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Rate Enhancement in Diels−Alder Reactions by Perchlorate Salts in Nonaqueous Solvents: An Alternate Explanation†

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Recent experimental observations regarding rate enhancement of the Diels−Alder reactions in presence of the salt−nonaqueous solvent media are analyzed on the basis of two fundamental properties, i.e. internal pressure of solvent media and the volume of activation of the reaction. Such solvent media are normally perchlorates dissolved in diethyl ether, acetone, ethyl acetate, etc., out of which the lithium perchlorate−diethyl ether system is being used more frequently. With due credence to other explanations like Lewis acid catalysis by cations such as Li^+ and the nature of solvents, the problem of rate enhancement has been examined from an entirely different angle and the significance of internal pressure and activation volume in explaining rate profile presented. Several cases, like obviation of high-pressure conditions for the synthesis of cantharidin by the use of lithium perchlorate−diethyl ether and the rate acceleration of other reactions in such media are discussed. The reasons of ineffective or less effective role of internal pressure in driving certain reactions are critically examined in terms of the magnitude of activation volumes. In general, the solvent system with high internal pressure at a specified concentration and with lower activation volume will enhance the reaction rate with greater magnitude than one with higher activation volume. Both the internal pressure and activation volume can offer an alternate plausible explanation for the rate enhancement of the investigated Diels−Alder reactions in presence of salt−nonaqueous solvents.

Diels−Alder (D−A) reactions are useful in synthesizing complex organic molecules of biological importance. With regard to these reactions, two fascinating observations have been recently reported pertaining to the effect of salt−solvent additives on their kinetic profiles. The first observation[1] is concerned with the dramatic rate acceleration of the reaction leading to the synthesis of cantharidin using an additive, i.e. $LiClO_4$−diethyl ether (LPDE) under ambient conditions of temperature and pressure. This is a milestone in terms of achievement over the classic work of Dauben, Kessel, and Takemura,[2] who synthesized cantharidin by applying an external ultrahigh pressure of $\sim$15 kbar (1 ba = 10^5 Pa). The second observation pertains to the accelerated rates of D−A reactions in aqueous media. An excellent discussion regarding use of the additives in aqueous media has been recently documented.[3,4] This rate enhancement in aqueous media has been ascribed to several effects like hydrophobic interactions,[5,6] miceller catalysis,[7a] hydrogen bonding,[7b] and solvent effects.[7c]

In nonaqueous solvents like diethyl ether (DE), it was demonstrated[8] that the rate enhancement was due to Lewis acid catalysis by the lithium cation. Contrary to this, however, recently a report[9] appeared describing lithium ion as a strong Lewis acid only in the gas phase and this effect was considerably moderated in the DE solution by the presence of the perchlorate counterion and complexation to DE. This has been supported by NMR experiments and MNDO calculations in confirmation with the published work on the lithium ion in the gas phase. Further, it may be noted that physicochemical data on dielectric constants of LPDE solutions at low concentrations showed no evidence of catalytic activity.[10,11] Another recent study described the role of some metal perchlorates in acetone (AC) on the D−A reactions,[8b] where systematic experimental data on several D−A reactions in four perchlorate salts with acetone, i.e. magnesium (MPAC), barium (BPAC), lithium (LPAC), and sodium (SPAC), were presented and analyzed on the basis of the nature of the solvent and the cations involved. It may be recalled that LPDE was employed earlier by Pocker and his group for achieving rate enhancement in some organic reactions.[10] However, the use of LPDE in obviating the necessity of external ultrahigh pressure

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[1] Grieco, P. A.; Nunes, J. J.; Gaul, M. D. *J. Am. Chem. Soc.* **1990,** *112,* 4595.

[2] Dauben, W. G.; Kessal, C. R.; Takemura, K. H. *J. Am. Chem. Soc.* **1980,** *102,* 6893.

[3] Review: Grieco, P. A. *Aldrichim. Acta* **1991,** *24,* 59.

[4] Waldmann, H. *Angew. Chem. Int. Ed. Engl.* **1991,** *30,* 1306 and references therein.

[5] Review: Breslow, R. *Acc. Chem. Res.* **1991,** *24,* 159 and references cited therein.

[6] Rizzo, C. J. *J. Org. Chem.* **1992,** *57,* 6382.

[7] (a) Grieco, P. A.; Garner, P.; He, Z. *Tetrahedron Lett.* **1983,** *24,* 1897. Grieco, P. A.; Yoshida, K.; Garner, P. *J. Org. Chem.* **1983,** *48,* 3137. (b) For example see: Kelly, T. R.; Meghani, P.; Ekkundi, V. S. *Tetrahedron Lett.* **1990,** *31,* 3381 and references cited therein. (c) Blake, J. F.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1991,** *113,* 7432 and references cited therein. The Monte Carlo simulation results for the aqueous D−A reaction are interesting.

[8] Desimoni, G.; Faita, G.; Righetti, P. P.; Tacconi, G. *Tetrahedron Lett.* **1991,** *47,* 8399. (b) Casaschi, A.; Desimoni, G.; Faita, G.; Invernizzi, A. G.; Lanati, S.; Righetti, P. P. *J. Am. Chem. Soc.* **1993,** *115,* 8002. (c) Forman, M. A.; Dailey, W. P. *J. Am. Chem. Soc.* **1991,** *113,* 2761. They demonstrated the role of internal pressure to be ineffective in some D−A reactions and claimed Lewis acid catalysis as a cause of rate enhancement.

[9] Pagni, R. M.; Kabalka, G. W.; Bains, S.; Plesco, M.; Wilson, J. Bartmass *J. Org. Chem.* **1993,** *58,* 3130. More recently Li^+ has been shown to contain a Lewis acid effect in nonaqueous solvents. For this see: Reetz, M. T., Gansauer, A., *Tetrahedron Lett.* **1993,** *49,* 6025.

[10] Pocker (Pocker, Y.; Ellsworth, D. L. *J. Am. Chem. Soc.* **1977,** *99,* 2276, 2284, and references cited therein, established that LPDE can accelerate the rates of a variety of organic reactions like isomerization and aminolysis under ambient conditions. They interpreted their results, treating LPDE as a mixture of mono- and diether adducts of LP. Also see: Weinstein, S.; Smith, S.; Darwish, D. *J. Am. Chem. Soc.* **1959,** *81,* 5511.

[11] Markowitz, M. M.; Hawley, W. N.; Boryata, D. A.; Harris, R. F. *J. Chem. Eng. Data* **1961,** *6,* 325.

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was not successfully explored until the inspirng work of Grieco et al.[1] on the synthesis of cantharidin. These authors supposed that internal pressure[12] generated by the additives like LPDE presses the reactants together to realize the reaction, comparable to that in aqueous media. Their suggestion, however, was not quantified to explain the rate enhancement.[8c]

In the above discussion, the catalytic effect due to the Li^+ cation as a Lewis acid seems to be the rate-promoting factor in the nonaqueous D–A reactions. Our main objective, however, in this study, is to emerge with an alternate possible explanation besides what has been offered on the basis of catalysis. We examine both the issues of obviation of ultrahigh pressure in a D–A reaction like the synthesis of cantharidin, and the rate enhancements in several D–A reactions by LPDE. Rate acceleration in aqueous media is excluded from this study. The problem of dealing with the effect of other nonaqueous perchlorate solutions on the rates of D–A reactions is also addressed in this article. We also attempt to answer two questions: (1) Why does a perchlorate solution at the specified concentration speed up a given reaction at a higher rate as compared to another reaction? (2) Why are some D–A reactions insensitive to a salt–solvent media?

In order to achieve these, we analyze two properties of the system, i.e. internal pressure (P_i) caused by the solvent mixture,[12] and the activation volumes ($\Delta V^{\ddagger}$) of the reaction.[13] The former has recently been shown to correlate the rate enhancement in aqueous D–A reaction,[14] besides its wide and proven applications in understanding the thermodynamic and transport properties.[15]

Calculations

1. Internal Pressure. In order to estimate the internal pressure, P_i, we employed the Tamman–Tait–Gibson (TTG) model, which has been successfully used to describe kinetic thermodynamic and transport properties.[14,15] The relevant internal pressure equation is:

$$P_i = [10^3(B_T + 1)10^Q\alpha_s V_s + 10^{-3}(\phi_E{}^\circ M + S_E M^{1.5})/A'] - 1 \quad (1)$$

where B_T is Tait parameter.[15] Function Q is given by

$$Q = a_0 M + a_1 M^{1.5} + a_2 M^2 \quad (2)$$

with

$$a_0 = -\bar{K}^0(B_T + 1)/A \quad (3a)$$

$$a_1 = -S_1/A \quad (3b)$$

$$a_2 = -S_2/A \quad (3c)$$

and

$$A = 315V_s \quad (4a)$$

$$A' = A/2.303 \quad (4b)$$

In the above equations, M is molarity, $\bar{K}^0$ is partial molal compressibility at infinite dilution, V_s is specific volume of solvent. Constants S_1 and S_2 are the parameters from Masson equation.[16] S_E is corresponding temperature derivative of S_1. α_s and $\phi_E{}^\circ$ are thermal expansion coefficient of solvent and apparent molal expansibility of salt at infinite dilution. T is absolute temperature.

Another accurate method to obtain the P_i and values is: $P_i = (T\alpha/\beta)$ where α and β indicate coefficient of thermal expansion and isothermal compressibility at temperature T. Both these quantities can be easily estimated from the use of Scaled Particle Theory,[17] abbreviated as SPT, where experimental data are unavailable. We have recently employed the SPT for calculating the required quantities for an organic salt–solvent system comprised of different component sizes.[17b] The hard core diameters for perchlorate salts and solvents are given elsewhere.[18] The TTG constants available for LPDE, LPAC (in acetone), LPEA (in ethyl acetate), and LPTF (in tetrahydrofuran) are reported in Table 1. For other systems, i.e. acetone solutions of magnesium perchlorate (MPAC), barium perchlorate (BPAC), and sodium perchlorate (SPAC), the P_i values were generated from the SPT model.[17] As a check of reliability, the P_i values for LPAC, LPDE, and LPEA were also computed by the SPT model. The agreement between two models is shown in Figure 1, with an average deviation value of 3% in P_i. The P_i versus M plots for these solutions show very high internal pressures, a tremendous quantity to drive a reaction.

Internal pressures, induced by the addition of the perchlorate salts in solvents, can be represented by fitting pressure and concentration data using a least squares technique to an equation of the form

$$P_{i,eff} = (P_i - P_i, \text{pure}) = q_0 M + q_1 M^2 + q_2 M^3 + q_3 M^4 \quad (5)$$

where q_0 to q_3 are adjustable constants and M is molarity. The $P_{i,pure}$ is internal pressure of a pure solvent and $P_{i,eff}$

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[12] For internal pressure see: Dack, M. R. J. *Chem. Soc. Rev.* **1975**, *4*, 211 and references cited therein.

[13] (a) Van Eldik, R.; Asono, T.; Le Noble, W. J. *Chem. Rev.* **1989**, *89*, 549. (b) Le Noble, W. J. *Progress in Physical-Organic Chemistry*; Interscience; New York, 1967; Vol. 5, p 207.

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[15] Leyendekkers, J. V. *J. Chem. Soc. Trans. Faraday I* **1983**, *79*, 1109, 1123. *Aust. J. Chem.* **1981**, *34*, 1785. *Thermodynamics of Sea Water as a Multicomponent Electrolyte Solution*: Marcel Dekker: New York, 1976. Leyendekkers, J. V.; Hunter, R. J. *J. Phys. Chem.* **1977**, *81*, 1657 and references cited therein.

[16] (a) Harned, H. S.; Owen, B. B. *The Physical Chemistry of Electrolyte Solutions*; Reinhold: New York, 1958. (b) $\bar{K}^0$ is obtained from linear extrapolation of apparent molal compressibility and ϕ_K as a function of concentration to zero concentration in dilute range. Constants S_1 and S_2 are obtained in a similar fashion. By using the constants listed in Table 1, the densities and sound velocities of the given salt–solvent systems can be accurately reproduced with an agreement of 50 ppm and 0.71 m s^{-1}, respectively, when compared to experimental data measured by pycnometer (for density) and interferometer (for sound velocity) at a bath temperature remaining constant to within 0.5 K. Density and sound velocity yield specific volume and compressibility at a given concentration, see: ref 16a. For data see: Lobo, V. M. M.; Quaresma, J. L. *Literature Data on Thermodynamic and Transport Properties*; Univ. of Coimbra Press: Coimbra Port, Portugal, 1985; Vol. 2, 1096 pp.

[17] (a) Lobowitz, J. L., Helfand, E.; Praestgaard, E. *J. Chem. Phys.* **1965**, *43*, 774 and references cited therein. (b) Kumar, A. *J. Am. Chem. Soc.* **1993**, *115*, 9243 and also see ref 14. (c) For additional data see ref 11 and Pocker, Y.; Buchholz, R. F. *J. Am. Chem. Soc.* **1970**, *92*, 2075 and 4033. Gmehling, J.; Rasmussen, P.; Fredenslund, A. *Ind. Eng. Chem. Process Des. Dev.* **1982**, *21*, 118.

[18] Marcus, Y. *Ion Solvation*; John Wiley: New York, 1986.

Table 1. Values of Constants Used in the TTG Equation for the Calculation of Internal Pressure (P_i) in $LiClO_4$ Solution in Several Solvents[16]

constants	diethyl ether LPDE	acetone LPAC	ethyl acetate LPEA	tetrafuran LPTF
B_T (bar)	969	2097	1290	1753
a_0	0.127	0.142	0.201	0.153
$a_1 \times 10^2$	−0.715	−2.24	−4.11	−3.58
$a_2 \times 10^3$	−1.64	−5.61	−7.20	−8.00
V_s ($cm^3\ g^{-1}$)	1.4132	1.2684	1.1178	1.1310
ϕ^0_E ($cm^3\ mol^{-1}\ K^{-1}$)	0.325	0.288	0.272	0.239
$\alpha_s \times 10^3$ (K^{-1})	1.603	1.423	1.342	1.142
$S_E \times 10^3$	8.03	6.13	6.70	4.20
P_i (kbar) of pure solvents	3.385	3.405	3.376	4.365

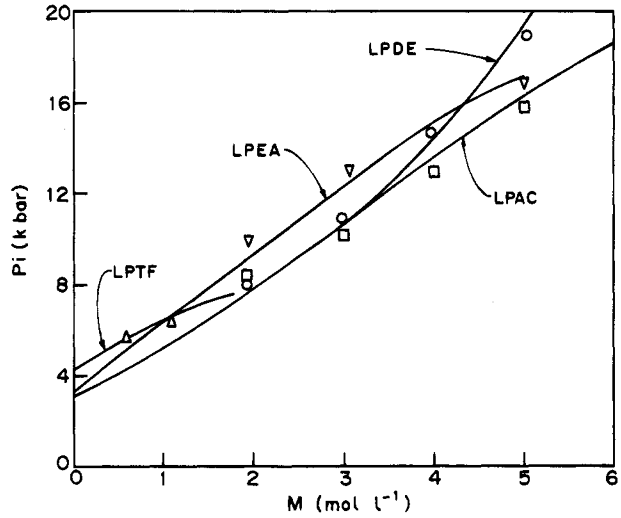

Figure 1. Internal pressure, P_i, as a function of concentration M for the solutions of LPDE, LPAC, LPEA, and LPTF. Lines are calculated by the TTG model; points from the SPT model. (○) LPDE; (□) LPAC, (▽) LPEA, (△) LPTF.

Table 2. Constants of Eq 5 for Calculating Effective Internal Pressure, $P_{i,eff}$ (bar), as a Function of Molarity, M, for Several Solvent Systems

system	q_0	q_1	q_2	q_3	σ (bar)
LPDE	1470	218.2	26.2	–	5
LPEA	2130	−39.5	–	–	11
LPEA	2229	431.3	−68.6	–	20
LPAC	1645	357.4	−33.7	–	30
MPAC	2316	2205	−468.5	–	58
BPAC	2934	−1383	1881	−421.7	57
SPAC	482.1	489.2	117.8	−19.5	22

is the effective internal pressure of a solution, which is caused by the addition of salt in a pure solvent. Constants q_0–q_3 are listed in Table 2 along with the standard deviations of fit.

2. Activation Volume. Activation volume $\Delta V^{\ddagger}$ data yield valuable information on the kinetics of reaction.[13] The $\Delta V^{\ddagger}$ can be obtained by the use of liquid phase nonideality calculations, besides high-pressure kinetics.[13b] In the method used in our work, activity coefficients were deployed to yield liquid phase nonidealities of components. We used a well-known model called a Universal Functional Group contribution model abbreviated as UNIFAC,[19] where the interactions between cation, anion, and their individual and mutual interaction with solvents are explicitly considered by the extended Debye–Hückel model. In order to check the reliability of this method, we calibrated the sets of calculations for three different reactions in different solvents. In Table 3 are listed the compounds used in the present work. The D–A reactions chosen for calibrating calculations with known kinetic data are (a) reaction of **1** and **2** in aqueous LiCl,[6] (b) **3** and **4** in LPDE,[8c] and (c) **12** and **13** in LPAC.[8c] Our calculated rate constants are in excellent agreement with the reported values yielding an average percent deviation, δ, for these reactions to be 3%. The δ values for these reactions are plotted in Figure 2 over a range of salt concentrations in solvent media.

The activation volume, $\Delta V^{\ddagger}$, for a reaction can easily be calculated[12,20,21] from the rate constant (ln k) in conjunction with $P_{i,eff}$, treating effective internal pressure coordinates equivalent to external pressure.

Results and Discussion

1. Cantharidin Synthesis. As noted earlier, cantharidin (**5**) was synthesized by the reaction of **6** with **7** under 15 kbar external pressure. In fact, as shown by our calculations in Figure 1, P_i the values induced by 5 M LPDE, LPAC, and LPEA are significantly high and comparable to the externally applied pressure. As a matter of fact, internal pressure acts like an external ultrahigh pressure and influences the rate of D–A reactions in the same direction as the external pressure.[12] Total effective internal pressures, for example, in a 5 M LPDE solution are 20 and 16 kbar, respectively. Grieco[3] noted that the same reaction could be realized with comparable ease in LPAC and LPEA. The reaction rate, however, was sluggish in LPTF. To explain this, we calculated the rate constants, k, in all the above solvents. In Figure 3 these values in the form of ln k are plotted against $P_{i,eff}$, where we note that the curves for LPDE, LPAC, LPEA, and LPTF fall close to each other or almost superimpose. For LPTF, however, due to the solubility limit of LP in TF (~1.6 M), a limited internal pressure (~7.5 kbar) was generated. The $\Delta V^{\ddagger}$ values for this reaction as calculated in our work are −26.3, −26.5, −26.9, and −26.0 $cm^{-3}\ mol^{-1}$ in LPDE, LPAC, LPEA, and

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(19) (a) There are several versions and modifications of the UNIFAC model available (for summary see e.g. Kumar, A. *Sep. Sci. Technol.* **1993**, *28*, 1799. We employed the calculational procedure given in Kikic I.; Fermegha, M.; Rasmussen, P. *Chem. Eng. Sci.* **1991**, *6*, 2775. In this method, a modified Debye–Huckel term is added to concentration independent UNIFAC terms. This term accounts for interactions between ions of salt and solvent. (b) For computation see: Hirata, M.; Ohe, S.; Nagayama, K. *Computer Aided Data Book of Vapor Liquid Equilibria*; Kodansha Ltd., Elsevier Sci. Pub. Co.: Tokyo, 1975. (c) For extensive tabulations of the values of group contributions see: *Models For Thermodynamic and Phase Equilibrium Calculations*; Sandler, S. I., Ed.; Marcel-Dekker Inc.: New York, 1993; Chapter 4. (d) For the values of parameters like dielectric constants of solvents and ionic radii, see ref 18.

(20) (a) Eckert, C. A. *Annu. Rev. Phys. Chem.* **1972**, *23*, 249. (b) Backman, C.-M.; Claesson, S.; Szwarz, M. *Trans. Faraday Soc.* **1970**, *66*, 3061.

(21) (a) This procedure of fitting $\Delta V^{\ddagger}$ data has been successfully attempted elsewhere. See: e.g. ref 13a and 13b. Another method to calculate $\Delta V^{\ddagger}$ is due to Benson, J. W.; Berson, A. *J. Am. Chem. Soc.* **1962**, *84*, 152, where the Tait expression is used. Extrapolation to normal pressure and some inconsistent mathematical derivations render this approach to be less correct than the method given in refs 13a and 13b. (b) The activation volume, in fact, is combination of solvation and other structural effects and is dependent on the reactants and reaction environment. See: refs 13, 22.

Table 3. Entry Numbers of Compounds

no.	compound	no.	compound
1	anthracene-9-carbinol	11	2,6-dimethylbenzoquinone
2	*N*-ethylmaleimide	12	2-3-dimethylbutadiene
3	9,10-dimethylanthracene	13	1,4-naphthoquinone
4	acrylonitrile	14	(*E*)-1-phenyl-4-[2-[(3-methyl-2-butenyl)oxy]benzylidene]-5(4*H*)-pyrazolone
5	cantharidin	15	*trans,trans*-1,4-diphenylbutadiene
6	furan	16	4-phenyl-1,2,4-triazoline-3,5-dione
7	2,5-dihydrothiophene-3,4-dicarboxylic acid anhydride	17	1,3-diphenylisobenzofuran
8	cyclopentadiene	18	styrene
9	methylmaleic anhydride	19	1-phenylallyl chloride
10	*trans*-piperylene	20	cinnamyl chloride

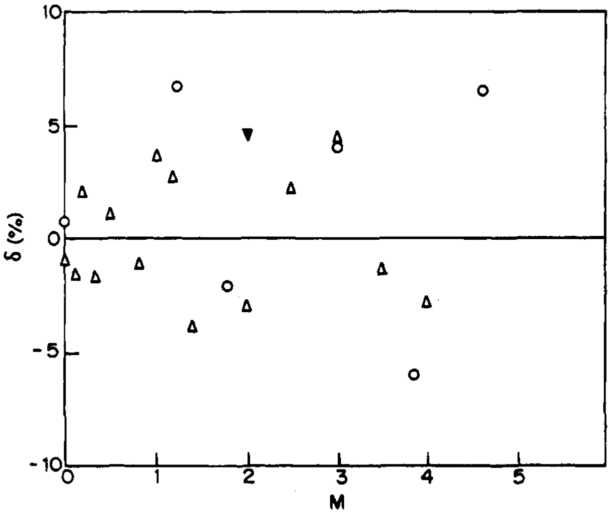

Figure 2. Plots of average percent deviation (δ) at several concentrations (*M*) for reactions (a) (▼) **1** + **2** in aqueous LiCl, (b) (○) **3** + **4** in LPDE, (c) (△) **12** + **13** in LPAC. δ is calculated from the differences of reported and calculated rate constants.

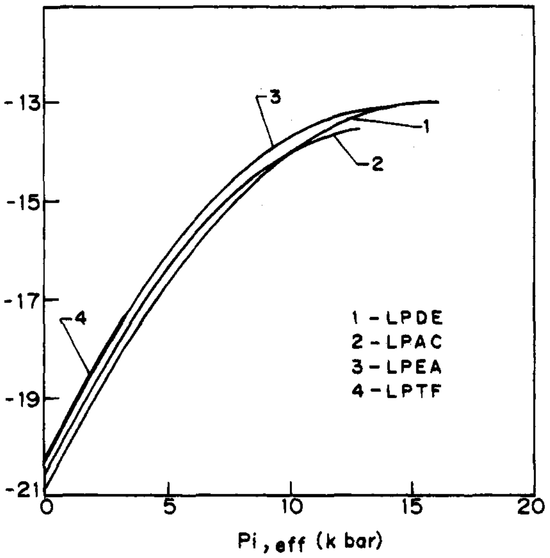

Figure 3. Plots of rate constants against effective internal pressure, $P_{i,eff}$ for the reaction of **6** and **7** leading to cantharidin in LPDE, LPAC, LPEA, and LPTF.

LPTF, respectively, yielding an average $\Delta V^{\ddagger}$ of -26.4 ± 0.3 cm^3 mol^{-1}. The D–A reactions in general are accompanied[13,22] by a negative $\Delta V^{\ddagger}$ which is also evident in this case. The negative $\Delta V^{\ddagger}$ indicates compact transition state. Now application of internal pressure or pressure on the negative $\Delta V^{\ddagger}$ would enhance the reaction rates, which is a true case, as seen in the reaction leading to cantharidin in LPDE-like solvent media. Thus, the use of LP-containing solvents in appropriate concentrations, could bring the reactants together in order to realize the reaction, which was, otherwise, not possible under ambient conditions.

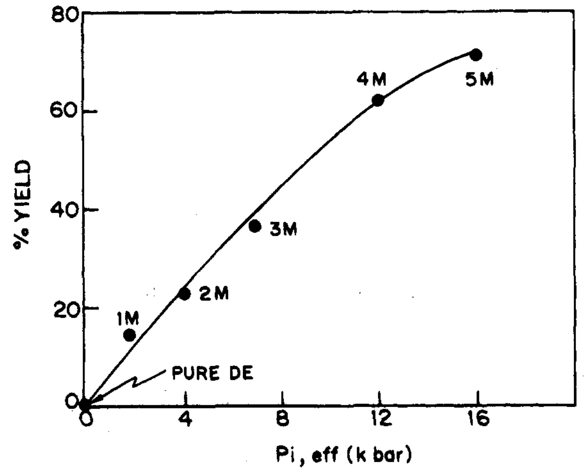

Figure 4. Percent yield plotted against $P_{i,eff}$ showing the effect of LPDE concentration for the synthesis of cantharidin.

As evident from Figure 3, ln *k* varies sharply up to 4 M of LP-solvent systems, but then starts to taper off.[23] A plot between the yields reported for this reaction and our $P_{i,eff}$ values, given in Figure 4, support the present results. The shapes of the ln *k* versus $P_{i,eff}$ curve in Figure 3 is almost identical to the curve plotted between the yield versus $P_{i,eff}$ in Figure 4 for the synthesis of cantheridin in LPDE. Our results both on the $\Delta V^{\ddagger}$ and $P_{i,eff}$ for the four solvent systems confirm the experimental observations[3] and thus help us in understanding the substitution of external pressure requirements by a simple solvent like LPDE. Other solvents, LPAC and LPEA, offer similar advantages like that of the LPDE system.

Besides the above example, some D–A reactions are reported to be accelerated in LPDE. These reactions,[1] otherwise, are completed in longer time. For example, reactions of **8** and **9** can be performed in 3 h with 90% yield in 5 M LPDE as compared to 94% yield after 24 h at 60 °C without LPDE. The $\Delta V^{\ddagger}$ for this reaction is -11.2 ± 0.8 cm^3 mol^{-1}. Another reaction, for illustration, involving **10** and **11**, which in water yields >20% after 24 h, can now be sped up to undergo reaction in 15 min with 80% yield, a remarkable achievement with LPDE. The $\Delta v^{\ddagger}$ for this reaction is -18.5 ± 0.8 cm^3 mol^{-1}.

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[22] McCabe, J. R.; Eckert, C. A. *Acc. Chem. Res.* **1974**, *7*, 251.

[23] The leveling off in the internal pressure values at higher solute concentrations was pointed out by Breslow (ref 5), where he indicated that solubility of solute in a solvent played a key role in deciding the internal pressure effects near saturation. I gratefully acknowledge a throughtful reviewer for his comment on the interesting observation noted in Figure 3 and its relevance with the Breslow remarks.

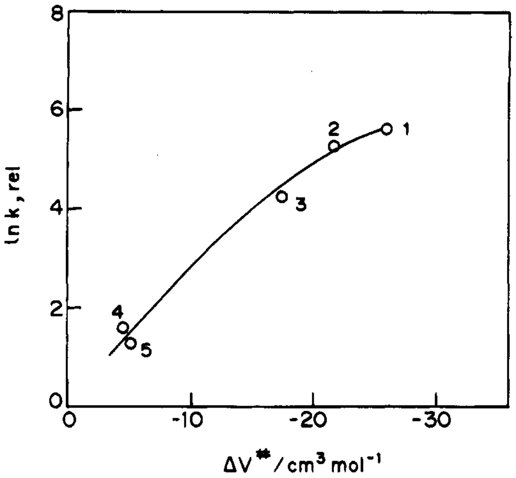

Figure 5. Plot of ln $k_{\rm rel}$ against $\Delta V^{\ddagger}$ for reactions (1) **6** + **7**, (2) **12** + **13**, (3) **4**, (4) **15** + **16**, and (5) **12** + **17** in a 3 M LPAC solution.

Considering the value of $P_{\rm i,eff}$ at 5 M LPDE and $\Delta V^{\ddagger}$ of the reaction, one can explain the of rate acceleration in these reactions.

2. Effect of Other Perchlorates. As discussed, several D–A reactions were kinetically investigated for their rate enhancement in the presence of MPAC, BPAC, LPAC, and SPAC solvent media.[8b] The results were discussed in terms of nature (electrophilic, nucleophilic, or nonspecific) of solvents and their relationship with cationic activity. We discuss the rate enhancement of a few D–A reactions first in LPAC alone and then of a single reaction in MPAC, BPAC, LPAC, and SPAC. For the purpose of illustration, we studied the reactions of **6** + **7**, **12** + **13**, **14**, **15** + **16**, and **12** + **17**, all in LPAC, where the $\Delta V^{\ddagger}$ values estimated from the present method were −26.4, −21.9, −16.6, −4.3, and −4.8 cm^3 mol^{-1}, respectively. The effective internal pressure, $P_{\rm i,eff}$, for example, by a 3 M LPAC solution being constant at ~7204 bar, enhances the rates of reactions depending upon the magnitude of $\Delta V^{\ddagger}$. The rate enhancements for reactions of **6** + **7**, **12** + **13**, **14**, **15** + **16**, and **12** + **17** are in the same order of decreasing $\Delta V^{\ddagger}$, indicating that higher accelerations are accomplished by more compact transition states at high internal pressure conditions. A plot between ln $k_{\rm rel}$ (relative rate constant $k_{\rm rel}$ = rate constant in presence of an additive divided by that in pure solvent) and $\Delta V^{\ddagger}$ for these reactions yields a smooth curve (Figure 5) at constant concentration, or constant $P_{\rm i,eff}$ of LPAC solution. Assuming that, for instance, the values of $\Delta V^{\ddagger}$ at constant pressure can be an indication of the reaction rates as a first approximation,[21b] an extrapolation of the curve in Figure 5 leads to zero rate at $\Delta V^{\ddagger} \rightarrow 0$. At positive $\Delta V^{\ddagger}$ values, the decrease in the rates will be obtained,[12] as clearly visible in Figure 5.

It is interesting to note that different rate enhancements for the same reactions are obtained at a specified concentration of several perchlorate–AC solvent systems. For an example, the reactions of **12** and **13** in MPAC, BPAC, LPAC, and SPAC at 1.4 M (maximum concentration of MP available in AC) yield the relative rate constants of 5.8, 4.32, 2.68, and 1.96, respectively. A solution of 1.4 M of MPAC, BPAC, LPAC, and SPAC each generate the $P_{\rm i,eff}$ of 6250, 5001, 3253, and 1809 bar, respectively. In Figure 6 we plot the ln $k_{\rm rel}$ for the reaction of **12** and **13** in presence of the above solvent systems as a function of $P_{\rm i,eff}$ at constant M = 1.4. The plot depicts the decreasing order of rate enhancement with decreasing $P_{\rm i,eff}$. This demonstrates the utility of internal pressure in explaining the rate enhancement. Further, the $\Delta V^{\ddagger}$ value for this reaction as determined by this procedure outlined above is −21.9 ± 0.6 cm^3 mol^{-1}, which confirms that the higher the internal pressure, the greater the rate enhancement, provided the $\Delta V^{\ddagger}$ is negative. Most of the D–A reactions are reported in LPDE or to some extent in LPAC, although the internal pressure generated by LPAC are lower than those by MPAC. The reason for avoiding the use of an MPAC kind of salt may be due to the poor solubility of MP in AC or other organic solvents. On the other hand, LP is highly soluble in the solvents like DE, AC, EA, etc. and thus likely to offer more efficient solvent systems.

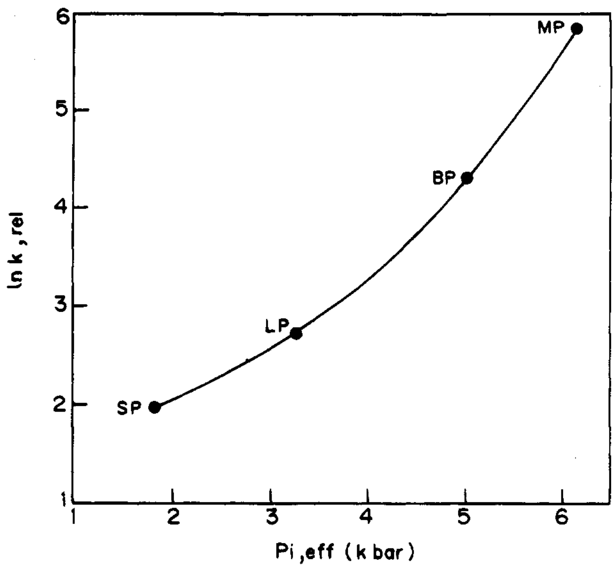

Figure 6. ln $k_{\rm rel}$ as a function of $P_{\rm i,eff}$ induced by MP, BP, LP, and SP in acetone for the reaction of **12** and **13**.

3. Concept of Internal Pressure Not Applicable to Some D–A Reactions. Initial suggestion of the role of internal pressure was not found to be applicable on reactions like **17** with **18**, when LPDE was employed as a reaction media.[8c] We decided to analyze the reason behind such an observation that such a high $P_{\rm i,eff}$ of 5 M LPDE was unable to drive this reaction. For this, we calculated $\Delta V^{\ddagger}$ as $-0.98 \approx -1$ cm^3 mol^{-1}, which is a very high value as compared to other cases. It was, thus, not surprising that very high internal pressure, when coupled with the above given $\Delta V^{\ddagger}$ value, failed to explain the influence of LPDE on the above reaction. Higher $\Delta V^{\ddagger}$ in such types of reactions may be ascribed[13,20a] to the fact that the sum of partial molar volumes (obtained from volume or density measurements of reactant mixture) almost cancels out the transition state volume, yielding a high value of $\Delta V^{\ddagger}$ (close to zero). Since the resultant $\Delta V^{\ddagger}$ is either zero or very high (compared to negative scale), no appreciable rate enhancement in these reactions is noticed.

Similarly, the D–A reaction between **3** and **4** in LPDE was explained in terms of the Lewis acid catalysis by Li$^+$ ion.[8c] The rate enhancement was about 9 times at 4.5 M LPDE as compared to pure DE. If we plot the ln $k_{\rm rel}$ as a function of $P_{\rm i,eff}$, a smooth nonlinear curve (Figure 7) is obtained, which is contrary to the linear variation noted in the aqueous D–A reaction.[14] The difference in shapes of the curves may primarily be due to the fact that the nature of interactions of salt with nonaqueous

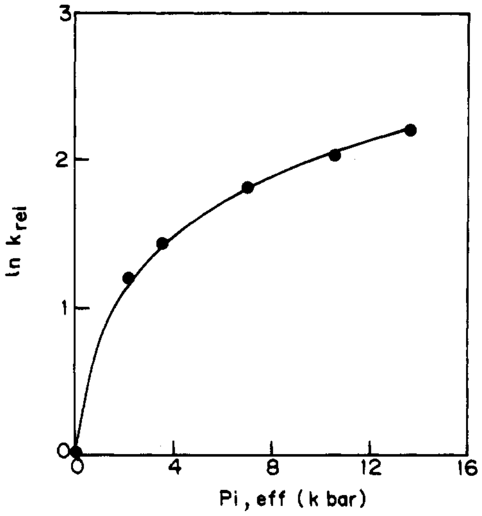

Figure 7. Variation of ln k_{rel} with respect to $P_{i,eff}$ for the reaction of **3** and **4** in LPDE.

and aqueous media are different.[16a] We also mention that in the case of the aqueous reaction, the reaction rates were noted to be linear with respect to internal pressure of different salts at a constant concentration of 2 M, whereas in the present study, the effect of varying concentrations of salt, i.e. LP in DE, is under investigation. Thus, the comparison of the shapes of curves does not appear to be meaningful at least at this state of work. Although Lewis acid catalysis by Li^+ has been stated to be the reason of the above rate acceleration,[8c,24] we can also analyze this by $\Delta V^{\ddagger}$. After confirming the rate constants by our method to within ±4% agreement, the $\Delta V^{\ddagger}$ is estimated as -9 cm^3 mol^{-1}, which is much higher than those noted for other D–A reactions, where enhancement is more pronounced. In fact, the reaction rate at ~1 M LPDE increases very sharply indicating the built up of a very high effective internal pressure of ~5300 bar by the addition of LP in DE making a 1 M solution.[25] But since $\Delta V^{\ddagger}$ is not very low, the reaction rates are not of very high magnitudes. Thus, internal pressure alone cannot describe the rate enhancement. Another vital property for such an explanation is to examine the activation volume of the reaction.

4. Impact of LPDE Kind of Solvents on Non-D–A Reactions. Since in our explanation we have stressed the need of $\Delta V^{\ddagger}$ and P_i, it is imperative to examine some non-D–A reactions, where the rate enhancements are in presence of LPDE kind of solvents. For illustration, we calculated the $\Delta V^{\ddagger}$ and $P_{i,eff}$ values for the isomerization reaction[10] of **19** to **20** in several LP-based solvents, i.e. LPDE, LPTF, LP–diethyl carbonate (LPDC), LP–propylene oxide (LPPO), and LP–dimethylformamide (LPDMF). The calculated $P_{i,eff}$ values in various solvents support the experimental results of Pocker[10] regarding a direct relationship between ln k_{rel} and $P_{i,eff}$. For example, in a 3 M LP solution (chosen for the ease of comparison) in several solvents, a plot of ln k_{rel} against $P_{i,eff}$ in different several solvents is shown in Figure 8. As evident from the plot, the rate enhancement can be easily described by the effective internal pressure generated by LP solutions in different solvents. The $\Delta V^{\ddagger}$ for this reaction is -80.3 cm^3 mol^{-1}, indicating that a tremendous rate enhancement occurs in these solvents, subject to the magnitude of internal pressure. It is also evident from Figure 8 that LPDE is the most efficient solvent system while the LPDMF is least productive.[26]

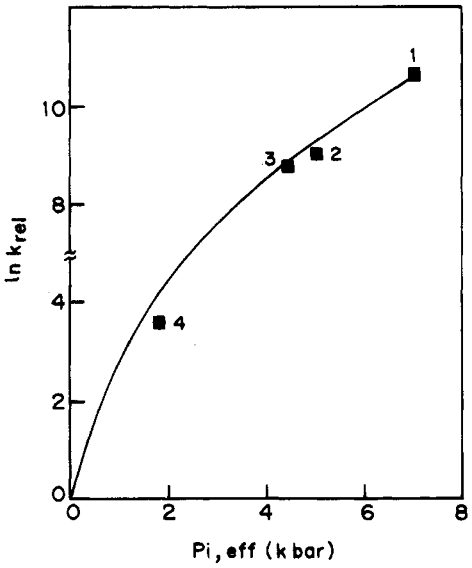

Figure 8. Relationship between ln k_{rel} and $P_{i,eff}$ of several LP-based solvent systems for the isomerization reaction of **19** to **20**. (1) LPDE, (2) LPDC, (3) LPPO (4) LPDMF. Solvent systems are at 3 M.

Conclusions

After a careful analysis of experimental data with the tools of thermodynamics and solution chemistry, we have attempted to attend the problem of rate enhancement in the D–A reactions with salt–nonaqueous solvent media from an entirely different angle. Important points of summary are:

1. Internal pressure generated by the salt–solvent (nonaqueous) media coupled with the volume of activation can explain the variations in reaction rates.

2. Higher internal pressure with lower activation volume will enhance the reaction rate with a higher degree than with the higher activation volume keeping the internal pressure constant.

3. Arguments presented above explain both the effect of a single solvent system on several D–A reactions and the effect of several solvent systems on a single D–A reaction.

4. More significantly, this approach is not contradictory to the explanations, proposed on the basis of Lewis acid catalysis. As a matter of fact, arguments presented in our approach offer an alternate possible explanation among others[7-10] for the description of kinetic profiles of Diels–Alder reactions in the salt–nonaqueous solvent media. We are, currently studying the roles of several potential salt–solvent systems on the D–A reactions for both the cases of rate enhancement and decrease to gain further insight into theoretical aspects. These results will be presented in a future communication.

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(24) We do not disagree with the explanation based on catalysis, but wish to examine the problem from the thermodynamic point of view.

(25) e.g. Herbrandson, H. F.; Neufeld, F. R. *J. Org. Chem.* **1966**, *31*, 1140.

(26) Discussion on the nature of these solvents in the presence of LP and its influence on the reaction is dealt in greater detail in ref 10, and our analysis receives support by their experimental data.