hydrogen in the trisubstituted olefin setting. This correlation seems firm for trisubstituted olefins containing a vicinal methyl and hydrogen.[14]

Good synthetic routes are available for enynols of the type reported in this work: (1) reaction of an enyne with ethylene oxide in liquid ammonia[15] and (2) the palladium-catalyzed coupling of an alkenyl bromide with a terminal homopropargyl alcohol.[10] Thus, the group IV transition-metal–organoalane reagents provide promise for the selective synthesis of substituted dienols that may be useful in the synthesis of selected natural products and as components of Diels–Alder reactions.

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work. We also thank the Ethyl Corp. for a gift of TMA and the E. I. du Pont de Nemours and Co. and the National Science Foundation (PRM-8114795) for funds with which to purchase gas chromatographs.

Registry No. $Al(CH_3)_3$, 75-24-1; $TiCl_4$, 7550-45-0; (3*Z*)-4-methylhexa-3,5-dien-1-ol, 925-53-1; (3*Z*)-4,5-dimethylhexa-3,5-dien-1-ol, 87351-54-0; (3*Z*)-6,7-dimethylocta-5,7-dien-3-ol, 87351-55-1; hex-5-en-3-yn-1-ol, 28916-38-3; 5-methylhex-5-en-3-yn-1-ol, 1559-16-6; 7-methyloct-7-en-5-yn-3-ol, 87371-34-4.

---

(14) (a) For typical supporting data, see Breitmaier, E.; Haas, G.; Voelter, W. "Atlas of Carbon-13 NMR Data"; Heyden: London, 1979; compounds 119 and 120, (*E*)- and (*Z*)-3-methyl-1,3-pentadiene. (b) Reference 1.[c] Rand, C. L.; Van Horn, D. E.; Moore, M. W.; Negishi, E. *J. Org. Chem* **1981**, *46*, 4093.

(15) Croxall, W. J.; Van Hook, J. O. *J. Am. Chem. Soc.* **1954**, *76*, 1700.

Communications

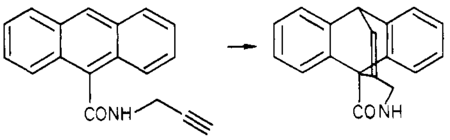
Vibrational Activation. 3. Effect of Solvent Density on the Rate of a Diels–Alder Reaction. Density as an Index of Porosity[1]

Summary: In a set of mixtures of tetraglyme and poly(ethylene glycol) monomethyl ethers, the rates of a Diels–Alder reaction vary linearly with solvent density, which in turn reflects the solvent's porosity because all the solvent molecules are built from the same units. We propose that the reaction goes faster in packed zones than in empty ones because translation of reactant molecules is impeded.

Sir: The vibrational activation theory[2] holds that bond-forming reactions are promoted by vibrational energy in the reactants and that high translational energy is detrimental; i.e., soft collisions are more likely to result in bond formation than are hard ones. High solvent viscosity, then, should promote bond-forming reactions. No conventional theory predicts this effect.[3]

With bimolecular reactions there is a problem in that the reactants cannot find each other if the viscosity is too high. Enzymes solve this problem by providing a microenvironment of high viscosity in which the reaction takes place rapidly, within a bulk medium of low viscosity that permits the reactants and products to come together and separate without hindrance. That is why enzymes need not only the few amino acids required at the active site but also the "ball of wax"—additional long polypeptide chains that are not involved in the chemistry but confer stiffness on the molecule as a whole. This question has aroused much speculation heretofore.[4]

The prediction that viscosity promotes bond-forming reactions was tested for two reactions and verified.[1] Both the Diels–Alder reaction (1) and the Claisen rearrangement of phenyl allyl ether (2) go faster as the solvent viscosity rises. This phenomenon cannot be accounted for by cage, polarity, or polarization effects.



(1)

It was recognized previously that macroscopic viscosity, as measured by the rate of fall of a heavy object, was but a crude measure of the microscopic viscosity experienced by individual molecules. What is needed, according to the theory, is an environment in which, like the cavity of an enzyme, translation is restricted so that collisions between reactants (in our special cases between two reacting sites within a single molecule) are soft rather than hard.

For further investigation, we used as a starting point the observation[1] that adding a small amount of polyethylene to Nujol markedly increased both the viscosity and the rate of reaction 1. It was apparent that there must be (ideally) two rates in this macroscopically homogeneous but microscopically heterogeneous solvent: a normal one for most of the molecules in the Nujol milieu and a high one for those in the polyethylene zones. In the new study, reaction 1 was run at 100 °C in mixtures of tetraglyme and poly(ethylene glycol) monomethyl ethers (PEGE's) of various molecular weights. The compositions of the mixtures were determined by experimentation to find the maximum attainable limits of solubility of the PEGE's of each molecular weight in tetraglyme at 100 °C. The data and results from three separate experiments are presented in Table I.[5]

---

(1) Part 2: Firestone, R. A.; Vitale, M. A. *J. Org. Chem.* **1981**, *46*, 2160.

(2) Firestone, R. A.; Christensen, B. G. *Tetrahedron Lett.* **1973**, 389.

(3) Leffler, J. E.; Grunwald, E.; "Rates and Equilibria of Organic Reactions"; Wiley: New York, 1963; pp 57 ff. Amis, E. S.; Hinton, J. F. "Solvent Effects on Chemical Phenomena"; Academic Press: New York, 1973; p 324.

(4) Luisi, P. L. *Naturwissenschaften* **1979**, *66*, 498 and references therein.

(5) The procedure used for the kinetic runs was exactly the same as that used for reaction previously.[1] Tetraglyme was freshly distilled. The PEGE samples, from Aldrich, were used as received. The water content of the PEGE of molecular weight 750, measured by azeotropic distillation with benzene, was <0.3%. Densities and viscosities were measured at 100 °C on pure solvent mixtures, i.e., without reactants or additives. Full-scale NMR spectra of all solvent mixtures, neat, showed no impurities. NMR spectra of product mixtures were spread out at 300 MHz and integrated by planimetry. We thank Dr. Byron Arison and Mr. Herman Flynn For the 300-MHz spectra.

Table I. Rate of Reaction 1 (66 h) vs. Solvent Density and Viscosity for Mixtures of Tetraglyme and PEGE's (All Experimental Data at 100 °C)

expt	PEGE %	PEGE M_r	density	η/η_0	k/k_0
1	0		0.958	1.00	1.00[a]
	1	750	0.958	1.00	1.00
	2	750	0.947	1.00	0.99
	4	750	0.952	1.08	0.99
	8	750	0.953	1.08	0.99
2	0		0.958	1.00	1.00[a]
	16	750	0.961	1.28	1.03
	32	750	0.984	1.87	1.06
	48	750	0.997	2.59	1.08
	64	750	1.014	4.04	1.14
	80	750	1.032	6.14	1.20
	96	750	1.050	9.36	1.22
3	0		0.958	1.00	1.00[a]
	32	750	0.984	1.87	1.11
	8	1900	0.955	1.27	1.01
	16	1900	0.959	1.77	1.01
	2	5000	0.947	1.09	0.98
	4	5000	0.950	1.10	0.97
	0.0625	10^5	0.947	1.03	0.97

[a] The control points for expts 1-3 had percent reactions of 47.4, 46.9, and 47.0, respectively.

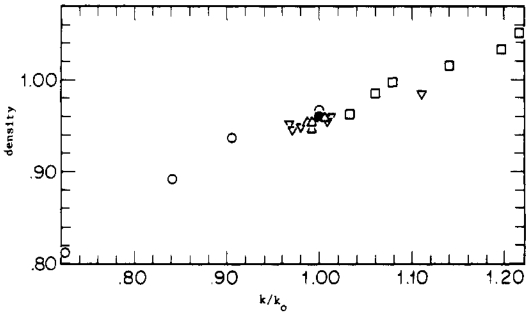


Figure 1. Data from Table I and ref 1: (△) Table I, expt 1; (□) Table I, expt 2; (▽) Table I, expt 3; (○) reference 6.

The most obvious conclusion is that the reaction rate does increase with viscosity, as before. However, the influence of viscosity is smaller than it was in the series of pure solvents—not surprising since this was also true for the mixed solvent Nujol + polyethylene—and not as regular, i.e., there is considerable scatter. But if k/k_0 is plotted against density instead of viscosity, the scatter all but vanishes (Figure 1).

Why is density significant? Because in all the mixtures used in the present study, every solvent molecule is built from the same basic unit, namely, $-CH_2CH_2O-$, with the same intrinsic mass and volume per unit. Therefore, differences in density can arise only from differences in packing of the solvent chains. Efficient packing makes for high density, while inefficient packing gives rise to a porous, less dense matrix. Here then is a new index of the microscopic environment that is not subject to the drawbacks of macroscopic viscosity.

We propose that each solvent in Table I be regarded as consisting of two microscopic phases, one of them closely packed molecules and the other the cavities created by imperfect packing. The two environments correspond, from the point of view of a reacting molecule, to the two macroscopic phases liquid and vapor. Reaction 1 goes faster in the closely packed zones because translation of the two reactive moieties relative to each other is impeded. It is already well-known that many nonpolar bond-forming reactions go faster in the liquid than the vapor phase, and the analysis in ref 1 of both published and new experimental data concluded that this phenomenon could not be explained by any conventional solvation or polarization effect.

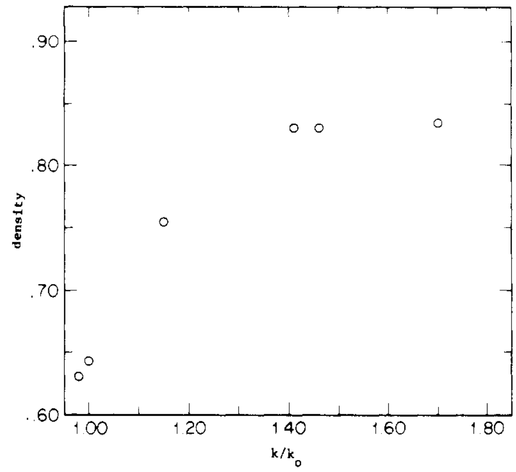


Figure 2. Data from ref 7.

In the previous study of reaction 1 in a series of unmixed solvents, the rate varied smoothly with macroscopic viscosity. Would it do likewise with density? Indeed it does, as see in Figure 1, in which the data from both ref 1[6] and the present work (Table I) are plotted together. The combined plot of 23 experimental points smoothly increases in rate by a factor of 1.68 while the density increases by a factor of 1.29. The slope at infinite dilution would probably be greater than that in Figure 1, because, as noted before,[1] the presence of considerable additives (including the reactant) in constant amount in each reaction tube compresses the range of solvent properties such as viscosity or density relative to the pure solvent mixtures.

It seems likely that microscopic viscosity (resistance to shear) plays a role as well as density (resistance to translation). Thus, a replot of the Claisen rearrangement data of ref 1, in four unmixed hydrocarbon solvents and Nujol + polyethylene, showing rate vs. density instead of viscosity[7] (Figure 2) shows a smooth but curved relationship, with a rate increment at the high end that cannot be accounted for by density alone.

Our conclusion is that reactions 1 and 2, and presumably other bond-making reactions, are accelerated by increased solvent density *and* viscosity, factors that impede translational motion of solute molecules. Both of these factors are also involved at high pressures and consequently affect the kinetics; see ref 1 for a discussion of this point. The fact that the present results were predicted by the vibrational activation theory supports, but does not yet prove, the theory. In any event, the phenomena are new, and presently without any alternative explanation.

---

(6) Data, all at 100 °C from ref 1 for reaction 1, 66 h (solvent, density, k/k_0): glyme, 0.812, 0.725; diglyme, 0.891, 0.841; triglyme, 0.938, 0.906; tetraglyme, 0.966, 1.00.

(7) Data from ref 1 for reaction 2 (solvent, density at 100 °C k/k_0 at 138 °C). Expt 1 (538 h), *n*-octane, 0.643, 1.00; isooctane, 0.631, 0.98; *n*-octacosane, 0.755, 1.15; Nujol, 0.831, 1.46. Experiment 2 (233 h), *n*-octane, 0.643, 1.00; Nujol, 0.831, 1.41; Nujol + polyethylene, 0.835, 1.70.

Raymond A. Firestone,* Susan G. Saffar

Membrane and Arthritis Research Department
Merck Sharp & Dohme Research Laboratories
Rahway, New Jersey 07065

Received July 8, 1983