High-Pressure Kinetic Studies of a Transition State. The Diels–Alder Condensation of Methoxybutadiene–Maleic Anhydride

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The kinetics of the Diels–Alder reaction of *trans*-1-methoxy-1,3-butadiene with maleic anhydride have been measured in five solvents and at pressures up to 20,000 psi. The results are used to show how solvent effects on the activation volume can lead to a better understanding of the structure and properties of the reaction transition state. Also, this provides a better measure of reaction polarity than the study of kinetic solvent effects alone.

A knowledge of the physical properties of the transition state provides the key for a detailed understanding of a reaction mechanism. Such information has direct engineering application in the design of chemical reaction systems— for example, in the prediction of substituent effects on reaction rates and in the prediction of kinetic solvent effects, as well as in catalysis and reactor design. Because the transition state is not isolable, its physical properties must be deduced from the effect of thermodynamic variables on the rate constant.

The temperature variation of the rate constant gives the activation energy, which can lead to calculations for the internal energy, entropy, and heat capacity of the transition state relative to the reactants. On the other hand, an equally important, if not even more valuable, approach is to measure the effect of pressure on reactions in solution. Although more difficult experimentally, if done accurately such determinations of activation volume can give information about both the atomic and electronic structure of the transition state, translatable into thermodynamic terms as partial molal volumes and activity coefficients in solution. One especially

good way to study such effects is the measurement of activation volume in a variety of solvents.

In this work we report the effects of pressure and solvent on the Diels–Alder condensation of maleic anhydride (MA) with *trans*-1-methoxy-1,3-butadiene (MB) to form the cyclic adduct 3-methoxy-*cis*-4-cyclohexene-1,2-dicarboxylic anhydride (MOCDA).

MB   MA   MOCDA
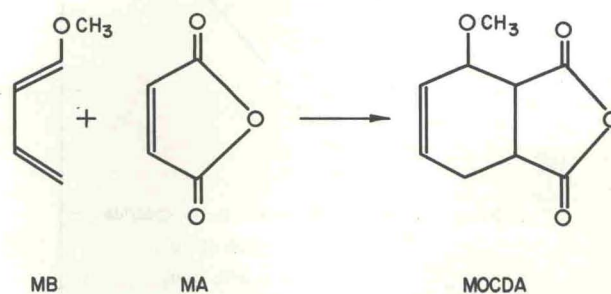
This reaction was chosen for a number of reasons. First, the Diels-Alder reaction represents a simple, single-step molecular addition, uncomplicated by competing or reverse reactions at moderate temperatures. Although the solvent effects are not as great as for ionic reactions (Gould, 1959), they are quite significant. Moreover, previous studies (Wong and

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Solvent	Pressure, psia						
	15	2500	5000	7500	10,000	15,000	20,000
Nitromethane	459	561	753	1020	1280	. . .	2940
Acetonitrile	200	245	287	378	451	647	. . .
1,2-Dichloroethane	105	139	. . .	237	285	408	557
n-Butyl chloride	32.7	43.9	55.8	75.5	95.3	148	208
Dimethyl carbonate	41.6	60.0	80.8	114	147	223	348

Eckert, 1969, 1971) have shown that for the addition of a nonpolar diene (butadiene) to MA solvent effects can be predicted well from solution theory. Also solvent effects on the activation volume of a similar reaction, isoprene with MA (Grieger and Eckert, 1970c), have substantiated the solution theory and yielded detailed information on that transition state. Finally, mechanistic studies (Grieger and Eckert, 1970b) have indicated that the transition state for this reaction could have an unusually high polarity.

The charge distribution in the transition state is a key property not only for mechanistic investigation but especially for making thermodynamic predictions of kinetic solvent effects. Most estimates of the polarity of transition states have been qualitative ones, based on the old rule of thumb that reactions for which the transition state is more polar than the reactants go faster in polar solvents, and *vice versa*. This rule was substantiated largely by studies on S_N reactions (Ingold, 1953), for which electrostatic interactions with the solvent far outweigh other factors which affect the reaction rate in solution. More recently, it has been recognized that for many reactions, the effect of solvent on the reaction rate may be greatly influenced by other types of interaction, such as London forces, hydrogen bonding, and formation of charge-transfer complexes (Parker, 1967; Reichardt and Dimroth, 1968). Nevertheless, solvent effect on the reaction rate is still often used as a criterion of transition state polarity, even for a free radical reaction for which the rate constant varies by less than a factor of 3 in a wide range of solvents (Niki, *et al.*, 1969).

Here we use the solvent effect on the activation volume in conjunction with partial molal volume measurements on the reactants to evaluate the volume in solution of the transition state. In terms of an electrostatic model for dipole interactions, this leads to an estimate of the absolute value of the dipole moment of the transition state.

Experimental Section

Reagent grade MA was recrystallized twice from ethyl ether and vacuum sublimed (mp 53°C). 1,1,3-Trimethoxybutane was dehydrogenated (Montagna and Hirsh, 1960) to make MB, which was washed, dried, and distilled to give 99% purity by gpc. The MB was all-trans by nmr. The product MOCDA was made by the reaction of MA with MB (mp 97–98°C). The solvents nitromethane, 1,2-dichloroethane, dimethyl carbonate, n-butyl chloride, and acetonitrile were purified, dried, and distilled by the methods of Perrin, *et al.* (1966). The hygroscopic acetonitrile contained no more than 0.01% water by Karl Fischer titration.

Kinetic measurements were made using the newly developed technique and equipment for high-pressure rate measurements reported previously (Grieger and Eckert, 1970a). This method employs *in situ* mixing of equilibrated reactants at high pressure, coupled with continual sampling for analysis; the resulting rate constants are more accurate than those determined by previous techniques because intrinsic errors due to heat of compression and uncertainty in reaction time are avoided.

For this study master solutions of MA and MB were prepared and stored in the dark at −15°C. All the high-pressure rate constants in a particular solvent were measured using similar initial concentrations of reactants, approximately 0.05 M. Copolymerization was inhibited by the addition of a trace of hydroquinone, which has been shown to have no effect on the rate of the Diels–Alder reaction (Stepek, 1964).

Analysis was done by gpc, using the ratio of peak areas for MA and MOCDA measured on a Beckman GC-5 chromatograph, equipped with dual 6 ft × $^1/_8$ in. columns with silicone DC-11 on a Teflon Gas-Pak F support and with dual flame ionization detectors. This method is independent of both sample volume and solvent losses due to evaporation in sampling. Moreover, it is more sensitive to the extent of reaction than analysis with an inert reference material. The calibration factor was determined by using several solutions of known concentration of MA and MOCDA. The standard deviation of the calibration factor was 1.6%. Reaction within the chromatograph was shown to be insignificant by simultaneous injection of MA and MB solutions.

Figure 1. Typical rate plot for the methoxybutadiene–maleic anhydride reaction

Results

Reaction rates were determined in five solvents at 35.00°C and at pressures up to 20,000 psi. In four of the solvents,

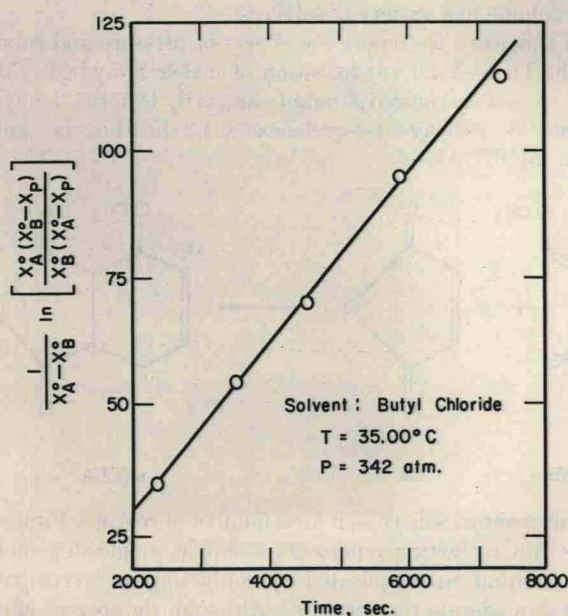## Table II. Activation Parameters and Partial Molal Volumes for the MA–MB Reaction

Solvent	Activation energy, E_a, kcal/mole	Activation volume, $\Delta v^{\ddagger}$, cc/mole	Partial molal volumes, cc/mole			
			$\bar{v}_{MA}{}^a$	$\bar{v}_{MB}{}^a$	$\bar{v}_{MOCDA}{}^a$	$\bar{v}^{\ddagger}$
Nitromethane	9.2	−43.0	72.4	100.4	144.6	130
Acetonitrile	10.5	−32.0	69.8	99.6	137.0	137
1,2-Dichloroethane	9.6	−43.7	72.2	100.8	142.6	129
n-Butyl chloride	10.7	−45.4	69.6	100.6	134.7	125
Dimethyl carbonate	. . .	−53.6	70.9	101.0	139.7	118

[a] Measured by high-precision injection dilatometry (Grieger, *et al.*, 1971).

rate constants were also determined at 10.00°C and at 1 atm to allow calculation of activation energies. Each rate constant was calculated from a least-squares fit of a straight line to a plot of the integrated second-order rate expression for unequal reactant concentrations. A typical rate plot is shown in Figure 1. Because use of pressure-independent concentration units allows straightforward calculation of activation volumes (Hamann, 1963), all rate constants are based on mole fractions. The results are presented in Table I.

Activation volumes (at zero pressure) can most readily be determined from a least-squares fit of a quadratic expression (Golinkin, *et al.*, 1966) of the form

$$\ln k_x = a + bP + cP^2 \qquad (1)$$

and from the thermodynamic relationship

$$\left(\frac{\partial \ln k_x}{\partial P}\right)_{T, P=0} = -\frac{\Delta v^{\ddagger}}{RT} = b \qquad (2)$$

A typical plot for the pressure variation of the rate constant is shown in Figure 2.

The volume of activation is rigorously the difference in partial molal volume between the transition state and the reactants.

$$\Delta v^{\ddagger} = \bar{v}^{\ddagger} - \bar{v}_{MA} - \bar{v}_{MB} \qquad (3)$$

In Table II are reported the values of the activation volume, found from eq 2, and the partial molal volumes of all species in solution. These have been used to calculate from eq 3 the partial molal volume of the transition state in each solvent,
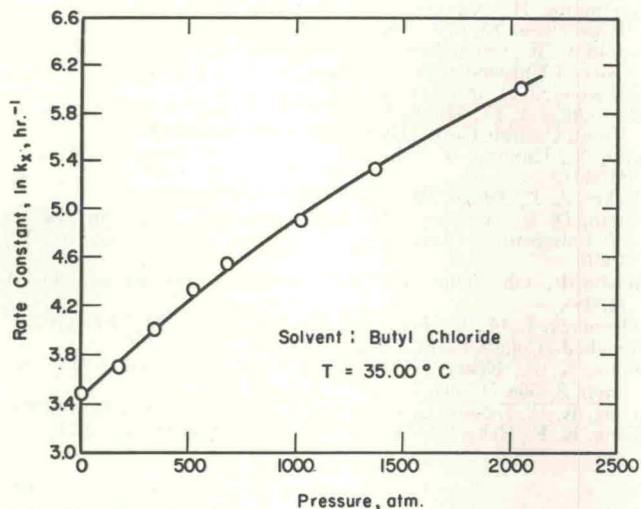
also given in Table II. Also, activation energies in four solvents are given in Table II.

Discussion

The Kirkwood (1934) model provides a simple expression for the Gibbs energy (work at constant T and P) required to place an ideal dipole μ at the center of a spherical cavity of radius r within a continuum of dielectric constant ϵ, as

$$\Delta g = -\frac{\mu^2}{r^3}\left(\frac{\epsilon-1}{2\epsilon+1}\right) \qquad (4)$$

This has often been used to represent the partial molal Gibbs energy of a dipolar solute at infinite dilution, where non-electrostatic effects are assumed negligible. Then the pressure derivative of eq 4 gives the electrostatic contribution to the partial molal volume

$$\bar{v} = \bar{v}_0 - \frac{\mu^2}{r^3}\frac{\partial}{\partial P}\left(\frac{\epsilon-1}{2\epsilon+1}\right) \qquad (5)$$

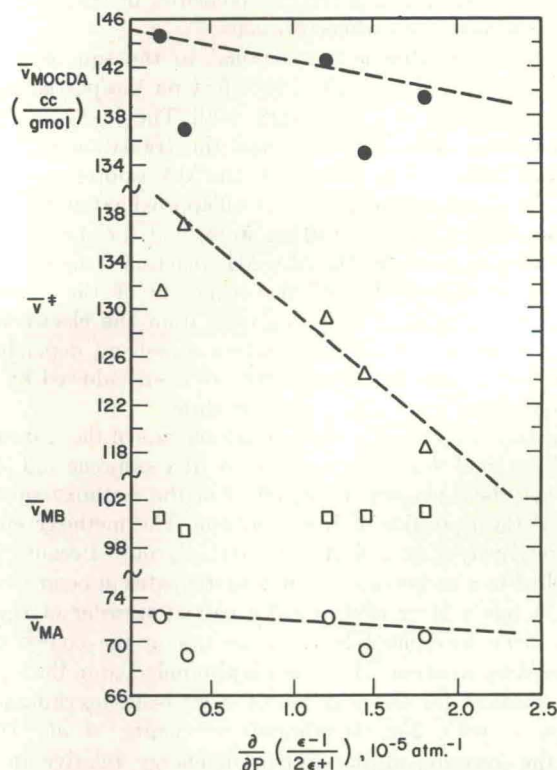where $\bar{v}_0$ is the volume of the solute in a solvent in which

Figure 3. Solvent effects on the partial molal volumes at infinite dilution for reactants, transition state, and product of the methoxybutadiene–maleic anhydride reaction

Figure 2. Effect of pressure on the rate constant of the methoxybutadiene–maleic anhydride reaction in n-butyl chloride

Table III. Dipole Moments for MA, MOCDA, and the Transition State

	Estimated from Figure 3	Lit. value[a]
MA	3 D	3.94 D
Transition state	8 D	...
MOCDA	5 D	5.25 D

[a] Wong and Eckert, 1970.

there is no electrostriction. Nonelectrostatic interactions which affect partial molal volumes, such as hydrogen bonding and formation of charge-transfer complexes, are expected to cause negative deviations in volume from the electrostatic model.

Plots of the partial molal volumes of MA, MB, MOCDA, and the transition state for the reaction vs. the pressure derivatives of the dielectric constant factors for the solvents are shown in Figure 3. Pressure derivatives of dielectric constants were calculated from reported data (Greiger and Eckert, 1970c; Hartmann, et al., 1968; Schornack and Eckert, 1970).

Dipole moments can be estimated from eq 5, using the slopes of the lines in Figure 3. The values used for r^3 are calculated from the molar volumes of the solutes, using a model of close-packed spheres. In drawing the lines it was assumed that deviations from eq 5 due to specific solvent–solute interactions would always be negative, thus in effect neglecting the low points. Such an application of the Kirkwood theory gives only a semiquantitative evaluation of the dipole moment, with a probable uncertainty of 10 to 25%. Even this, however, is of sufficient accuracy to be quite useful in comparing the relative polarities of reactants and transition states for various reactions.

Because the slope is proportional to the square of the dipole moment, the electrostatic effect on the partial molal volume of MB ($\mu \approx 1$ D) is very small. The dipole moments estimated for MA, MOCDA, and the transition state are shown in Table III. In contrast to the MA–isoprene reaction, for which the dipole moments are all approximately the same size for MA, for the transition state, and for the product, the transition state for the MA–MB reaction is significantly more polar than either of the reactants or the product. Deviations of partial molal volumes from the electrostatic model, which show a similar pattern of solvent dependence for MA and MOCDA, apparently are overshadowed by the electrostatic effect for the transition state.

The large difference in the dipole moments of the transition states for the Diels–Alder reactions of MA–isoprene and MA–MB may be explained by the effect of the methoxy substituent at the 1 position of the butadiene. The methoxy entity is a relatively strong electron-donating group. Because it is attached to a carbon atom which participates in bond formation, it has a large effect on the partial transfer of charge from diene to dienophile which occurs in the course of a Diels–Alder reaction. This effect is also reflected in the higher rate constant for the reaction of trans-1-methoxybutadiene compared with 2-methoxybutadiene (Craig, et al., 1961) and the lowering of the activation energy relative to the isoprene reaction.

In conclusion, it has been shown that the concurrent determination of pressure and solvent effects on the rate of a chemical reaction can yield important information about the structure and properties of the transition state. For example, although the solvent effects on the rate constant of this reaction at atmospheric pressure are somewhat larger than for the isoprene–MA reaction, no quantitative estimate of the relative polarity of the two transition states can be made from solvent effects alone. However, accurate measurement of the solvent effect on the partial molal volume of the transition state not only allows estimation of its dipole moment, but also gives some indication of solvent–transition state interactions.

Nomenclature

a, b, c = empirical constants
E_a = activation energy, kcal/g mole
g = molar Gibbs energy, cal/g mole
k_x = rate constant based on mole fraction, hr^{-1}
P = pressure, psia
r = radius of spherical cavity, cm
R = gas constant
T = temperature
$\Delta v^{\pm}$ = activation volume, cc/g mole
$\bar{v}$ = partial molal volume, cc/g mole
$\bar{v}_0$ = volume in nonelectrostricted solvent, cc/g mole
ϵ = dielectric constant
μ = dipole moment, D

SUBSCRIPTS

MA = maleic anhydride
MB = trans-1-methoxy-1,3-butadiene
MOCDA = 3-methoxy-cis-4-cyclohexene-1,2-dicarboxylic anhydride

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