

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA, LOS ANGELES 7, CALIF.]

Pressure Effects on Reaction Rates. The Compressibility of Transition States

BY SIDNEY W. BENSON^{1a} AND JEROME A. BERSON^{1b}

RECEIVED JUNE 21, 1963

A theoretical calculation is made of the contribution of very weak bonds in molecules to over-all liquid compressibility. It is shown that they contribute negligibly up to pressures of 3000 atm. An examination is made of the effect of $P\Delta V$ work on shifting the position of the transition state along the reaction coordinate of those reactions in which the transition state is not a volume extremum. It is concluded that the perturbations of the transition state parameters, ΔF^\ddagger and ΔV^\ddagger , are negligibly small in the ranges of pressure commonly employed. Consequently, there is no basis for the objection of Walling and co-workers to the use of our previous model. The position taken by Walling that ΔV^\ddagger is not related to the effect of pressure on an equilibrium between reactants and transition state is critically re-examined and found untenable. It is also concluded that the pressure dependence of the rearrangement of the hydroxydicyclopentadienes has no necessary implication for the mechanism of the Diels-Alder reaction.

In two recent papers,² Walling and co-workers disagree with our treatment³ of pressure effects on the rates and equilibria of liquid-phase reactions. The present paper examines the bases of Walling's objections and points out why we continue to adhere to our earlier position.

Our theory³ proposes that the transition state can be treated as a normal molecule and that its compressibility is expressed by the Tait equation. Walling and Tanner^{2b} contend that for reactions in which the over-all volume change ΔV for the reaction varies monotonically with passage through the transition state (transition state not a volume extremum), there will be an apparent abnormal compressibility associated with the activated complex. This is presumed² to arise from the shift of the maximum in the free energy-reaction coordinate diagram that results from the contribution of the $P\Delta V^\ddagger$ term.

For purposes of numerical comparison, we note that for a reaction in which ΔV^\ddagger is 25 cc./mole, the total $P\Delta V^\ddagger$ work at 2500 atm. is about 1.5 kcal. This is a very small quantity compared to ΔF^\ddagger , which is in the range of 20–30 kcal. for most reactions near room temperature. Hence, the $P\Delta V^\ddagger$ term in general represents a very small perturbation on the reacting system.⁴ Because of this, it is to be expected that the effect of such pressures in deforming the transition state will be small and comparable to that on ground state molecules. An estimate of just how small this effect is can be obtained by the following calculation.

Following Walling and Tanner,^{2b} the free energy of activation at pressure P is written as

$$\Delta F_p^\ddagger = \Delta F_0^\ddagger + P\Delta V^\ddagger \quad (1)$$

where ΔV^\ddagger is the volume difference between points on the reaction curve and the reactants at some value of the reaction coordinate x , and where ΔF_0^\ddagger is the free energy of activation at zero pressure. We define the quantity Δx as the difference between the positions (x_0 and x_p) of the transition states along the reaction coordinate at pressure zero and at pressure P ; thus, Δx is the shift in position of the transition state produced by a pressure change. We then expand ΔF_0^\ddagger and ΔV^\ddagger as functions of the reaction coordinate x about x_0 , using a Taylor's series in Δx . This gives

(1) (a) This work has been supported in part by grants from the U. S. Atomic Energy Commission and the National Science Foundation to this author. (b) This work has been supported in part by a grant from the Petroleum Research Fund of the American Chemical Society. Grateful acknowledgment is hereby made to the donors of this fund. Requests for reprints should be addressed to this author at the Department of Chemistry, University of Wisconsin, 1112 W. Johnson St., Madison 15, Wis.

(2) (a) C. Walling and H. J. Schugar, *J. Am. Chem. Soc.*, **85**, 607 (1963), (b) C. Walling and D. D. Tanner, *ibid.*, **85**, 612 (1963).

(3) S. W. Benson and J. A. Berson, *ibid.*, **84**, 152 (1962).

(4) In terms of these magnitudes, the illustrative diagram (Fig. 4) used by Walling and Tanner² to show the effect of $P\Delta V^\ddagger$ on shifting ΔF^\ddagger is highly misleading, since their depicted values of $P\Delta V^\ddagger/\Delta F^\ddagger$ are about 0.3 to 0.5.

$$\Delta F_{x_p}^\ddagger = \Delta F_{x_0}^\ddagger - \frac{1}{2}k(\Delta x)^2 + P(\Delta V_0^\ddagger + \sigma_p \Delta x) \quad (2)$$

where $\sigma_p = [\partial \Delta V^\ddagger / \partial x]_{x_0, p}$, and $k = -[\partial^2 \Delta F_0^\ddagger / \partial x^2]_{x_0}$. We omit higher-order terms in the ΔV^\ddagger expansion and note that σ_p may be positive or negative. Also, since ΔF_0^\ddagger is a maximum at the transition state, $(\partial \Delta F_0^\ddagger / \partial x)_{x_0} = 0$, and $k > 0$. At the new transition state at pressure P , the free energy of activation is again an extremum, so that differentiating eq. 1 we have

$$\partial(\Delta F_p^\ddagger) / \partial x = -k\Delta x + P\sigma_p = 0$$

Thus x is shifted at pressure P by the amount

$$\Delta x = P\sigma_p / k \quad (3)$$

We now can make a numerical estimate of the pressure effect on the transition state parameters. The quantity σ_p may be thought of as the reaction cross-section in the vicinity of the transition state. It is the quantity which gives the over-all volume of reaction when multiplied by Δx_r , the change in x required to convert reactants to products. For purposes of illustration we shall take an extreme case most likely to give large shifts, Δx . Let us select a reaction in which ΔV changes uniformly at the pressure P , with $\Delta x_r = 4 \text{ \AA}$, and ΔV^\ddagger about 38 cc./mole, $\sigma_p \sim \pm 16 \text{ \AA}^2$. If the transition state has extremely compressible bonds, the force constant in this region will be feeble. This force constant is given by $k = 2\Delta F_0^\ddagger / (\Delta x^\ddagger)^2$; ΔF_0^\ddagger is given the reasonable value 20 kcal./mole, and Δx^\ddagger , the change in x required to achieve the transition state, is given the value $\Delta x_r/2$ or $\sim 2 \text{ \AA}$. The value so derived for k is 7×10^3 dynes/cm., corresponding to a vibration frequency of about 47 cm.⁻¹ for a reduced mass $\mu = 50$ a.m.u. This is an unusually weak restoring force and corresponds to a highly compressible bond. The shift of the transition state, Δx , associated with raising the pressure to 2500 atm., may now be calculated from eq. 3 and is found to be 0.06 \AA . The corresponding shift in ΔV^\ddagger associated with this is $\sigma_p \Delta x =$ about 0.6 cc./mole, or well within the limit of experimental error of measurement of ΔV^\ddagger . The free energy of activation ΔF_p^\ddagger is shifted by an amount derived from eq. 2 and 3 and given in eq. 4. It is clear

$$\begin{aligned} \Delta \Delta F_p^\ddagger &= \Delta F_{x_p}^\ddagger - (\Delta F_{x_0}^\ddagger + P\Delta V_0^\ddagger) \\ &= -\frac{1}{2}k(\Delta x)^2 + P\sigma_p(\Delta x) = +\frac{1}{2}k(\Delta x)^2 \\ &= 0.018 \text{ kcal./mole} \end{aligned} \quad (4)$$

that even with an extremely compressible transition state, the shifts are negligibly small. With a more realistic force constant of about 10^5 dynes/cm., all the changes would be still smaller.

Although it might be argued that the transition state, with one or more weak bonds, might be abnormally sensitive to pressure deformation, it seems difficult to

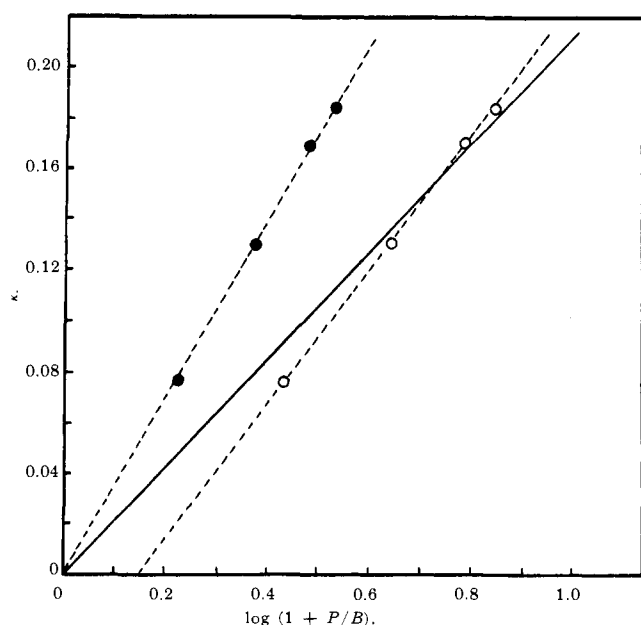


Fig. 1.—Tait plot of the bulk compression (κ) of liquid cyclopentadiene as a function of pressure: the solid line is the theoretical one for $C = 0.216$; open circles represent the data with $B = 599$ kg./cm.² and $C = 0.216$; filled circles represent the data with $B = 1500$ kg./cm.² and $C = 0.354$.

support such a view. Compressibilities in the pressure range under discussion represent mainly the squeezing out of free volume or holes between molecules⁵ and not significant changes in length of covalent bonds. The case of intermolecularly hydrogen-bonded liquids such as water and alcohols, in which weakly bonded dimers and higher aggregates are abundant, is especially instructive. These materials do not show abnormal compressibility, and in particular, their behavior is well accommodated by the Tait equation.⁶

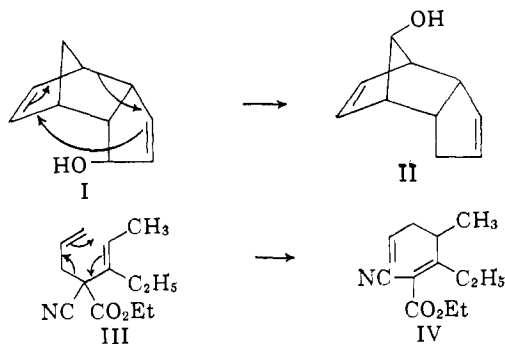
The contention^{2b} that the transition state cannot be treated as a normal molecule implies that transition state theory, which assumes equilibrium between ground state and activated complex, is inapplicable to the study of pressure effects on kinetics. This position is made more explicit in the discussion^{2a} of the dimerization of cyclopentadiene. Walling and Schugar^{2a} note that their data for this reaction do not fit the standard thermodynamic relationship $(\partial\Delta S^\ddagger/\partial P)_T = -(\partial\Delta V^\ddagger/\partial T)_P$ and use this discrepancy to support their view that "it is probably not correct to consider ΔV^\ddagger as measured as being related to the effect of pressure on the equilibrium between two species which can be treated as normal molecules." We find this position untenable for two reasons.

The first has to do with the reliability of the experimental determination of ΔV^\ddagger . Walling and co-workers^{2a, b} note that the data for the dimerization of cyclopentadiene require an unreasonable Tait B -value for the transition state in order to be fitted by the ψ -function we propose.³ This is not surprising, since Walling^{2a} uses the data of Raistrick, *et al.*,⁷ for the compressibility of the *ground state* (cyclopentadiene monomer) and chooses the Tait parameters $B = 599$ kg./cm.², $C = 0.216$, for the calculation of our³ function ψ . But the data⁷ and parameters^{2a} do not fit the Tait equation. The points lie badly off the line passing through the origin with slope 0.216. The line actually formed by these points does not pass through the origin and has a slope much steeper than 0.216 (Fig. 1). The

data can be fitted with $B = 1500$ kg./cm.² and $C = 0.354$, values that are quite unreasonable for this molecule.³ We conclude that either cyclopentadiene itself has an abnormal compressibility, or the data are in error. In either case, the calculation of the ψ -function, which requires Tait-like response to pressure of both ground and transition states, is clearly unjustified. It is for this reason that these data were not included in our previous paper.³ Furthermore, calculations of ΔV^\ddagger for this reaction by *any procedure* seem hazardous with the present data.

Our second objection is a theoretical one. The position taken by Walling, *et al.*,² can very well be extended to temperature and its conjugate variable entropy. The argument would run somewhat as follows: "In a reaction in which the transition state entropy is not a minimum or maximum along the reaction coordinate, a change in temperature will shift the transition state to a new configuration and hence to a new value of ΔS^\ddagger as well as ΔH^\ddagger . This will contribute an abnormal value of ΔC_p^\ddagger to the transition state for such systems and hence will make the values of ΔS^\ddagger and ΔH^\ddagger difficult to interpret in terms of structures of normal molecules." Accompanying such a proposal, it would be appropriate to show a schematic diagram such as Walling and Tanner's Fig. 4, with their F replaced by H , their ΔF^\ddagger replaced by ΔH^\ddagger , and their $P\Delta V^\ddagger$ replaced by $T\Delta S^\ddagger$. The reciprocal structure of thermodynamics would seem to require this as a logical consequence of Walling's position. On this basis, one would refrain from ever trying to interpret either ΔS^\ddagger or ΔV^\ddagger in terms of molecular models. In fact, pressing these types of arguments one step further, we can object that even normal molecules change their internal energy levels with temperature and so are also not amenable to thermodynamic description.

Finally, even if the serious problems³ associated with the determination of ΔV^\ddagger of a reaction are ignored, there remains the problem of the interpretation of the experimental quantity one chooses to call " ΔV^\ddagger ," or even of the qualitative rate increase or decrease observed to result from the application of pressure. Walling and Schugar^{2a} find that the rearrangement of β -1-hydroxydicyclopentadiene (I) to *anti*-8-hydroxydicyclopentadiene (II),⁸ which is formally a Cope rearrangement, is slightly pressure retarded, in contrast to Cope rearrangements in open-chain systems, *e.g.*, III \rightarrow IV, which are pressure accelerated.⁹ From this they conclude that the Woodward-Katz rearrangement (I \rightarrow II) is a partial retro-Diels-Alder reaction, since the latter would also be pressure retarded. In our view, this conclusion is unjustified, since the open-chain 1,5-hexadiene Cope rearrangement systems are poor models for predicting the behavior of a 1,5-hexadiene such as β -1-hydroxydicyclopentadiene (I). In the latter, the reacting ends of the 1,5-hexadiene system



(8) R. B. Woodward and T. J. Katz, *Tetrahedron*, **5**, 70 (1959).

(9) C. Walling and M. Naiman, *J. Am. Chem. Soc.*, **84**, 2628 (1962).

(5) R. Ginell, *J. Chem. Phys.*, **34**, 1249 (1961).

(6) Reference 3 and references cited therein.

(7) B. Raistrick, R. H. Sapiro, and D. M. Newitt, *J. Chem. Soc.*, 1770 (1939).

are held in rigid proximity to each other by the molecular framework, in contrast to the open-chain cases, where the ends must first be brought together to achieve the transition state for a concerted process. The contrast between the two cases is manifested in the entropies of activation, those for the open-chain Cope rearrangement being large and negative¹⁰ and that of the I → II reaction being small and positive.^{2a} The

entropy changes and qualitative pressure effects are about what might be expected for the two kinds of reaction on any grounds and have no bearing on the question of whether the I → II rearrangement uses the same energy surface as the Diels-Alder retrogression of I to cyclopentadiene and hydroxycyclopentadiene.

(10) E. G. Foster, A. C. Cope and F. Daniels, *J. Am. Chem. Soc.*, **69**, 1893 (1947).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, JOHN CARROLL UNIVERSITY, CLEVELAND 18, OHIO]

Determination of Dissociation Constants of Ion Pairs from Kinetic Data of Bimolecular Nucleophilic Substitutions. I. The Importance of Solvation and Ion Pairing on the Nucleophilic Reactivity of the Halide Anions

BY WILLIAM M. WEAVER AND J. DOUGLAS HUTCHISON¹

RECEIVED JULY 18, 1963

The dissociation constants for the ion pairs of lithium chloride, bromide, and iodide in DMF at 0° have been determined from the variation, with concentration of the halides, of the second-order rate constants derived from their reaction with methyl toluenesulfonate in DMF at 0°. The rate of reaction of the halide anions is visibly in the order I⁻ < Br⁻ < Cl⁻. The significance of this order compared to the reverse order which is normally reported is discussed.

The nucleophilicities of the halide ions are of considerable interest because the usual order of reactivity [I⁻ > Cl⁻] is opposite to that predicted by the generalization—the more basic a nucleophile the greater its nucleophilicity. Further, the ease with which iodide ion in acetone replaces chloride from an alkyl chloride is inconsistent with the easy displacement of iodide from an alkyl iodide compared to the sluggish displacement of chloride from an alkyl chloride by a common nucleophile. These irregularities have been ascribed by various authors to: (1) polarizability,²⁻⁵ (2) solvation,^{3,6} and (3) ion pairing.⁷

In the present report an effort to evaluate the importance of the above has been made by studying the rates of reaction of methyl *p*-toluenesulfonate (methyl tosylate) with lithium chloride, bromide, and iodide in dimethylformamide (DMF). Moreover, a method for determining the dissociation constant of ion pairs from kinetic data alone is described.

Results

In DMF, the relative rates of reaction of the lithium halides (at 0.04 *M*) with methyl tosylate are visibly in the order Cl⁻, 7.8 > Br⁻, 3.2 > I⁻, 1.0. (After correction for ion pairing, the relative rates are Cl⁻, 9.1 > Br⁻, 3.4 > I⁻, 1.0.) This, of course, is directly opposite that observed with sodium halides in aqueous dioxane reacting with ethyl tosylate⁸ where the order is Cl⁻, 0.14 < Br⁻, 0.32 < I⁻, 1.0; and likewise opposite to that observed with lithium halides reacting with *n*-butyl *p*-bromobenzenesulfonate in anhydrous acetone⁷ where the order is Cl⁻, 0.16 < Br⁻, 0.92 < I⁻, 1.0. In addition, it was found that the presence of 9.1% by volume of water in the DMF (5 *M* H₂O) caused a 24-fold reduction in the observed rate for displace-

ment by chloride ion but only a twofold retardation of the iodide. This retardation does not arise from the hydrolysis of the methyl halides since methyl iodide (1.6 *M*) in 20% H₂O–80% DMF was only 0.35% hydrolyzed after 1 hr. at 0°. Consequently, with but 9% water in DMF the usual order of reactivity is restored, for, now, iodide is twice as reactive as chloride.

It was also found that *n*-butyl iodide is converted nearly quantitatively (99%) to *n*-butyl chloride by lithium chloride in anhydrous DMF after but 1 hr. and with but a 16% excess of lithium chloride.

As anticipated, the rate constants for the bimolecular reaction of halide anions with methyl tosylate in DMF are dependent on initial concentration of lithium halide. This was ascribed to ion pairing, and from the degree of variation of rate constants with initial concentration of the halide, the dissociation constants of the lithium halides in DMF at 0° were computed to be: LiCl, *K* = 0.180; LiBr, *K* = 0.385; and LiI, *K* = 1.80.

Method.—An examination of Table I and Fig. 1 clearly shows that, in DMF, not only is chloride ion a

TABLE I
OBSERVED AND SPECIFIC RATE CONSTANTS OF THE METHYL
TOSYLATE-LITHIUM HALIDE REACTION AT VARIOUS
CONCENTRATIONS OF HALIDE IN DMF AT 0°

	[C], mole l. ⁻¹	10 ³ × <i>k</i> _{obsd} ± <i>s</i> , ^a l. mole ⁻¹ sec. ⁻¹	<i>K</i>	α ^b	<i>k</i> ₂ × 10 ⁴ , l. mole ⁻¹ sec. ⁻¹
LiCl	0.03933	4.54 ± 0.04	0.180	0.845	5.38
	.0985	3.84 ± .01	.180	.713	5.33
	.1940	3.23 ± .09	.180	.605	5.36
	.3911	2.61 ± .02	.180	.486	5.37
LiCl + 5.0 <i>M</i> H ₂ O	.3678	0.116 ± .003			
LiBr	.03947	1.84 ± .02	0.385	0.914	2.00
	.2167	1.43 ± .03	.385	.714	2.00
LiI	.03818	0.581 ± .017	1.80	.979	0.593
	.3880	0.500 ± .007	1.80	.846	0.591
LiI + 5.0 <i>M</i> H ₂ O	.1764	.276 ± .007			

^a Standard deviation, *s* = √Σ[*d*²]/(*N* - 1) where *d* = deviation from mean value and *N* = number of determinations.

^b Degree of dissociation, *i.e.*, ratio of "free" ion to total concentration.

better nucleophile than bromide, which is better than iodide, but also that the observed rate constants de-

(1) Based on the M.S. Thesis of J. Douglas Hutchison, John Carroll University, August, 1963.

(2) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, p. 140.

(3) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York, N. Y., 1959, p. 260.

(4) F. G. Bordwell, "Organic Chemistry," The Macmillan Co., New York, N. Y., 1963, p. 208.

(5) J. E. Leffer and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, p. 250.

(6) H. R. McCleary and L. P. Hammett, *J. Am. Chem. Soc.*, **63**, 2254 (1941).

(7) S. Winstein, L. G. Savedoff, S. Smith, I. D. R. Stevens, and J. S. Gall, *Tetrahedron Letters*, **9**, 24 (1960).