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Rate Acceleration and Subsequent Retardation of Diels−Alder Reactions in $LiClO_4$−Diethyl Ether: An Experimental Investigation

Anil Kumar* and S. S. Pawar

Physical Chemistry Division, National Chemical Laboratory, Pune 411 008, India

akumar@ems.ncl.res.in

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The experimental kinetic data for several Diels−Alder reactions show why a 5 M $LiClO_4$−diethyl ether (LPDE) solution offers maximum enhancement of reaction rates, endo/exo ratios, and yields. These reactions, if carried out in LPDE solutions of concentrations higher than 5 M, show a substantial decrease in these kinetic parameters. This decrease is attributed to the very high viscosity of LPDE solutions near saturation, though this interpretation is not consistent when considered in terms of sizes of the diene and dienophile. The monoetherates, dietherates, and higher other clusters in LPDE solutions and their relationship with the Lewis acid catalysis by Li^+ offer a more plausible explanation of both the enhancement and the decrease of the rate of Diels−Alder reactions in this medium.

Introduction

Diels−Alder chemistry offers a powerful strategy for synthesizing six-membered ring systems with excellent stereochemical control.[1] In principle, Diels−Alder reactions should not be influenced by different solvents, as these reactions involve isopolar-activated complexes.[2] Contrary to this, however, Rideout and Breslow[3] demonstrated a remarkable rate enhancement of Diels−Alder reactions in water. Later, Breslow and co-workers[4] studied the kinetics of these reactions in aqueous salt solutions and concluded that LiCl enhanced the reaction rates, while $LiClO_4$ and guanidinium chloride (GnCl) retarded them. Later, Grieco, Nunes, and Gaul[5] found a dramatic rate acceleration of several sluggish Diels−Alder reactions by employing a 5 M $LiClO_4$−diethyl ether solution, popularly known as LPDE. The conventional synthesis[6] of cantharidin under high external pressure (≈15 kbar) was achieved under normal temperature and pressure with an improved yield when 5 M LPDE was used as a solvent medium for carrying out the reaction.[5] Obviation of high pressure requirements and huge rate enhancements of slow Diels−Alder reactions in 5 M LPDE have led to its use for several other organic reactions.[7] The spectacular rate variations in Diels−Alder reactions carried out in such solvent media have been ascribed to solvent polarity, hydrophobic packing, enforced hydrophobic hydration, Lewis acid catalysis, etc.[8−14] A careful literature search reveals that several Diels−Alder reactions have been carried out in a specific 5 M LPDE solution only for achieving maximum rate enhancement and not in solutions of LPDE of other concentrations. However, no quantitative support for the use of a 5 M LPDE solution only for achieving maximum rate acceleration has been offered in the literature to date.

The main objectives of this work are to address the following three questions. (1) Is the concentration of 5 M LPDE critical for maximizing the rate enhancement of Diels−Alder reactions? (2) What will happen if other

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* To whom correspondence should be addressed. Fax: +91 20 589 3044.

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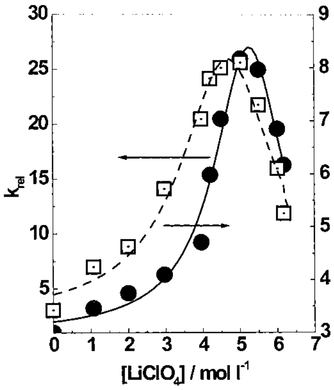
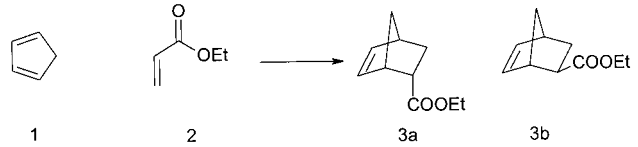


Figure 1. k_{rel} (●) and endo/exo (☐) ratios as a function of [$LiClO_4$] in LPDE for the reaction of **1** with **2**.

Scheme 1



salt concentrations are chosen for carrying out such a reaction. (3) What is the comparative performance of other solvent media in giving maximum rate enhancement, and at which concentrations does this occur? During the course of this study, some interesting experimental results were obtained in this laboratory and are reported in this paper and hoped to be of general use to chemists. This work is a part of systematic investigations being carried out in this laboratory on delineating the origin of forces responsible for spectacular rate variations of Diels−Alder reactions in different salt solutions.[14]

Results and Discussion

To achieve the objectives cited above, several Diels−Alder reactions were carried out in $LiClO_4$ solutions prepared in diethyl ether and other organic solvents. Largely, the reactions are conducted in concentrated $LiClO_4$ solutions. As rate data for several reactions studied here were obtained in solutions of low concentrations of $LiClO_4$ by earlier authors, the measurements were extended up to solubility limits. The solubility data suggest that it is possible to prepare LPDE solutions up to 6.06 M at room temperature.[15]

The starting point of this investigation is the pioneering work of Grieco, Nunes, and Gaul,[5] who first studied the reaction of cyclopentadiene **1** with ethyl acrylate **2** in 5 M LPDE only to give a 93% isolated yield of cycloadduct **3** with an endo/exo ratio of 8:1 (Scheme 1). Their criteria for estimating the progress of this reaction were yields and endo/exo products. No direct kinetic data were collected to support their claim. To quantify the effect of LPDE on the progress of this reaction, this reaction was carried in LPDE solutions of different concentrations. In Figure 1 are plotted the relative rate constant, k_{rel} (rate constant in $LiClO_4$ solution/rate constant in pure solvent), and endo/exo ratios as a function of concentration of $LiClO_4$, [$LiClO_4$], for the reaction of **1** with **2**. A 9-time increase in the reaction rates is observed in 4 M LPDE. Surprisingly, a drastic rate increase of 26 times is witnessed in 5 M LPDE when compared to that in pure diethyl ether. It is important to note that a sharp increase in rate constants can be marked in LPDE solutions with concentrations above 4 M LPDE. The k_{rel} value, which was about 9 in 4 M LPDE, more than doubles in 4.5 M LPDE and triples in 5 M LPDE. The reaction rate begins to fall if the reaction is carried out in 5.5 M LPDE. The increase in k_{rel} between 4.5 and 5 M LPDE is quite strong suggesting that LPDE offers a spectacular advantage around concentrations between 4.5 and 5 M. The slow decrease in k_{rel} observed between 5 and 5.3 M LPDE indicates that a maximization of reaction rate has already been achieved in 5 M LPDE. Furthermore, kinetic measurements in nearly saturated 6 M LPDE reveal that the reaction rate falls to $k_{rel} = 16$ from its value of 26 in 5 M LPDE. The rate retardation effect in Diels−Alder reactions carried out in very concentrated LPDE solutions has been recorded for the first time and is an important point of this investigation.

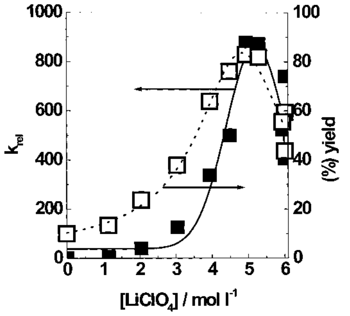
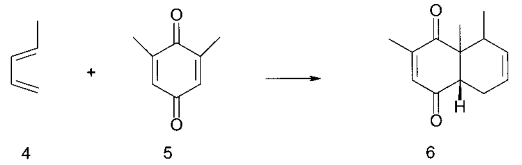


Figure 2. k_{rel} (■) and % yield (☐) as a function of [$LiClO_4$] in LPDE for the reaction of **4** with **5**.

Scheme 2



Analogous behavior of the concentration dependence of endo/exo ratios and yields is observed for the above reaction in different LPDE solutions. The endo/exo ratio (8.1:1), which is the highest in 5 M LPDE, reduces to 5.2:1 in 6 M LPDE. Similarly, the yield of **3** increases to 91% in 5 M LPDE before declining to 69% in 6 M LPDE (not shown).

Another reaction studied is that of transpiperylene **4** with 2,6-dimethyl benzoquinone **5** (Scheme 2) in 5 M LPDE, which affords an 80% yield after 15 min as compared to <20% yield after 24 h in water.[5] The k_{rel} values and yields in LPDE solutions of different concentrations obtained in the current study are demonstrated in Figure 2. The reaction becomes 125 times faster in 3 M LPDE as compared to 5 times faster in 1 M LPDE. A 4.5 M LPDE solution accelerates the reaction by about 500 times with a maximum enhancement of about 880 times occurring in 5 M LPDE as compared to that in diethyl ether alone. In LPDE solutions above 5 M, the k_{rel} value falls to about 400 times in 6.06 M LPDE as compared to that in pure solvent. Again, a slow decrease in reaction rates between 5 and 5.2 M LPDE is noted. Analogous behavior can be seen in the case of yields of cycloadduct **6** (Scheme 2). The yield, which is 38% in 3

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(15) Willard, H. H.; Smith, G. F. *J. Am. Chem. Soc.* **1923**, *45*, 286.

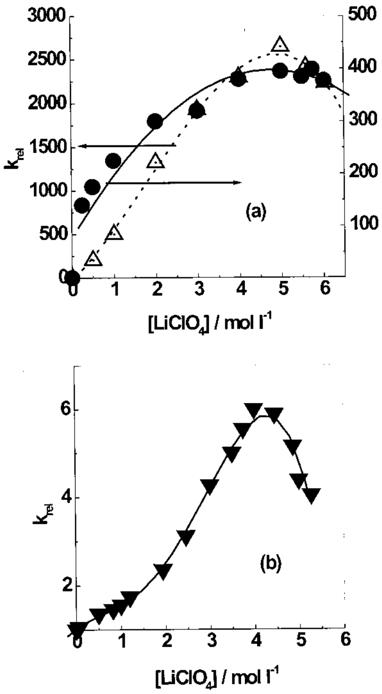
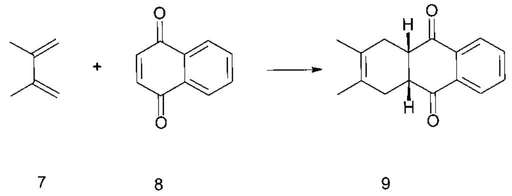
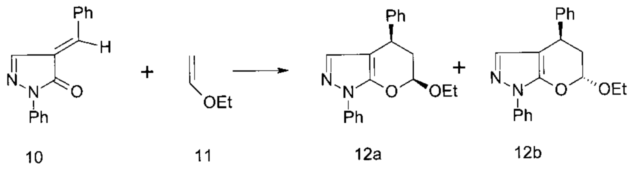


Figure 3. Dependence of k_{rel} on [LiClO$_4$] in LPDE for reactions of (a) **7** with **8** (Δ) and of **10** with **11** (●) and of (b) **7** with **13** (▼).

Scheme 3



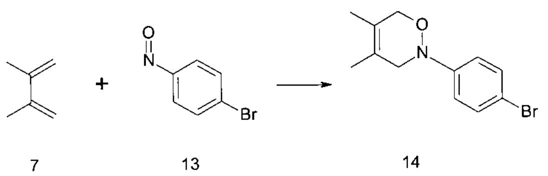
Scheme 4



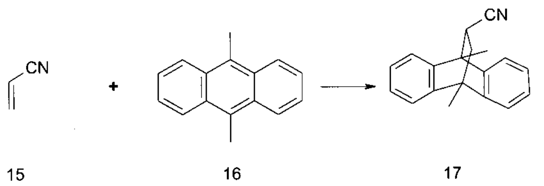
M LPDE, doubles in 4.5 M LPDE before reaching a maximum of 83% in 5 M LPDE. In 6.06 M LPDE, where the reaction rate falls dramatically as compared to that noted in 5 M LPDE, a substantial decrease in the yield from 83 to 43% is witnessed.

The reaction of 2,3-dimethylbutadiene **7** with 1,4-naphthoquinone **8** (Scheme 3) is accelerated about 1300 times in 2 M LPDE solution as compared to that in diethyl ether alone.[16] The kinetic data obtained in this study, when plotted in Figure 3a for this reaction, show a huge acceleration in the rates by about 2600 times in 5 M LPDE. When the same reaction is carried out in 5.5 and 6 M LPDE, the reaction rate declines to 2500 and 2200 times, respectively, from 2600 times noted in 5 M LPDE.

Scheme 5



Scheme 6



The reaction of 1-phenyl-4-benzylidene-5-pyrazolone **10** with ethyl vinyl ether **11** (Scheme 4) is greatly influenced by the concentration of LiClO$_4$ in diethyl ether[16] (Figure 3a). A 2 M LPDE solution enhances the reaction rate by 300 times, reaching a maximum of about 400 times in 5 M LPDE, as seen from the plot drawn in Figure 3a. No changes in reaction rates are noted in the concentration range from 5 to 5.5 M, and therefore the k_{rel} vs salt concentration curve becomes invariant in this concentration range. A slow retardation of reaction rates is observed in 6 M LPDE.

It is interesting to find out whether the rate retardation in very highly concentrated LPDE exists for Diels−Alder reactions with mild increases in reaction rates. An example of mild rate enhancement for the reaction of **7** with 4-bromonitrosobenzene **13** (Scheme 5) is shown in Figure 3b. This reaction proceeds about 2.5 times faster in 2 M LPDE as compared to that in diethyl ether.[16] The present results show that if this reaction is carried out in higher concentrations of LPDE, a maximum acceleration of 5 times in ≈4.75 M LPDE with reference to that in pure diethyl ether is observed. The reaction slows down in LPDE of concentrations between 5 and 6 M giving only an acceleration of 4 times.

Forman and Dailey[12a] were the first to demonstrate that the rate acceleration of Diels−Alder reactions carried out by Grieco and co-workers[5] in 5 M LPDE was due to Lewis acid catalysis. They showed Li$^+$ acting as a Lewis acid by demonstrating a linear dependence of the second-order rate constant on the concentration of LiClO$_4$ for the reaction of acrylonitrile **15** with 9,10-dimethylanthracene **16** (Scheme 6) in LPDE solutions up to a maximum concentration of 4.55 M. These authors did not carry out the reaction in LPDE solutions above the concentration of 4.55 M. Their explanation that Lewis acid catalysis is responsible for the dramatic rate enhancement of Diels−Alder reactions in LPDE-type media has been widely accepted.[1,7] Their experiments were extended further in this laboratory beyond 4.55 M LPDE. The temperature-dependent rate data from 28 to 43 °C obtained in the present study, together with the rate constant obtained in 4.55 M LPDE at 28 °C from Forman and Dailey,[12] are plotted in Figure 4 in the form of k_{rel} vs [LiClO$_4$]. The k_{rel} still increases in 5 M LPDE before declining by 17% in 6 M LPDE. An examination of Figure 4 suggests that the degree of rate retardation in the LPDE solutions of concentrations between 5 and 6 M becomes weak with an increase in temperature (from 28 to 43 °C).

An attempt was also made to examine whether this effect also exists in solutions of LiClO$_4$ in other solvents. The reaction of **1** with **2** was examined in high concentra-

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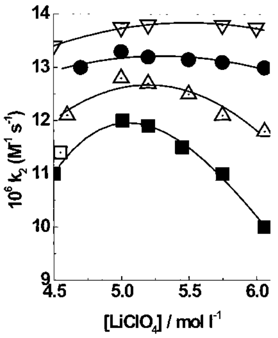

Figure 4. Second-order rate constant, k_2, for the reaction of **15** with **16** in concentrated LPDE solutions at various temperatures: (□) from ref 12a at 4.55 M at 28 °C, (■) 28 °C, (△) 33 °C, (●) 38 °C, and (▽) 43 °C.

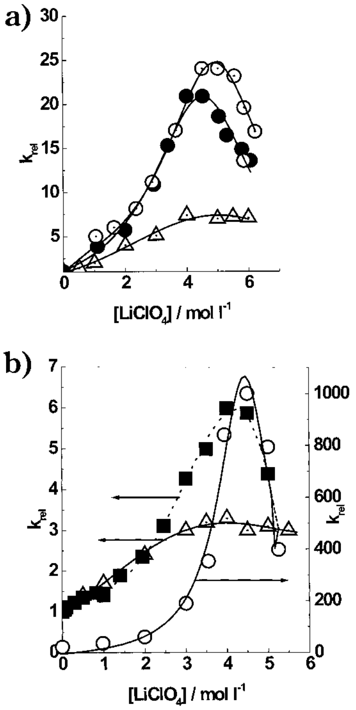

Figure 5. k_{rel} − $[LiClO_4]$ plots for the reactions of (a) **1** with **2** in LPAC (●), LPEA (○), and LPME (△), and (b) for the reactions of **7** with **8** in LPAC (○) and **7** with **13** in LPAC (■) and in LPME (△).

tions of $LiClO_4$ in ethyl acetate (LPEA) and acetone (LPAC) (see Figure 5a). In LPEA, the reaction was fastest in 4.25 M solution. This rate was accelerated by about 24 times as compared to that in pure ethyl acetate. It may be noted that a 26-time acceleration in the rate was achieved in 5 M LPDE. If this reaction is carried out in 5 M LPAC, the rate is 21 times faster than that in acetone alone before k_{rel} falls to a value of ≈13 in 6 M LPAC. A decrease in the rates of reactions carried out in very highly concentrated acetone and ethyl acetate solutions of $LiClO_4$ is observed. In both LPEA and LPAC, the reaction becomes slow in highly concentrated salt solutions, i.e., 4.5 and 4 M, respectively, as compared to 5 M LPDE. The concentration dependence of the endo/exo ratios and yields in LPEA and LPAC show trends comparable to those noted using LPDE. $LiClO_4$ is soluble in methanol up to about 6.7 M at room temperature.[15] The effect of LPME is less pronounced than those of LPDE and LPAC on the kinetic data for the reaction of **1** with **2**. The k_{rel} values for this reaction in LPME shown in Figure 5a reach a maximum of ∼7 in 4 M LPME. As seen in the above reaction, no further rate enhancement takes place above 4 M LPME.

Furthermore, the reaction of **7** and **8** was carried out in LPAC (Figure 5b). A huge rate enhancement of about 800 times in 4 M LPAC as compared to that in acetone alone was noted in earlier work.[17] However, when this reaction was carried out under identical conditions in LPAC with concentration above 4 M, the interesting results shown in Figure 5b were observed. A maximum rate enhancement of about 1000 times is obtained in 4.5 M LPAC. A further increase in the concentration of LPAC decreases the reaction rates. In short, a 1000-fold rate enhancement at 4.5 M is reduced to 400 times at 5.25 M LPAC. One should note that the concentration zone between 4 and 4.5 M LPAC is very sensitive to the rate enhancement, while the zone between 4.5 and 5 M is sensitive to retardation of the rate of this reaction.

The reaction of **7** with **13** reaches a maximum rate acceleration of about 6 times in 4 M LPAC solution before declining to about 4 times in 5 M LPAC as compared to that in acetone alone (Figure 5b).[17]

The reaction of **7** and **13** occurs about 3 times faster in a 4 M solution of $LiClO_4$ in methanol (LPME) (Figure 5b). No further noticeable change in k_{rel} is seen in the LPME solutions of concentrations higher than 4 M.

It has been suggested that the tapering of the k_{rel} vs salt concentration at high concentrations may be the result of the solubility of salt in the solvent used to prepare the solution in which the reaction is carried out.[4d,14e] As the reaction rates for many Diels−Alder reactions reach a maximum in 5 M LPDE and the solubility of $LiClO_4$ in diethyl ether is about 6.06 M, the tapering effect may not be due to solubility factor alone. As seen above, the reaction rates for several Diels−Alder reactions decline in LPDE solutions above 5 M only.

Does the viscosity of concentrated LPDE solutions play any role in reducing the reaction rates, endo/exo products, and yields? The literature data show that the viscosity of a saturated LPDE solution is about 800% higher than that of pure diethyl ether at 25 °C.[15] The viscosity of 5 M LPDE increases by about 15 times as compared to that of pure DE. There is, however, a very sharp exponential increase in viscosity between 5 and 6.07 M solutions. A 42-fold rise in viscosity is seen in 5.3 M LPDE and becomes 250-fold in 5.8 M LPDE solution. A 500-fold increase in the viscosity of a 5.95 M LPDE solution is enhanced to about 800-fold in 6.07 M LPDE, a saturated solution of $LiClO_4$ in diethyl ether. Two zones showing the changes in viscosity of LPDE solutions are demonstrated in Figure 6. Remarkable differences between the viscosities of LPDE solutions below and above the concentrations of 5 M LPDE are noticeable.

A significant development in the effect of viscosity on the rates of Diels−Alder reactions was made by Firestone and co-workers.[19] Swiss and Firestone[19a] reported the rate enhancement of dimerization of cyclopentadiene with viscosity of several hydrocarbon solvents up to 1 cP with a subsequent drop in the solvents with viscosities >1 cP. A similar observation was made for the 1,3-dipolar

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(17) Casaschi, A.; Desimoni, G.; Faita, G.; Invernizzi, A. G.; Lanati, S.; Righetti, P. P. *J. Am. Chem. Soc.* **1993**, *115*, 8002.

(18) Ekelin, K.; Sillen, L. G. *Acta Chem. Scand.* **1953**, *7*, 987.

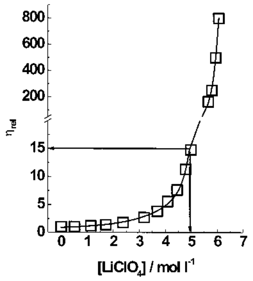

Figure 6. Concentration dependence of the relative viscosity, η_{rel}, for LPDE solutions; the break on the y-axis is shown to cover the huge viscosity enhancement (data from ref 15).

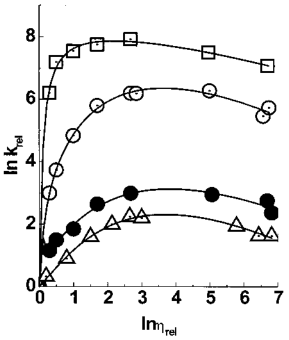

Figure 7. Correlation of ln k_{rel} with ln η_{rel} for the reactions of **1** with **2** (●), **4** with **5** (○), **7** with **8** (□), and **15** with **16** (△) in LPDE solutions.

cycloaddition of diphenyldiazomethane with ethylphenylpropiolate. The viscosity-induced rate enhancement and subsequent decrease in these two reactions cannot be explained in terms of current kinetic theory. Variation of ln k_{rel} on the ln η_{rel} (η_{rel} = relative viscosity = viscosity of solution/viscosity of pure solvent) for the reactions of **1** with **2**, of **4** with **5**, and of **7** with **8** in LPDE solutions is shown in Figure 7. The reaction rates, in general, rise up to a value of viscosity of 3.5 cP corresponding to 5 M LPDE. Then, the reaction rates level off in the viscosity range from 3.5 to 42 cP corresponding to concentrations of 5 to 5.3 M LPDE. Retardation of the reaction in the viscosity range from 42 to 190 cP is observed (near the solubility range). As shown in Figure 6, the viscosity of LPDE solution does not rise dramatically up to a concentration of 5 M. As the viscosity of nearly saturated LPDE solution is too high ($\approx$800 times with respect to that of diethyl ether), the reactants cannot find each other (because of diffusional problems) in such a highly viscous syrup, which leads to reduction of reaction rates.[19,20] The observed rate in a highly viscous solution decreases as the rate of diffusion is inversely proportional to the viscosity of a medium. Such models have been discussed by many authors, more notably by Hynes.[20] The rate reduction of the reaction of **15** with **16** in LPDE solutions with concentrations above 5 M can also be explained in a similar fashion. A similar effect was also noted in LPAC, LPEA, and LPME, though the viscosity enhancement of these solutions near their saturation limits is not as high as that of LPDE.

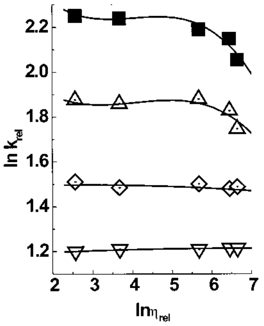

Figure 8. ln k_{rel} vs ln η_{rel} for the reaction of **15** with **16** at (■) 28 °C, (△) 33 °C, (◇) 38 °C, and (▽) 43 °C.

If viscosity plays an important role in retarding the reaction rates, it should be supported by the temperature-dependent rate and viscosity data. In Figure 4 are shown the second-order rate constants as a function of concentration of $LiClO_4$ from 4.5 M to near saturation at 28, 33, 38, and 43 °C. The viscosity of LPDE solutions decreases with increases in temperature, thereby allowing lesser dense reaction media to be used for the reaction.[21] The curve of ln k_{rel} vs ln η_{rel} at different temperatures is plotted in Figure 8. An examination of Figures 4 and 8 suggests that the portions of plots that were highly curved in very high LPDE concentrations at the lowest temperature (28 °C) tend to become straight with increases in the temperature of the reaction emphasizing the role of viscosity.

However, one notes certain contradictions when attempting to describe the rate variations in terms of viscosity.[22] The reaction of **4** with **5** slows down by about 54% between 5 and 6 M LPDE. An about 38% fall in the rates is noted in the case of reaction of **1** and **2**. On the other hand, a 17% fall in the rates is observed for the reaction of **15** and **16** with an approximately equal fall in the rates for the reaction of **7** with **8**. The rate drop for the reaction of **10** with **11** is less than 10%. If the higher viscosity were the primary source of hindrance to the diffusion of the diene and dienophile, one would expect that the reaction with the larger molecule would exhibit a larger drop as compared to that of the smaller ones. Larger molecules will offer larger molecular surface areas interacting with the solvent medium. Accordingly, the reaction of **10** with **11** should have shown a larger drop in the rates than that of **1** with **2** as compound **10** is larger in size than **1**. In connection with such contradictions, it is important to recall the contribution of Swiss and Firestone,[19a] who critically examined the roles of both macroviscosity and microviscosity[23] on the reaction rates. While macroviscosity is a bulk property, microviscosity

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[19] (a) Swiss, K. A.; Firestone, R. A. *J. Phys. Chem. A* **1999**, *103*, 5369. (b) Firestone, R. A.; Swiss, K. A. *J. Phys. Chem. A*, **2001**, *105*, 3430. (c) Firestone, R. A.; Vitale, M. A. *J. Org. Chem.* **1981**, *46*, 2160. (d) Firestone, R. A.; Christensen, B. G. *Tetrahedron Lett.* **1973**, 389. For other supporting references, see, for example: (e) Sternbach, D. D.; Rossana, D. M. *Tetrahedron Lett.* **1982**, 23, 303. (f) Dunams, T.; Hoekstra, M.; Pentaleri, M.; Liotta, D. *Tetrahedron Lett.* **1988**, 29, 3745.

[20] There are several models to describe the viscosity-dependent reaction rates. For examples, see: (a) Truhlar, D. G.; Hase, W. L.; Hynes, J. T. *J. Phys. Chem.* **1983**, *87*, 2664. (b) Van der Zwan, G.; Hynes, J. T. *Chem. Phys. Lett.* **1983**, *101*, 367. (c) Grote, R. F.; Hynes, J. T. *J. Chem. Phys.* **1982**, *77*, 3736. Bagchi, B.; Biswas, R. In *Advances in Chemical Physics* Prigogine, I., Rice, S. A.; John Wiley: New York, 1999; Vol. 109 and refs cited therein.

[21] Temperature-dependent viscosity data show a 25% decrease in ln η near saturation per 5 °C increase in temperature. The viscosities of LPDE solutions at 25 °C are taken from ref 18.

[22] An anonymous reviewer is thanked for pointing this out to the authors.

[23] For microviscosity, see: Sun, Y.-P.; Saltiel, J. *J. Phys. Chem.* **1989**, *93*, 8310.

is defined as the viscosity experienced by the diene and dienophile in a given solvent medium. The sizes of the diene and dienophile and properties of solvent (salt solution in this case) determine whether the macro- and microviscosity can be alike or not.[24] How the microscopic viscosity can be estimated in the current situation involving salts is presently not clear to the authors.[25] Its estimation, however, can help in delineating the viscosity effect on the kinetics of Diels−Alder reactions. The ion−solvent and ion−ion interactions in relation to their impact on the microviscosity in changing ionic concentrations are subjects of future study. As the dienes and dienophiles employed in this study were not selected on the basis of their sizes, it is difficult to compare the effect of individual reactants in terms of microviscosity. Our proposal that the viscosity of the medium (not the microviscosity) plays role is a preliminary and tentative explanation and is not consistent when considered in conjunction with microviscosity.

Can Lewis acid catalysis explain the retardation of reactions in LPDE solutions of concentrations above 5 M? The spectacular rate enhancement in 5 M LPDE has already been attributed to the Lewis acid catalysis.[12a] It is established that LPDE solution exists as a dietherate, $Li^+(OC_2H_5)_2ClO_4^-$, below the concentration of 4.25 M.[7d] The rate enhancement in this concentration range can be understood in terms of decreasing ether coordination of Li^+, thus rendering a “partly naked” ion as a more powerful Lewis acid. Above 4.25 M, a mixture of dietherate and monoetherate, $Li(OC_2H_5)ClO_4^-$, becomes gradually richer in monoetherate with an increase in concentration. As $LiClO_4$ can be solvated by a smaller mole fraction of ether than of water, the effect begins at a lower concentration and contributes to the large rate accelerations. Higher clusters have also been reported in LPDE solutions.[7d] In very highly concentrated LPDE solutions, the clusters come together to grow almost to a lattice driven by the lack of solvent.[18] This cluster formation at these concentrations adversely affects the degree to which Li^+ would be available at these concentrations as a Lewis acid catalyst. As less active Li^+ is expected to be available in the clusters, a fall in the rates is noticed.[22]

Does this situation exist in Diels−Alder reactions carried out in aqueous salt solutions? Recent work[14c] from this laboratory on the reaction of cyclopentadiene with methyl acrylate showed that the endo/exo ratios increased with increases in the concentrations of LiCl, NaCl, NaBr, and $CaCl_2$ up to a concentration of about 4 M. The log(endo/exo) vs [salt] plots leveled off in solutions with concentrations higher than 4 M. The solutions of LiCl, NaCl, and NaBr are less viscous than those of $CaCl_2$ in the full concentration range extending up to solubility.[26] Thus, it seems that a decrease of qjthe endo/exo ratios is not clearly seen in aqueous LiCl, NaCl, and NaBr solutions of the above concentrations. The log(endo/exo) − [salt] plot in aqueous $CaCl_2$ is not steep throughout the concentration range, possibly due to increases in viscosity by 3.6 and 8.3 times in 4 and 5 M solutions, respectively.

Conclusion

The kinetic results obtained on several Diels−Alder reactions carried out in different $LiClO_4$-containing solvent media quantitatively suggest the concentrations of such media that can be employed for maximizing the reaction rates and yields. This study is expected to offer valuable guidelines to synthetic organic chemists for achieving the optimum reaction conditions required in their synthetic work, as the limiting conditions of LPDE are quite clear from this investigation. It is hoped that these studies will provide further insight into the origin of forces responsible for the salt effects on Diels−Alder reaction kinetics. A quantitative estimation of the microviscosity in a salt solution and its correlation with the reaction rates will be a step forward in this direction.

Experimental Section

The kinetic data were collected by the methods employed in the original papers. Therefore, their details are not reproduced here. $LiClO_4$ was recrystallized twice from distilled water in the form of $LiClO_4 \cdot 3H_2O$ and then dried at 140 °C for 8h before $LiClO_4$ solutions were prepared in UV-grade solvents that were procured commercially. The salt was stored in a sealed bottle in a desiccator until used since it was necessary to keep it in a completely anhydrous state *(CAUTION: $LiClO_4$ is potentially explosive and must be handled with care)*.[27] The dienes and dienophiles used in this work were procured from M/S Aldrich or Merk, unless otherwise indicated. Cyclopentadiene (**1**) was freshly cracked from its dimer, while 1-phenyl-4-benzylidene-5-pyrazolone (**10**) and 4-bromonitrosobenzene (**13**) were prepared according to the procedure described elsewhere.[28] 2,6-Dimethyl benzoquinone (**5**), 1,4-naphthoquinone (**8**), and 9,10-dimethylanthracene (**16**) were commercially recrystallized products. Other dienes and dienophiles were freshly distilled prior to their use.

The rates of the reaction of **1** with **2** were determined by the procedure outlined elsewhere.[3] This study was performed under pseudo-first-order conditions with 4 mmol of **1** and 39.5 mmol of **2.** A volumetric pipet was used to measure accurately 2 mL of **2** in the salt solution, which was then transferred to a cuvette. A 15 μL volume of **1** was added, and the cuvette was capped and mixed. The progress of the reaction was followed at 250 nm, in which a first-order disappearance of **1** was observed over two half-lives. The pseudo-first-order rate constant was recorded to be first-order in **2**. The endo/exo ratios were determined using NMR as described in an earlier work.[14c]

The reaction of **4** (0.6 M) with **5** (2×10^{-4} M) was investigated under pseudo-first-order conditions. A 3.5 mL volume of **4** (in a definite amount of salt solution) was measured using a volumetric pipet and transferred to a cuvette. Then, 25 μL of **5** dissolved in salt solution was added. The cuvette was capped. After vigorous shaking, the disappearance of **5** was monitored at 250 nm.[29]

The progress of the reaction of **7** with **8** was examined by a procedure taken from the literature.[16] Quantities of 12 mmol of **7** and 48 mmol of **8** were used in this reaction. A definite amount of **8** was added to 10 mL of salt solution. Then, the solution was prepared by adding **7** to a weighed 5 mL volumetric flask. After the flask was reweighed, it was filled with the salt solution. Three samples of **8** were placed in a thermostat, in which definite amounts of **7** ranging from 0.25

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[24] Akesson, E.; Hakkarainen, A.; Laitinen, E.; Helenius, V.; Gillbro, T.; Korppi-Tommola, J.; Sundstrom, V. *J. Chem. Phys.* **1991**, *95*, 6508.

[25] The microviscosity determination in pure organic liquid though is relatively simple. See ref 19a.

[26] Isono, T. *J. Chem. Eng. Data* **1984**, *29*, 45.

[27] Schumacher, J. C. *Perchlorates−Their Properties, Manufacture and Uses*, ACS Monograph Series; American Chemical Society: Washington, DC, 1960.

[28] (a) Desimoni, G.; Gamba, A.; Righetti, P. P.; Tacconi, G. *Gazz. Chim. Ital.* **1971**, *101*, 2635. (b) Desimoni, G.; Astolfi, L.; Cambieri, M.; Gamba, A.; Tacconi, G. *Tetrahedron* **1973**, *29*, 2627. (c) Desimoni, G.; Faita, G.; Righetti, P. P.; Toma, L. *Tetrahedron* **1990**, *46*, 7951.

[29] Flaig, W.; Salfeld, J.-C.; Baume, M. E. *Annalen der Chemie* **1958**, 117.

to 0.75 mL were added. In the beginning and at definite intervals (after quenching of samples), the absorbance of **8** was monitored at 350 nm. An agreement of ± <5% was noted in the rate constants collected in this work and those reported in dilute salt solutions.[16]

Quantities of 0.01 mmol of **10** and 5.5 mmol of **11** were used for the measurement of kinetic data. To 10 mL of salt solution was added **10**. The solution of **11** was prepared in an accurately weighed 5 mL volumetric flask containing 3 mL of the required salt solution. The concentration of **11** was accurately calculated by reweighing the flask. Then, the flask was filled with the salt solution. Using a pipet, we placed 2 mL of the salt solution of **10** in three cuvettes, into which constant amounts from 0.25 to 0.75 mL of **11** were added. After the flask was vigorously shaken, the absorbance of **10** was measured at 410 nm to examine the progress of the reaction of **10** with **11**. The reaction rates in the lower salt concentrations collected in the present work agreed to ±2% with the reported values.[16]

Quantities of 5 mmol of **7** and 0.15 mmol of **13** were employed in the reaction of **7** with **13**. To 10 mL of salt solution was added a definite amount of **13**. The solution of **7** was prepared by addition into an accurately weighed 5 mL volumetric flask containing 3 mL of the required salt solution. The concentration of **7** was accurately calculated by reweighing the flask. Then, the flask was filled with the salt solution. Using a pipet, we placed 2 mL of the salt solution of **13** in three cuvettes, into which constant amounts from 0.25 to 0.75 mL of **7** were added. After the flask was vigorously shaken, the absorbance of **13** was measured at 740 nm to examine the progress of the reaction of **7** with **13**.[16] The experimental rate constants obtained in this study agreed to ±2.5% with the reported data in lower salt solutions.[16]

The reaction of **15** (0.7 M) with **16** (2×10^{-4} M) was carried out under pseudo-first-order conditions and was monitored by measuring the absorbance at 398 nm to follow the disappearance of **16**. The procedure is analogous to that given for the reaction of **1** with **2**. The details are provided by Forman and Dailey.[12a] Agreement of the rate constant obtained in 4.55 M LPDE in the current work was noted to be better than 1.5% when compared with rate data collected in lower salt solutions.[12a]

An average of three readings were treated as a final rate data recorded in tables and shown in figures. A Julabo constant-temperature bath was used for maintaining the temperature of the reaction mixtures.

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Supporting Information Available: Experimental kinetic data for different reactions and viscosity data of LPDE solutions at 28, 33, 38, and 43 °C. This material is available free of charge via the Internet at http://pubs.acs.org.

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