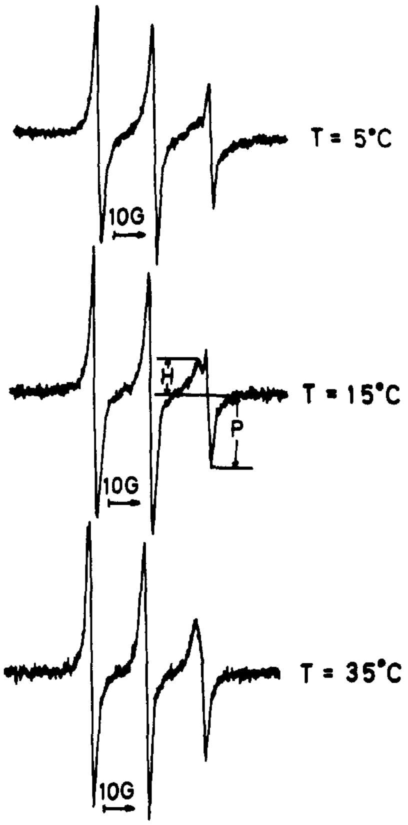

Figure 2. ESR spectra of **2** (2.72×10^{-4} M) in the sonicated aqueous solution of **1** (5.39×10^{-3} M).

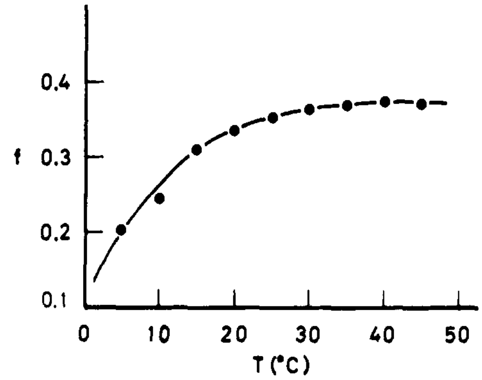

Figure 3. Correlation of spectral parameter f for **2** with temperature; measured in the sonicated aqueous solution of **1**.

(JEOL JES-ME-3, X-band); 4-(cyclohexylacetoxyl-2,2,6,6-tetramethylpiperidine-1-oxyl (**2**)[10] was used as a spin probe. The ESR spectral change with temperature is shown in Figure 2; signal P arises from **2** dissolved in the aqueous region and signal H is due to **2** placed in the hydrophobic interior of bilayer membrane. The spectral parameter, f, equal to $H/(H + P)$, approximately shows the fraction of the spin-labeled probe distributed to the membrane interior. Such a phenomenon was observed for the phospholipid bilayer system by using 2,2,6,6-tetramethylpiperidine-1-oxyl.[9] In Figure 3 is plotted f value against temperature; the f value tends to decrease below 20 °C, and hence the phase transition for the vesicular assembly of **1** must occur below 20 °C.

Our present amphiphile, as a modification of the phospholipids, may form the bilayer aggregates similar to those observed for the naturally occurring lipids. Single-compartment vesicles are quite stable in aqueous media at room temperature (above 20 °C) owing to the hydrogen belt effect provided by an amino acid residue. Since the present vesicles involve asymmetric centers in the hydrophobic region, they may provide an asymmetric recognition site for various guest molecules.

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Raman Phonon Spectroscopy of Solid-State Reactions: Thermal Rearrangement of Methyl *p*-Dimethylaminobenzenesulfonate in Solid State

Sir:

In this communication we propose a new approach utilizing laser Raman phonon spectroscopy that can be used to understand details of reaction dynamics in solids. The use of Raman spectroscopy itself in investigating solid-state reactions is not new. The novel feature of the present approach is the use of phonon spectra to derive the reaction mechanism. It is also shown that the new approach leads to a concept of phonon assisted reactions in solids. Such information is not readily available from X-ray diffraction techniques used widely in the past[1-9] to study organic solid-state reactions. We apply the method to investigate the thermal rearrangement reaction of methyl *p*-dimethylaminobenzenesulfonate (MSE) into *p*-trimethylammonium benzenesulfonate zwitterion (ZWT).

Phonons are low-frequency intermolecular vibrations of a crystal. The phonon spectral pattern contains both structural and the dynamical information. First, from the structural point of view, the Raman phonon spectra can be used to derive the mechanism of the reaction: (i) homogeneous where a solid solution of the reactant and the product forms; (ii) heterogeneous, in which the product forms its own lattice and no solid solution results. Our previous study of phonon spectra in organic solid solutions reveals that the phonon bands exhibit an amalgamation behavior.[10,11] The amalgamation behavior implies that the phonon frequencies change monotonically as the concentration of solid solution is changed. In the case where no solid solution forms, the unchanged phonon bands of the two compounds superimpose. Furthermore, the short-range character of the interactions that determine the phonon motions in molecular solids make these bands ideal for distinguishing between a truly random solid solution and segregated

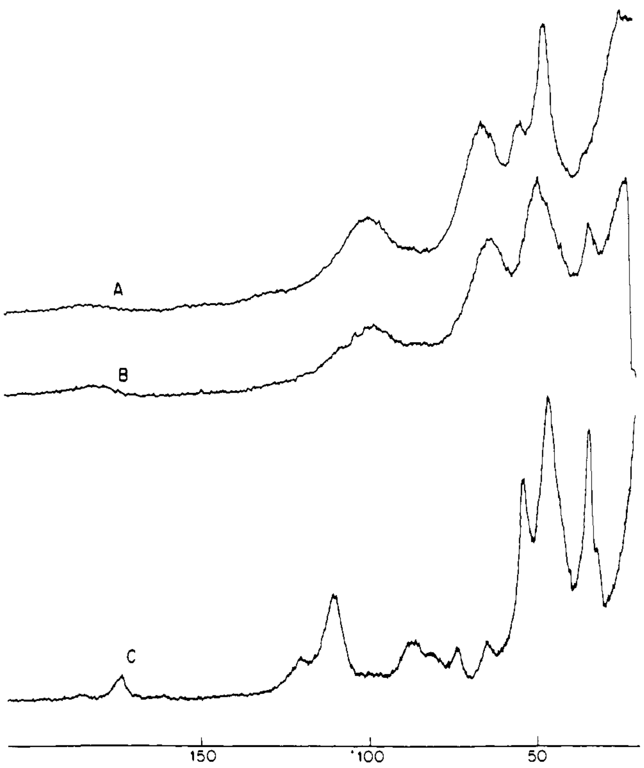

Figure 1. Raman phonon spectra at −152 °C of (A) MSE, (B) partially rearranged (~40%) MSE, and (C) ZWT.

microscopic domains.[10] Thus, the phonon amalgamation criterion can conveniently be used to distinguish solid solutions on molecular scale (truly homogeneous reactions) from randomly distributed microscopic aggregates. Such information is not easily available from optical or ordinary X-ray diffraction methods which provide information on a space averaged structure. Though a detailed careful analysis of diffuse X-ray scattering[12] may provide information regarding random solid solution, the method has not widely been applied to molecular solids. The reason is that diffuse scattering study[12] requires more than just the routine method of X-ray diffraction.

From the dynamical point of view, reactions can be phonon assisted. As the large amplitude phonon motions in the solids are analogous to the molecular collisions in the gas phase, softening of a phonon mode may enhance a thermal reaction in the solid. Mode softening is a term which implies that, as the temperature is raised, the phonon frequency shifts toward a zero value and the phonon becomes overdamped (i.e., the spectral transition due to the phonon shows a rapid broadening). Although the concept of mode softening has previously been used[13] to explain phase transitions in solids, its application to solid-state reactions is new. The softening of a specific phonon mode can result in a large amplitude displacement along this phonon coordinate whereby the reactants are brought close enough for the reaction to occur. The present work provides the first evidence which links a thermally enhanced solid-state reaction with phonon mode softening.

The thermal rearrangement reaction of MSE into ZWT is greatly enhanced in the solid state compared with that in the solution.[14,15] The reason is favorable stacking of the molecules in a chain in the crystal[14] which facilitates the transfer of methyl group from the oxygen atom of one molecule to the nitrogen atom of the adjacent molecule along the chain. For the study, the Raman spectra of the samples of MSE and ZWT, prepared employing the reported procedure,[14] were recorded on a Spex Model 14018 double monochromator using 5145-Å line of a Coherent Radiation argon ion laser as the excitation source. Our study of phonon spectra reveals a strong orientation dependence and care had to be taken in selecting the orientation such that meaningful correlation of the phonon spectra of the reactant and the product could be made. Figure 1 shows the phonon spectra of MSE, a partially rearranged sample, and ZWT. The spectrum of the partially rearranged sample, although broader than that of MSE and ZWT, can be seen to contain phonon bands of the reactant and the product unshifted in frequency. Spectrum B clearly shows the ~33-cm^{-1} phonon of the product (spectrum C) unshifted in frequency. The broadening observed in spectrum B may be due to disorder produced when the molecular relaxation occurs to form the product lattice. No phonon amalgamation in any partially converted sample is observed. This result shows that the thermal rearrangement of MSE into ZWT proceeds by a heterogenous transfer mechanism. This result is consistent with the mechanism proposed by Sukenik et al.[14] which predicts a long-range cooperative rearrangement, rather than a local rearrangement.

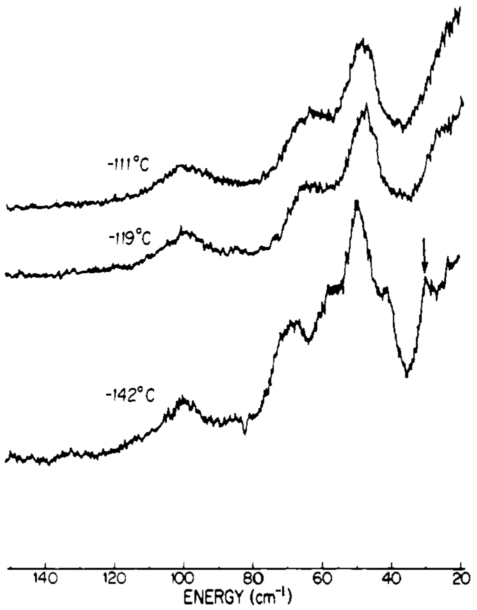

Figure 2. The temperature dependence of Raman phonons of MSE. The soft mode is indicated by an arrow.

Figure 2 shows the Raman phonon spectra of MSE at different temperatures. It can be seen that the transition at 27 cm^{-1} (163 K) shifts to a lower frequency, broadens, and finally merges into the Rayleigh wing as the temperature is raised. We do not believe that this observation is merely due to a rise in Rayleigh background. We have investigated, using identical experimental conditions, several chemically stable systems which exhibit very low frequency modes ($\leq$20 cm^{-1}) and have found them behaving differently.[11] We, thus, conclude that the observed temperature dependence of the 27-cm^{-1} mode of MSE is indicative of a mode softening and is consistent with our hypothesis that mode softening may play an important role in the thermal reactions.

Further studies utilizing MSE-d_3 and experiments up to liquid helium temperatures are underway to investigate details of the mode softening as well as the role of methyl motions in determining the reactivity.

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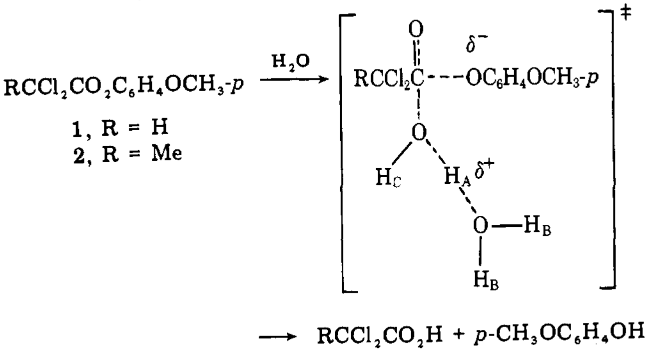
Hydrolysis of Two Acyl Activated Esters in Water-Rich 2-*n*-Butoxyethanol-Water Mixtures. Effects of Hydrophobic Interactions on Enthalpies, Entropies, and Heat Capacities of Activation[1]

Sir:

Hydrophobic association in aqueous media is of fundamental importance in (bio)chemistry, but the origin of the phenomenon is still not well understood.[2] For many organic reactions in typically aqueous (TA) solutions,[3] there is now ample evidence that the peculiar behavior of thermodynamic activation parameters (such as $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, $\Delta V^{\ddagger}$, and $\Delta C_p{}^{\ddagger}$) has its origin predominantly in effects due to hydrophobic interactions.[4] Herein we report the observation of large, positive heat capacities of activation ($\Delta C_p{}^{\ddagger}$) for the neutral hydrolysis of *p*-methoxyphenyl dichloroacetate (**1**) and 2,2-dichloropropionate (**2**) in 2-*n*-butoxyethanol (2-BE)-H_2O at n_{H_2O} = 0.98. These *positive* maxima contrast sharply with the *negative* extrema in $\Delta C_p{}^{\ddagger}$ which are invariably conjoined with a variety of solvolyses (mainly of the S_N type) of neutral substrates in TA solutions.

The pH-independent pathway for hydrolysis of **1** and **2** involves a water-catalyzed nucleophilic attack of water on the ester carbonyl.[5] Recently, further support for this mechanism has been provided by the results of proton inventory studies[6] which show that three protons (H_A, H_B's) contribute to the overall isotope effect.



1, R = H
2, R = Me

Recent studies by Desnoyers et al.[7] of the binary system 2-BE-H_2O have revealed that the concentration and temperature dependence of the apparent molal heat capacity and the apparent molal volume are those expected for a TA solution. In fact they are rather similar to those of *t*-BuOH-H_2O, but the various transitions are more pronounced. The sharp peaks in the thermodynamic quantities at about n_{H_2O} = 0.98 are even reminiscent of those of a pseudomicrophase transition and seem to be consistent with a clathrate model for hydrophobic hydration and interaction.[7] In view of these challenging solvent properties, we have measured rates and thermodynamic activation parameters for the neutral hydrolysis of **1** and **2** in this medium (Table I). Notice that $\Delta G^{\ddagger}$ increases continuously with decreasing n_{H_2O} but that $\Delta H^{\ddagger}$ and $-T\Delta S^{\ddagger}$ exhibit mirror-image behavior and pass through extrema near n_{H_2O} = 0.98. Similar behavior is found for hydrolysis in *t*-BuOH-H_2O,[5c,8] but there is one surprising difference. Whereas plots of $-\ln (kT^{-1})$ vs. T^{-1} show straight lines (with slope $\Delta H^{\ddagger}R^{-1}$) in pure water and at n_{H_2O} = 0.95, there is a strong curvature[9] in these plots (portrayed for **2** in Figure 1) at the "magic mole fraction" in 2-BE-H_2O (n_{H_2O} = 0.98). Analysis in the usual way[10] yields large and *positive* heat capacities of activation: for **1**, $\Delta C_p{}^{\ddagger} = 224 \pm 51$ cal deg^{-1} mol^{-1}, and for **2**, $\Delta C_p{}^{\ddagger} = 342 \pm 51$ cal deg^{-1} mol^{-1}. These changes of $\Delta C_p{}^{\ddagger}$ with n_{H_2O} are *opposite* in sign to those found previously for a number of solvolytic reactions (largely S_N1 or S_N2) in TA solutions.[10,11] Whatever the interpretation of the negative

Table I. Neutral Hydrolysis of **1** and **2** in 2-*n*-Butoxyethanol-H_2O Mixtures (25 °C)[a]

compd	n_{H_2O}	$k_{obsd} \times 10^5$, s^{-1}	$\Delta G^{\ddagger}$, kcal mol^{-1}	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, eu	temp range, °C
1	1.000	307	20.88	7.9	−44	25-48
1	0.995	235	21.04	7.6	−45	25-48
1	0.980	36.2	22.15	2.2[b]	−67[b]	20-48
1	0.950	4.67	23.36	10.4	−44	24-46
1	0.900	2.63	23.70	10.7	−44	25-48
2	1.000	115	21.46	7.8	−46	25-48
2	0.995	84.6	21.65	7.2	−48	26-48
2	0.980	6.19	23.20	0.8[c]	−75[c]	20-48
2	0.950	0.65	24.53	9.5	−50	30-45

[a] Determined in the presence of 6.0-10.0 × 10^{-3} M HCl to avoid hydroxide-ion catalysis. All rate constants pertain to water reactions since the solvolysis of **1** and **2** in 2-BE is extremely slow. [b] $\Delta C_p{}^{\ddagger}$ = 224 ± 51 cal deg^{-1} mol^{-1}. [c] $\Delta C_p{}^{\ddagger}$ = 342 ± 51 cal deg^{-1} mol^{-1}.

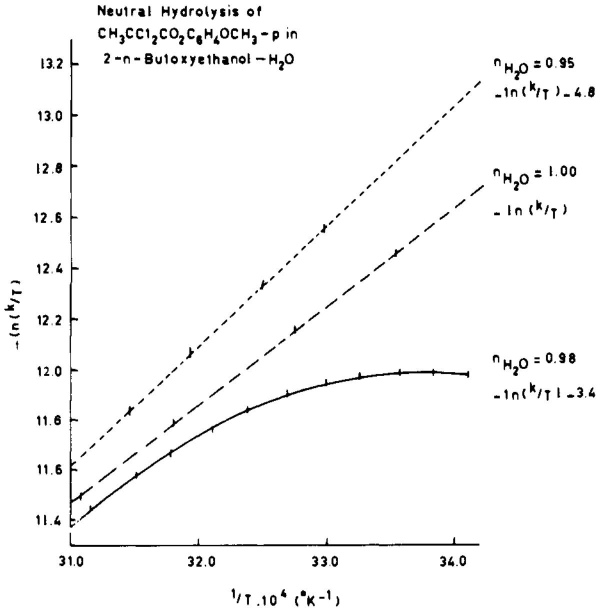


Figure 1. Plots of $-\ln (k/T)$ vs. $(1/T)$ for the neutral hydrolysis of **2** in 2-*n*-butoxyethanol-H_2O. The experimental error in $\ln (k/T)$ is indicated by the lengths of the vertical stripes.

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