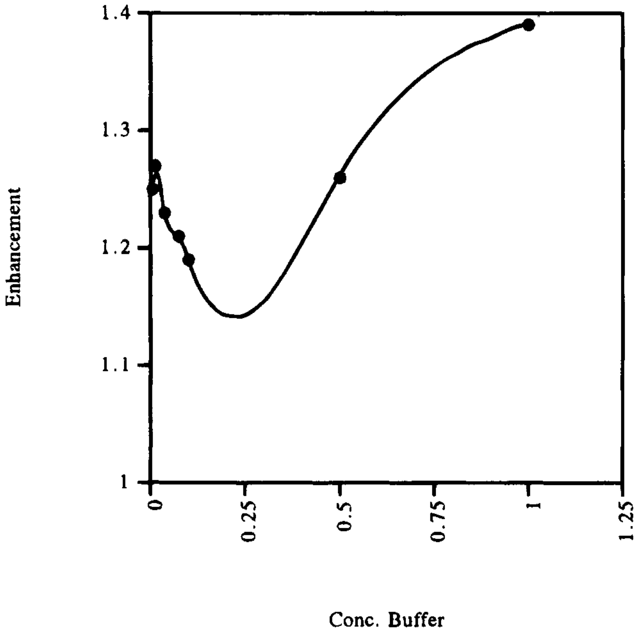

Figure 2. Rate enhancement in the reaction of 2,3-dimethyl-1,3-butadiene and ethyl acrylate as a function of pH 7 buffer concentration at 0.5 M alkene/diene concentrations.

We next varied the concentration of the buffer while keeping the concentration of the alkene/diene fixed at 0.5 M. These results are shown in Figure 2. Beginning with a 1.0 M concentration of buffer (above this concentration, inhomogenous solutions were obtained), we found that the increase in rate diminished from about 39% to about 18% as the concentration of buffer approached 0.1 M. Interestingly, the rate increased at very dilute solutions, but the increase is relatively small. This small enhancement in rate is too small to prove that the rate shown for 0.25 M is a minimum, which would suggest that a special effect operates in very dilute concentrations of salt. Although such an unspecified effect is generally consistent with these results, further work is required to verify the minimum in rate suggested by our data in Figure 2.

We next examined the rate of reaction in aqueous ethanol using different pH buffers compared to the rate of reaction without buffer. We were interested in effects due to changes in pH, but this study uses different types of salts which limits the value of the study. Nonetheless,

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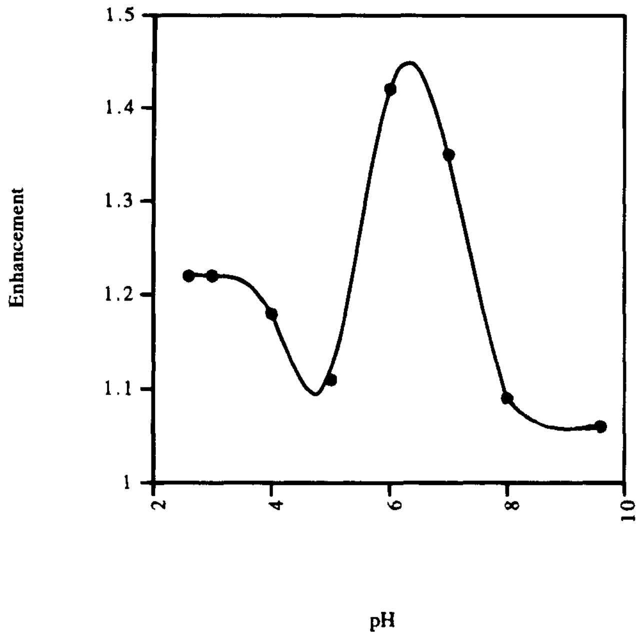


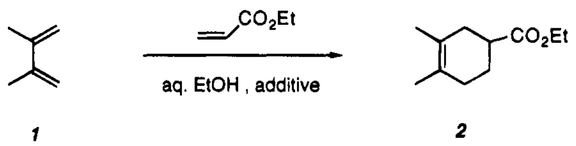
Figure 3. Rate enhancement in the reaction of 2,3-dimethyl-1,3-butadiene and ethyl acrylate as a function of pH buffers at 0.5 M alkene/diene concentrations.

our results are shown in Figure 3 and indicate that maximum rate enhancement occurred with neutral pH buffers. As with Figure 1, solubility problems occurred when buffers with a pH greater than 10 were used. The rate data for pH 9 is, therefore, not necessarily a minimum for the basic pH range. This could be due to changes in the type of salt, but it is interesting that, even in acidic media, the rate enhancement is diminished. Clearly, ethyl acrylate will be hydrolyzed at acidic and basic pH, which can interfere with the analysis. The enhancement in rate at neutral pH is clear, however. We therefore believe that the rate enhancement effects noted in this study, which occur at neutral pH, are not due to acid or base catalysis but rather to the influence of the anion or cation of the added salt.

These results suggested that the concentration of the alkene/diene was critical and that the salts in a pH 7 buffer induced a modest rate enhancement. Since the buffer contained a mixture of K_2HPO_4 and NaH_2PO_4, a key question was whether both of the salts would lead to a rate enhancement independently. We therefore examined the reaction of **1** with ethyl acrylate using a 7.3 mM solution of sodium dihydrogen phosphate (NaH_2PO_4) and then several reactions using a 7.3 mM solution of potassium monohydrogen phosphate (K_2HPO_4). We found that NaH_2PO_4 gave a 38% increase in the rate whereas K_2HPO_4 gave only a 19% increase. We also examined potassium dihydrogen phosphate (KH_2PO_4) at 7.3 mM and found a 46% increase in rate. These results suggest that the $H_2PO_4^-$ anion is responsible for the increase in rate. These results are presented in Table 1, along with those we obtained by adding several other additives to the aqueous ethanol solution.

From this data, only KH_2PO_4, NaH_2PO_4, and LiCl show significant rate enhancements, although both $NaHSO_3$ and tetrabutylammonium bromide show about a 30% increase in rate at these low concentrations. All of the other salts used in this study lead to a modest (10–15%) increase in rate of reaction in dilute solutions, relative to the rate of reaction without an additive. The results with LiCl are, of course, in accord with those of Breslow except that the concentration of the solution and the magnitude of the effect is much smaller. Interestingly, the effect observed with LiCl seems to be due to the lithium rather than the chloride anion (compare LiCl, NaCl, NH_4Cl, $ZnCl_2$, and $MgCl_2$), whereas the effect of the dihydrogen phosphates seems to be due to the anion ($H_2PO_4^-$) rather than the cation (potassium or sodium). All of the salts discussed up to this point contained monovalent anions, but we also examined several divalent salts and observed only modest rate enhancements with all of them (see Table 1). We have also examined the rate of this reaction in pure water, with and without added buffer, and in pure ethanol, with and without added buffer. The rate of reaction in pure ethanol, with no added salt, was about the same (about 1% slower) when compared to the rate of reaction with 1:1 aqueous ethanol with no added buffer. When the pH 7 buffer was added, the reaction was about 10% slower. When the reaction was observed in pure water, no correlation could be found since the rate data were not linear for either a first order or a second order reaction. The ethyl acrylate disappeared in this process, however, and some Diels–Alder product was observed. Since the reactants were visibly insoluble, the rate data is unreliable for comparison with the data from the aqueous ethanol system. Interestingly, when the pH 7 buffer was added to the reaction in water, the second order plot did not give a good correlation. Plotting a first order reaction (ln *A* vs time), however, gave an excellent linear correlation. The expected Diels–Alder adduct was isolated, and it appears that the time of reaction is shorter than in the aqueous ethanol system. The results of these studies show that the rate of reaction with aqueous ethanol is generally faster than the rate of reaction in pure ethanol and that the reaction in pure water cannot be correlated due to insolubility. The reaction in buffered water is faster than the aqueous ethanol reaction, but since it follows first order kinetics rather than second order, a direct comparison is ruled out for this work. In this latter case, a different mechanism may be operative, but this demands further study before it can be correlated with the aqueous ethanol results.

Table 1. Rate Enhancement in the Reaction of 2,3-Dimethyl-1,3-butadiene and Ethyl Acrylate (0.5 M) in Aqueous Ethanol Containing Various Additives at Concentrations of 7.3 mM



salt	relative rate	salt	relative rate
none	1.00	NaCl	1.15
KH_2PO_4	1.46	LiCl	1.49
NaH_2PO_4	1.38	$ZnCl_2$	1.20
K_2HPO_4	1.19	$MgCl_2$	1.11
$NaHSO_3$	1.28	NH_4Cl	1.15
$NaHSO_4$	1.18	*n*-Bu_4NBr	1.30
Na_2SO_4	1.14	urea	1.15
$MgSO_4$	1.17		

We were interested in the reaction when tetrabutylammonium bromide was used as an additive. As noted above, Breslow observed that *n*-Bu_4NCl was a salting in agent that increased the rate of the reaction, probably by contributing to easier cavity formation and direct solvation of the substrate. We observed a 30% increase in rate using a 7.3 mM solution of *n*-Bu_4NBr, which is not surprising given Breslow's results. When we examined the reaction of **1** with ethyl acrylate at 7.3 mM, 0.1

M, and 0.5 M solutions of n-Bu_4Br in aqueous ethanol, we found that the greatest rate enhancement occurred in the most dilute solution (relative rate: 1.30, 1.18, and 1.14, respectively). Interestingly, ammonium chloride did not give a significant enhancement in rate. Combined with the results in Figure 2, it appears that there may be an effect (or effects) in dilute solution that leads to the rate enhancement. Although most of our results can be explained by the usually invoked salting out phenomena, a different explanation may be necessary for these dilute systems. The solutions used for the reactions in Table 1 appeared to be homogeneous at the reflux temperature of the medium, but this does not rule out the presence of microemulsions or microaggregates. In previous studies, salting in usually resulted in a diminished rate of reaction rather than an increased rate, whereas salting out leads to rate enhancement. Traditional salting out phenomena appear unlikely in a homogeneous or nearly homogeneous system, although salting out could also include microaggregates and microemulsions in a strict sense. Indeed, the presence of a microaggregate or a microemulsion, as described above,[15] seems to be a likely explanation for these effects. It is also possible that the salts could increase the solubility of the alkene and diene or increase the surface contact of the electrolyte and organic substrates, as suggested previously.[16]

It is noted that the rates of Diels–Alder reactions in mixed solvents have been reported in the literature. As mentioned above, Breslow showed that the solubility of aromatics was increased in 10 and 20% aqueous ethanol. Presumably, the solubilities of ethyl acrylate and 2,3-dimethyl-1,3-butadiene are also increased in 1:1 aqueous ethanol. The observation that the reaction is faster in aqueous ethanol than in pure ethanol is consistent with the concept of increased solubility in the mixed solvent. The addition of salts to the pure ethanol solution slowed the reaction even further, again consistent with diminished solubility of the salts, and possibly the reactants. Schneider reported rate enhancement in the reaction of diethyl fumarate and cyclopentadiene in both aqueous dioxane and aqueous methanol (10, 30, and 60% solutions).[28] Johnson studied the influence of solutes (LiCl, KCl, NaCl, cyclodextrins, etc.) on the rate of reaction of cyclopentadiene and fumaronitrile in water, which was slower with added MCl.[29] The rate of reaction was slower with decreasing concentration of MCl. This reaction was also studied in 1:1 aqueous methanol and 1:1 aqueous ethanol. In both cases, the reaction was slower than it was in pure water but faster than it was in pure ethanol.[29] This is consistent with our observations. Johnson's study showed a decrease in ΔG relative to pure water, with a decrease in ΔH and a more unfavorable ΔS. Relative to pure ethanol, ΔG increased and ΔH decreased.

In conclusion, we cannot absolutely specify the mechanism by which these effects occur in dilute solution. They may be identical to previous results obtained in concentrated solution, or they may be unique. More work is required to answer this question. We also cannot rule out the transition state destabilization proposed by Engberts. It is not clear how the rate enhancements induced by phosphate anions, lithium cations, and tetrabutylammonium cations in the reaction of dimethylbutadiene and ethyl acrylate can be unified under a discussion of "traditional" hydrogen bonding effects. Blake and Jorgensen's proposed enhancement of rate acceleration as a function of increased charge transfer and/or polarization[25] is consistent with our results, however. Despite the mechanistic ambiguity, we have made several new observations that contribute to the interesting area of aqueous Diels–Alder chemistry. Dilute solutions of buffers, particularly salts of the $H_2PO_4^-$ anion, lead to rates 35–40% above the rate of reaction in aqueous ethanol without addition of the salt. Presumably, phosphate is a salting out agent, with a predictable increase in the rate of the reaction. Dilute solutions of both lithium chloride and tetrabutylammonium bromide lead to about 30–35% rate enhancements. Several other salts give very low levels of rate enhancement. The rate enhancement in dilute solutions shows a clear dependence on the concentration of the alkene/diene substrates, showing a maximum at 0.5 M. Our results suggest that this effect is not catalyzed by acid or base but is due to the presence of the phosphate anion or the lithium or tetraalkylammonium cation of the added salt. Our results strongly suggest that neutral solutions of the added salt are more effective in these reactions.

Experimental Section

Instrumentation. Kinetics were followed by HPLC analysis of samples using a Varian 2510 HPLC pump and a UV detector. A micro-pak S1-15 (15 cm × 4 mm) analytical column, at room temperature, was used with eluant consisting of 1% ethyl acetate/hexane pumped at 1.5 mL/min. The NMR spectroscopy was done on a Brüker AC-270 FT-NMR instrument at 270.13 and 67.3 MHz and reported in ppm downfield from tetramethylsilane (TMS) which was used as an internal standard. Infrared spectra were recorded on a Perkin-Elmer 1600 series FT-IR instrument.

The reaction of 2,3-dimethyl-1,3-butadiene and ethyl acrylate to give **2** is well-known.[5] Cycloadduct **2** was isolated by column chromatography and identified via NMR and IR techniques.

Materials. Ethyl acrylate, 2,3-dimethyl-1,3-butadiene, and methyl methacrylate were obtained from Janssen Chemical Co., and the pH buffer caplets (Metrepak pHydroin buffers) were obtained from Micro Essential Laboratory, Brooklyn, NY. Water was distilled and deionized and was saturated with argon prior to use. Ethanol was anhydrous and used as obtained from Baker.

Kinetics Measurements. The reaction was generally run at 0.5 M in **1** and ethyl acrylate in 300 mL of solvent (150 mL of water and 150 mL of ethanol). For those reactions involving salts, the appropriate salt was dissolved in water, and 150 mL of this solution was taken and mixed with 150 mL of ethanol. The reaction mixture was heated to reflux, 20 mL aliquots were removed at various times and cooled to ambient temperature, and a known amount of methyl methacrylate was added as an internal standard. This sample was injected into the HPLC instrument. The concentration of both **1** and ethyl acrylate in each aliquot was determined against the internal standard. The second order rate constant was determined by plotting time vs $1/A$ and gave a good linear fit (correlation ≥ 0.98). Both ethyl acrylate and **1** were used, and identical results were obtained. Each reaction was monitored for at least six half-lives. For each of the reactions involving salt solutions, an identical reaction was run using only aqueous ethanol (without the salt additive) and the second order rate constant of the reaction determined by plotting time vs $1/A$). The relative rates reported in our study were obtained by taking the ratio of $k_{\text{salt}}/k_{\text{no-salt}}$, and this ratio was used to determine increases in the rate of reaction. For Figures 1–3 and in Tables 1, this ratio is used for the relative rate enhancement.

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