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# Activation Volume and Transition State Character in Several Proton and Hydride Transfer Reactions

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**Abstract:** Volumes of activation have been measured for the dedeuteration of chloroform, fluoroform, acetophenone, phenylacetonitrile, methyl phenylacetate, $Me_2SO$, indene, phenylacetylene, diphenylmethane, and 2-nitropropane. None of them has $\Delta V^*$ as low as $-10$ mL/mol, and it may be inferred that their transition states are product-like. In two examples of hydride transfer, reduction of acetophenone by borohydride and the Cannizzaro reaction of benzaldehyde, $\Delta V^*$ is substantially negative, which implies a central transition state. These results support a theoretical prediction by Swain.

## Introduction

In many important organic reactions the rate is limited by a step in which a proton is removed from one of the reactants. There has been much interest in the character of the transition states for these reactions, and the subject has been extensively reviewed.[1,2] In a smaller but still very important group of reactions the rate is limited by transfer of hydrogen in the form of hydride ion. In this field too there is extensive literature on the question whether the transition state comes early or late.[3]

Experimental evidence for the location of the transition state on the reaction coordinate for proton transfers comes mainly from primary kinetic isotope effects,[4] solvent isotope effects,[5] Brønsted parameters,[6-8] stereochemistry,[9] and activation entropy.[6] For hydride transfers the evidence is based on the primary kinetic hydrogen isotope effect,[10] Hammett relationships,[11,12] activation entropy,[13] and numerous studies of steric effects which are described in a recent review.[14] Despite the great quantity and variety of evidence there is much difference of opinion about the nature of the transition state for both kinds of reaction. All of the authors cited above have been candid about the weak points of the various mechanistic tests. It is well known, for example, that moderate or small kinetic isotope effects are equally consistent with early and late transition states. The Brønsted parameters, on the other hand, are not two valued, but they can be very difficult to measure. The evaluation of $\beta$ requires a measurement of catalysis by general bases which is often overshadowed by lyate catalysis, and the evaluation of $\alpha$ requires p$K$ values for weak acids of very different strength in the same solvent. For deprotonation of nitroalkanes Bordwell[15] has reported $\alpha$ values substantially greater than one, and under the customary interpretation such values convey no meaning in terms of transition state structure. The Hammett $\rho$ scale is also monotonic, but there is no firm basis for anticipating what value $\rho$ should have for a highly product-like transition state. The observed values are usually considerably less than the theoretical maximum.

When the evidence is confusing or inconclusive it is probably better to have more kinds of evidence than a greater amount of the same kind. One method for investigating reaction mechanisms which has not yet been applied in any systematic way to the present problem is the measurement of the effect of pressure on reaction rate and the evaluation of the volume of activation. The utility of the method derives from the possibility of comparing the molar volumes of transition states with those of stable molecules. This gives information about changes in bonding and electrical polarization. More than 1000 measurements of activation volume have been reported to date, and the empirical basis for interpreting them is fairly secure.[16,17] The complete formation of a new bond causes a volume decrease which is usually in the range of 10–15 mL/mol, and the activation volume for a simple bond-forming step is usually a substantial fraction of the overall decrease. The case of bond breakage is reciprocal, and expansions on the order of 10–15 mL/mol are the rule. The formation of a pair of ions produces a contraction of about 20 mL/mol in water and 40 mL/mol in organic solvents. This phenomenon, which is called electrostriction, is considerably reduced by delocalization of charge as in carboxylate ions. For reactions of certain types the interpretation of activation volumes is complicated and uncertain. If there are strong contrary effects as in bond breakage accompanied by ionization it is difficult to estimate the amount of structural reorganization in the transition state unless the volume change is extremely negative. As it happens, most such reactions do have large negative activation volumes. There is also a problem if the rate-limiting step is preceded by an equilibrium. In such cases it is necessary to evaluate the volume change of the reversible reaction. A smaller uncertainty arises when an electronic charge in a reactant becomes more or less localized in the transition state and thus affects the volume of electrostricted solvent. This effect can often be anticipated and quantitatively estimated.

The isotopic exchange reaction of a neutral weak carbon acid catalyzed by an oxy anion is well suited to a study of activation volumes because ionic charge is conserved, and the first step is rate limiting. It is still necessary, however, to cope with changes in localization of the charge. The reduction of a ketone by sodium borohydride is also suitable. A recently proposed

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Table I. Activation Volumes (mL/mol)

| substrate | base | solvent | $\Delta V^*$ |
|---|---|---|---|
| Hydrogen Exchange | | | |
| $CDCl_3$ | $HO^-$ | HOH | +9 |
| $CDF_3$ | $HO^-$ | HOH | +3 |
| $C_6H_5COCD_3$ | $HO^-$ | HOH | −1 |
| $C_6H_5COCD_3$ | $EtO^-$ | EtOH | −1 |
| $C_6H_5COCD_3$ | $ArO^-$ | MeOH | −5 |
| $C_6H_5CD_2CN$ | $AcO^-$ | MeOH | −4 |
| $C_6H_5CD_2CO_2Me$ | $MeO^-$ | MeOH | −3 |
| $CD_3SOCD_3$ | $HO^-$ | HOH | +2 |
| $(CH_3)_2CDNO_2$ | $AcO^-$ | HOH | −1 ± 2 |
| $(CH_3)_2CHNO_2$ | $AcO^-$ | HOH | −1 ± 2 |
| indene-*1,1,3*-$d_3$ | $MeO^-$ | MeOH | −4 ± 2 |
| $C_6H_5C_2D$ | $HO^-$ | MeOH-HOH | −1 ± 2 |
| $Ph_2CD_2$ | $MeO^-$ | MeOH-$Me_2SO$ | −3 ± 2 |
| Hydride Transfer | | | |
| $C_6H_5COCH_3$ | $BH_4^-$ | $Me_2CHOH$ | −11 |
| $C_6H_5CHO$ | $HO^-$ | MeOH-HOH | −27 |
| Ester Interchange | | | |
| $C_6H_5CH_2CO_2Et$ | $MeO^-$ | MeOH | −12 |

model for the transition state[3] has the hydride transferred along a line perpendicular to the carbonyl group at a distance of 2.30 Å. A search for other types of hydride transfer reaction did not yield any equally satisfactory examples, but we elected to study the Cannizzaro reaction despite the fact that it has a reversible addition preceding the rate-limiting step. We hoped that the overall volume change from reactants to transition state would be so extreme as to permit only one interpretation. It will be seen below that this hope was fulfilled.

An ingenious concept based on molecular orbital theory has led Swain[18] to predict that hydride transfer will have a central transition state and proton transfer will not. Application of a unified experimental approach to both kinds of reaction can provide a potentially valuable test of the theory.

## Results and Discussion

All measurements of activation volume are collected in Table I. The first group of entries pertains to base-catalyzed dedeuteration of carbon acids, and in general the activation volume is low or even positive. In the discussion which follows we will rationalize these results on the basis of a very product-like transition state. The last three entries are for borohydride reduction of acetophenone, the Cannizzaro reaction of benzaldehyde, and base-catalyzed ester interchange. All have very substantial negative activation volumes which befit central transition states having a higher degree of bonding than either products or reactants. Because many of the reactions have special features, it is advantageous to discuss them individually or in small groups.

**Ethyl Phenylacetate Ester Interchange.** Although second-order rate processes with no change in state of ionization usually have activation volumes near −10 mL/mol, it is always welcome to have a closely related model for reference. Ester interchange is concurrent with dedeuteration of methyl phenylacetate in methanol, and for the purpose of chemical labeling we substituted the ethyl ester. This reaction is thought to have a central transition state resembling the product of addition of methoxide ion to the carbonyl group. Its activation volume is −12 mL, which makes it a typical case, and all of the examples which follow can be compared to it.

**Chloroform and Fluoroform.** The rate of alkaline hydrolysis of chloroform is limited by $k_2$ in the following scheme.

$$HO^- + CHCl_3 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Cl_3C{:}^- \xrightarrow{k_2} CCl_2 + Cl^-$$

Many papers by Hine and others[6] have been devoted to the details of this and related reactions including studies of hydrogen isotope exchange in the first step. The effect of pressure on the overall reaction was measured by le Noble,[19] who reported an apparent activation volume of +16 mL/mol. This value is surprisingly high for a single bond-breaking step, but it can better be understood in conjunction with our value of +9 mL for the initial step. This reaction has a rate-limiting step preceded by a somewhat faster equilibrium so that the apparent activation volume for the overall reaction is the sum of the volume changes for the equilibrium and the formation of the transition state between $Cl_3C{:}^-$ and $Cl_2C$. If we assume a very product-like transition state for the first step and subtract 9 mL from the apparent activation volume of +16 mL, we get a very reasonable value of +7 mL for the stretching of the C-Cl bond in the rate-limiting step.

A substantial positive activation volume for the H-D exchange was completely unexpected. Both authors of this report obtained a value of +9 mL in independent measurements. It is highly inconsistent with an early transition state and is only consistent with a late transition state provided that the sum of the partial molar volumes of $Cl_3C{:}^-$ and $H_2O$ is at least 9 mL greater than that of $HO^-$ and $CHCl_3$. This condition would obtain if the ionic charge of $Cl_3C{:}^-$ is dispersed to a degree comparable to that of a carboxylate ion by delocalization into the d orbitals of chlorine. Decreased solvation is indicated by the activation entropy, +15 eu, which is most unusual for a reaction wtih second-order kinetics.[6]

As a further test of this explanation we examined fluoroform, which lacks accessible d orbitals and ought not to show such a great decrease of electrostriction. Its activation volume of +3 mL is indeed substantially lower, but since it is also positive we are again obliged to infer a very late transition state. The activation entropy is near zero,[20] which indicates less desolvation and less dispersal of charge than in the case of chloroform. On the basis of the Hammond postulate we would expect an even later transition state for fluoroform than for chloroform because their estimated $pK_a$ values[6,20] are 31 and 25, respectively.

**Acetophenone, Phenylacetonitrile, and Methyl Phenylacetate.** The activation volumes for dedeuteration of this group of compounds are negative but near zero, which again suggests late transition states. An attempt was made to reveal changes in electrostriction by variation of solvent and base. Because aqueous and nonaqueous media are markedly different in volume of electrostriction by ionic solutes it has been possible to establish a correlation between the solvent dependence of activation volume and changes in electrical polarity accompanying various reactions.[21] If the negative charge initially localized in $HO^-$ were to become delocalized in the transition state, then solvent would be released, but the volume increase would be greater for ethanol than for water by an amount perhaps as great as 10 mL. When the test was applied to acetophenone by comparing the medium, $HO^-$ in $H_2O$, with $EtO^-$ in EtOH, no significant difference was found. A second test involved substitution of *p*-chlorophenoxide ion for ethoxide. It is known that phenoxide ions show decreased electrostriction as a consequence of delocalization because the volume change of ionization in water is as much as 9 mL higher than for ionization of water.[22] If the charge of the carbanion is more localized than that of *p*-chlorophenoxide, then the activation volume should become more negative. A decrease of 4 mL was in fact observed.

The high reactivity of phenylacetonitrile made it impractical to use an oxy anion having a localized charge, but it is interesting to note that acetate ion, which has a highly delocalized charge, gave an activation volume of −4 mL, which is nearly the same as for acetophenone with *p*-chlorophenoxide. Consequently, we ascribe this negative volume change to an increase of electrostriction rather than to partial bonding of the base to the substrate.

**Indene, Phenylacetylene, and Diphenylmethane.** The activation volumes for this group of compounds range from −1 to −4 mL/mol and suggest that the deuterons are not completely removed in the transition state, but the results are probably uncertain within 2 mL rather than the usual 1 mL for reasons which are different for each compound. Indene and phenylacetylene were the only two compounds listed in Table I which showed a detectable curvature in the plot of the logarithm of the rate constant vs. pressure; consequently, there is some uncertainty in the extrapolation to zero pressure. For diphenylmethane the high temperature and exotic solvent system which are both necessary for reasonable reaction rates made the reaction somewhat unclean and the rates less reproducible than usual. The high reactivity of phenylacetylene made it necessary to use Tris buffer and take into account the effect of pressure on the concentration of hydroxide ion. Fortunately it has been shown that pressure has a negligible effect on the hydronium ion concentration in Tris buffers[23] so that hydroxide concentration can be calculated from the relation $\Delta \mathrm{pOH}/\Delta P = -\Delta V/2.3RT$, where $\Delta V$ is the volume of ionization of water and has a value of −21 mL/mol. Since our medium contains methanol as cosolvent we measured the volume of ionization dilatometrically and obtained a value of −25 mL/mol.

The value of −4 mL for the activation volume of dedeuteration of indene seems small in comparison to our expectation of −10 or −12 mL for a central transition state, but it comes the nearest to giving an indication of bonding in all the hydrogen exchange reactions we have studied.

The case of phenylacetylene seems similar to that of chloroform. The activation volume of −1 mL is consistent with a very late transition state, but there is some uncertainty associated with its indirect determination. Delocalization of charge would not be expected in this case.

**Dimethyl Sulfoxide and 2-Nitropropane.** The acidity of these compounds is associated with their coordinate-covalent bonding. The activation volume of +2 mL for $\mathrm{Me_2SO}$ suggests a very late transition state with some delocalization of charge as in the case of chloroform. Of all the reactions involved in this study, the deprotonation or dedeuteration of 2-nitropropane by acetate ion would seem most likely to have a central transition state since the p$K$ (7.7) is only slightly above that of acetic acid (4.8). Another point of symmetry is that delocalization of charge on the carboxylate ion should be nearly the same as on nitronate ion. It is somewhat surprising, therefore, to find that the activation volume is near zero. The value for dedeuteration was checked by measurements on deprotonation using iodine as a scavenging agent for nitronate ions.

**Borohydride Reduction of Acetophenone.** With the aid of much published information on factors affecting the rate and course of reduction of carbonyl compounds by borohydride, Perlberger and Müller[3] have recently proposed a transition state model in which the reacting hydrogen approaches on a line perpendicular to the plane of the carbonyl group and which has a free-energy maximum at 2.3 Å. The activation volume for this reaction is −11 mL/mol, which is normal for a second-order reaction without ionization and is nearly equal to the −12 mL found for ester interchange of ethyl phenylacetate. The obvious conclusion is that the transition state is central and characterized by an increase of bonding.

**Cannizzaro Reaction of Benzaldehyde.** The accepted mechanism for the Cannizzaro reaction follows:

$$\mathrm{RCHO} + \mathrm{HO^-} \underset{\text{fast}}{\rightleftharpoons} \mathrm{RCH(OH)O^-}$$

$$\xrightarrow[\text{slow}]{\mathrm{RCHO}} \mathrm{RCH_2O^-} + \mathrm{RCO_2H} \xrightarrow[\text{fast}]{} \mathrm{RCH_2OH} + \mathrm{RCO_2^-}$$

**Table II.** Calculated Volumes of Reaction

| reaction | $\Delta V$, mL/mol |
|---|---|
| $\mathrm{CH_3COCH_3 + HOH \rightarrow CH_3OCH_2CH_2OH}$ | −12.5 |
| $\mathrm{CH_2{=}CHCH_2OH + HOH \rightarrow CH_3CHOHCH_2OH}$ | −12.8 |
| $\mathrm{C_6H_5CHO + HOH \rightarrow}$ guaiacol | −10.5 |
| $\mathrm{CH_2{=}CHCO_2H + HOH \rightarrow CH_3CHOHCO_2H}$ | −13.7 |

For the sake of variety this hydride transfer reaction was selected for study despite the occurrence of an equilibrium preceding the rate-limiting step. A survey of the field did not suggest any other possibilities which would meet all of the criteria mentioned in the Introduction. The volume change for the equilibrium step, although not easily measurable, should be predictable within 1–2 mL on the basis of model reactions. It should be approximately equal to the volume change for reactions of the type $\mathrm{A + H_2O \rightarrow AH_2O}$, which are listed in Table II. The volume changes were calculated from the molar volumes of the neat liquids, and they include infeasible as well as real reactions. The apparent activation volume for the Cannizzaro reaction of benzaldehyde is −27 mL/mol. If an allowance of −12 mL is made for the equilibrium addition of hydroxide, the volume change in the second step would be −15 mL, which indicates a high degree of bonding. This result is concordant with the −12 mL found for borohydride reduction of acetophenone.

**An Explanation of the Disparity in Activation Volumes of Proton and Hydride Transfers.** A set of molecular orbitals for the transition state in proton and hydride transfers has been proposed by Swain[18] and is shown in Figure 1. The molecular orbitals are formed by combination of p orbitals on the outer two nuclei (carbon and oxygen or boron in the present application) and the s orbital of hydrogen in the center. The three atomic orbitals form three molecular orbitals of which only the lowest, $\sigma_1$, is bonding. For hydride transfer there is only one electron pair shared by hydrogen and the two outer electrophilic atoms, and this pair occupies the bonding orbital. In the case of proton transfer the outer atoms are nucleophilic, and there is a second electron pair which is forced to enter $\sigma_2$. The repulsion of the pairs is expected to weaken and lengthen the bond. Swain's theory thus predicts a central transition state for hydride transfer and a reactant-like or product-like transition state for proton transfer. Since the free energy for removal of a proton from a weak carbon acid by a strong base is highly positive we expect the transition state to be product-like.

## Experimental Section

**Chloroform.** Deuterated chloroform was prepared by combining 10 mL of 1.0 N NaOD in 99.8% $\mathrm{D_2O}$ with 25 mL of chloroform and stirring at room temperature overnight. Analysis by density indicated 78% deuteration. Reaction mixtures were prepared by dissolving 0.40 mL of $\mathrm{CDCl_3}$ and 1.00 mL of 0.0568 N NaOH in 100 mL of water. A 5-mL portion of reaction mixture was allowed to react for 2–3 h at 26.0 °C under pressures ranging from 0.1 to 125 MPa. The reacted sample was analyzed by extracting with 1 mL of $\mathrm{CCl_4}$, drying the extract with $\mathrm{MgSO_4}$, and measuring the IR absorbance in a 0.2-mm cell with a Perkin-Elmer 421. The most useful characteristic bands are at 1219 $\mathrm{cm^{-1}}$ for $\mathrm{CHCl_3}$ and 911 $\mathrm{cm^{-1}}$ for $\mathrm{CDCl_3}$. Analyses of known synthetic mixtures were correct within 1.5%.

**Fluoroform.** Deuteration of fluoroform is usually done indirectly, but we proceeded with base-catalyzed exchange by using drastic conditions. A pressure vessel of 130 mL capacity was charged with 10 mL of 0.2 N NaOD in $\mathrm{D_2O}$ and 0.6 MPa of $\mathrm{CHF_3}$ vapor, and the vessel was heated for 5 h at 220–240 °C. The gas was then transferred to a rubber bladder for storage at atmospheric pressure. The mass spectrum was measured with a Varian EM-600, and the intensities of mass numbers 51 ($\mathrm{CHF_2^+}$) and 52 ($\mathrm{CDF_2^+}$) were recorded. The gas was initially 50% deuterated, and most of the alkali was consumed during the preparation.

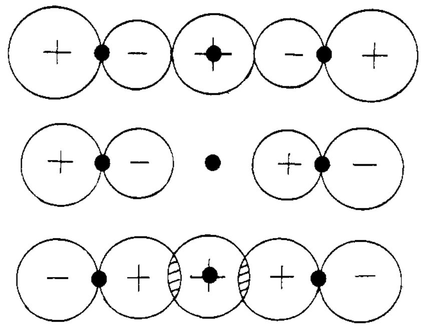

Figure 1. Molecular orbitals for hydrogen transfer.

A special reaction cell shown in Figure 2 was used to measure the rate of dedeuteration of fluoroform. The glass bell was loaded with 4 mL of 0.85 N NaOH and sufficient mercury to fill it. The bell was then raised in an upright position into the outer glass tube until the mouth of the bell touched the rubber septum. The assembly was then inverted, and additional mercury was placed in the outer tube for the purpose of transmitting pressure and sealing the contents. A hypodermic syringe with a long needle was used to inject 6 mL of $CDF_3$ gas inside the bell and later to withdraw it. When the cell was pressurized the fluoroform dissolved in the aqueous alkali, and when the pressure was released a substantial fraction of it effervesced and collected at the top of the bell. The entire pressure vessel was shaken gently to promote mixing. In one test a dye marker was used to reveal the thoroughness of mixing, and the results were satisfactory. Reaction mixtures were analyzed by mass spectrometry as described above. The range of pressures was 3-133 MPa, and the temperature was 65.0 °C.

**Acetophenone.** A mixture of 10 mL of acetophenone and 10 mL of NaOD solution (1 N) in $D_2O$ was mechanically stirred for 24 h at 50 °C. The acetophenone layer was dried and distilled and analyzed by mass spectrometer. The intensities of the parent peaks for $PhCOCD_3$, $PhCOD_2H$, $PhCODH_2$, and $PhCOCH_3$ indicated 74% deuteration under the assumption that their peak heights are proportional to their mole fractions. It was also assumed that isotope exchange in a large pool of protons would obey the simple rate law $dX/dt = -kX$, where $X$ is the fraction of $\alpha$-deuterons. Any errors resulting from these assumptions would have a negligible effect on the determination of activation volume because the reaction times at various pressures were adjusted to give nearly equal fractions of reaction.

The rate of dedeuteration in water was measured by reacting 10-mL portions of 0.0053 N NaOH containing 0.4 mL of deuterated acetophenone. After 2.5 h at 27.4 °C and pressures up to 117 MPa the reaction was stopped by adding a drop of acetic acid. The acetophenone was extracted with ether, and the ether layer was dried and concentrated to a small volume for analysis by mass spectrometry.

Dedeuteration in ethanol employed samples containing 20 mg of deuterated acetophenone in 2 mL of freshly diluted 0.001 N NaOEt. Reaction times were about 2 h at 19.5 °C and pressures to 113 MPa. The reaction was quenched by bubbling several milliliters of air saturated with acetic acid vapor through the solution. The solvent was removed by evaporation on a water bath, and the residue was analyzed by mass spectrometry as above.

For dedeuteration by 0.2 N sodium *p*-chlorophenoxide the solvent was 40% water/60% methanol. Samples with a volume of 5 mL were reacted for about 2 h at 100.5 °C and pressures up to 133 MPa. The method of workup and analysis was the same as for aqueous alkali solutions.

**Phenylacetonitrile.** A solution of 5 mL of phenylacetonitrile in 35 mL of $CH_3OD$ containing 0.05 N $CH_3ONa$ was allowed to stand at room temperature for 3 h. Deuterated phenylacetonitrile was isolated by simple distillation, and the mass spectrogram indicated 73% replacement of $\alpha$-hydrogen by deuterium. Reaction mixtures contained 50 mg of deuterated phenylacetonitrile in 1 mL of 0.2 N methanolic KAc. After reaction for about 2 h at 48.8 °C it was worked up like acetophenone. Mass spectral analysis is somewhat more complicated because of overlapping peaks. The method of treating the data is described by Nibbering and de Boer.[24]

**Methyl Phenylacetate.** A solution of 7.5 g of methyl phenylacetate in 40 mL of $CH_3OD$ containing 0.5 N $CH_3ONa$ was allowed to react at room temperature for 1 h. The deuterated product was isolated by distillation. The mass spectrogram indicated 75% replacement of $\alpha$-H by D. Reaction mixtures contained 100 mg of ester in 3 mL of 0.0258 N $CH_3ONa$ in methanol. The reaction time was about 2 h at 27.7 °C and pressures up to 123 MPa. The workup and analysis were the same as for acetophenone in methanol.

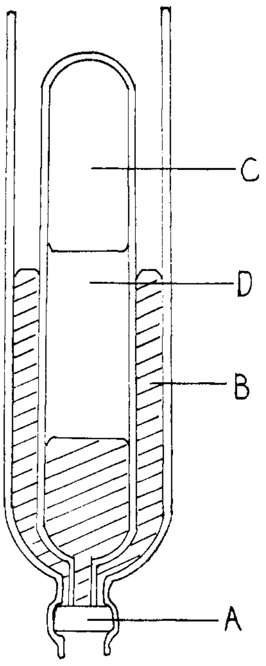

Figure 2. Reaction cell for $CHF_3$: (A) rubber septum, (B) mercury, (C) vapor space, (D) aqueous alkali.

**Dimethyl Sulfoxide.** Deuterated dimethyl sulfoxide (99.5%) was purchased from Fisher Scientific Co. Reaction mixtures contained 100 mg of sulfoxide in 1 mL of 0.85 N aqueous NaOH. After reaction for about 2 h at 71.0 °C under pressures up to 128 MPa the base was neutralized, and the water was evaporated by an air stream with slight warming. The residue was distilled in a small Kugelrohr, and all mass spectral parent peaks from $d_6$ through $d_0$ were measured.

**2-Nitropropane.** A mixture of 15 mL of 2-nitropropane and 15 mL of 2 N KOD in $D_2O$ was equilibrated by stirring for 24 h at room temperature. After purification the 2-nitropropane was analyzed by density and found to contain 0.9 deuterons per molecule. The rate of dedeuteration was measured by reacting 10-mL samples containing 100 $\mu$L of 2-nitropropane in 1 M aqueous sodium acetate at 65.0 °C for 3 h. Analysis was by IR with the same procedure used for chloroform. The most useful bands are at 1103 and 878 $cm^{-1}$ for the undeuterated and deuterated compounds, respectively.

The rate of deprotonation was measured by the method of Bell[25] using reaction mixtures containing 225 $\mu$L of 2-nitropropane and 3 mL of 0.0358 M $KI_3$ diluted to 50 mL with 1 M NaAc containing sufficient HAc to lower the pH to 7.3. The temperature was 21.0 °C and the time was 4 h. Pressures up to 133 MPa were used for both dedeuteration and deprotonation.

**Indene.** A mixture of 5 g of indene and 5 mL of 1 N $CH_3ONa$ in $CH_3OD$ was allowed to stand for 1 h, and the methanol was distilled off. A second 5-mL portion of $CH_3OD$ was added, and the procedure was repeated twice using 15 mL of $CH_3OD$ in all. Replacement of three exchangeable hydrogens was 84% complete. Reaction mixtures contained 50 mg of deuterated indene in 1 mL of 0.0833 N $CH_3ONa$ in methanol. The temperature was 29.5 °C and the reaction time was near 2 h. The workup and analysis were the same as for acetophenone in methanol. Data reduction is complicated by overlapping peaks as in the case of phenylacetonitrile, and it was necessary to observe all peak heights from mass number 115 through 119. As a precaution against error in the treatment of the data we adjusted the reaction times by trial and error to give almost identical mass spectra at several pressures. Under these conditions the ratio of rate constants is inversely proportional to ratio of reaction time.

**Phenylacetylene.** A solution of 3 g of sodium phenylpropiolate in 7 mL of $D_2O$ was heated in a sealed tube for 4 h at 125 °C. The layer of phenylacetylene which separated was dried and distilled. Deuteration was 100% of theoretical. Reaction mixtures contained 40 mg

**Table III.** Summary of Reaction Rate Constants

| | | | | | |
|---|---|---|---|---|---|
| $CDCl_3$ in $5.68 \times 10^{-4}$ N Aqueous NaOH at 26.0 °C | | | | | |
| *P*, MPa | 3.3 | 66.7 | 93.3 | 112 | 125 |
| $k \times 10^5$, $s^{-1}$ | 10.3 | 8.3 | 8.0 | 7.7 | 6.8 |
| $CDF_3$ in 0.85 N Aqueous NaOH at 65 °C | | | | | |
| *P*, MPa | 20.0 | 53.3 | 80.0 | 100 | 130 |
| $k \times 10^5$, $s^{-1}$ | 7.5 | 7.3 | 7.0 | 7.0 | 6.5 |
| $C_6H_5COCD_3$ in 0.0053 N Aqueous NaOH at 27.4 °C | | | | | |
| *P*, MPa | | 3.3 | | 117 | |
| $k \times 10^5$, $s^{-1}$ | 6.30 | 6.50 | 6.65 | 6.75 | |
| $C_6H_5COCD_3$ in 0.001 N NaOEt in Ethanol at 19.5 °C | | | | | |
| *P*, MPa | 3.3 | 111 | | | |
| $k \times 10^5$, $s^{-1}$ | 15.9 ± 0.28 | 16.6 ± 0.10 | | | |
| $C_6H_5COCD_3$ and 0.2 N Sodium *p*-Chlorophenoxide in 60/40 MeOH-HOH at 100.5 °C | | | | | |
| *P*, MPa | 3.3 | 53.3 | 111 | | |
| $k \times 10^5$, $s^{-1}$ | 11.3 ± 0.15 | 12.3 | 16.6 ± 0.10 | | |
| $C_6H_5CD_2CN$ in 0.2 N KAc in Methanol at 48.8 °C | | | | | |
| *P*, MPa | 3.3 | 53.3 | 133 | | |
| $k \times 10^5$, $s^{-1}$ | 10.3 ± 0.22 | 11.1 | 12.6 ± 0.15 | | |
| $C_6H_5CD_2CO_2Me$ in 0.0258 N $CH_3ONa$ in Methanol at 27.7 °C | | | | | |
| *P*, MPa | 3.3 | 66.7 | 123 | | |
| $k \times 10^5$, $s^{-1}$ | 12.0 ± 0.16 | 12.5 | 13.7 ± 0.16 | | |
| $CD_3SOCD_3$ in 0.85 N Aqueous NaOH at 71.0 °C | | | | | |
| *P*, MPa | 3.3 | 128 | | | |
| $k \times 10^5$, $s^{-1}$ | 11.3 ± 0.31 | 16.1 ± 0.36 | | | |
| $(CH_3)_2CDNO_2$ in 1 M Aqueous NaAc at 65 °C | | | | | |
| *P*, MPa | 0.1 | 133 | | | |
| $k \times 10^5$, $s^{-1}$ | 4.4 | 5.0 | | | |
| $(CH_3)_2CHNO_2$ in 0.94 M Aqueous NaAc with $KI_3$ at 21.0 °C | | | | | |
| *P*, MPa | 0.1 | 33 | 100 | 133 | |
| $k \times 10^6$, $M^{-1} s^{-1}$ | 2.44 | 2.56 | 2.58 | 2.58 | |
| Indene-*1,1,3*-$d_3$ in 0.0833 N $CH_3ONa$ in Methanol at 29.5 °C | | | | | |
| *P*, MPa | 3.3 | 26.7 | 53.3 | 130 | |
| $k \times 10^5$, $s^{-1}$ | 8.70 ± 0.13 | 9.05 | 9.65 | 10.62 ± 0.11 | |
| $C_6H_5C_2D$ in Tris Buffer (See Text) at 27.0 °C | | | | | |
| *P*, MPa | 3.3 | 26.7 | 53.3 | 128 | |
| $k \times 10^5$, $s^{-1}$ | 6.00 | 7.92 | 10.1 | 19.7 | |
| $Ph_2CD_2$ and $CH_3ONa$ in MeOH/$Me_2SO$ (See Text) at 109.0 °C | | | | | |
| *P*, MPa | 6.6 | 133 | | | |
| $k \times 10^5$, $s^{-1}$ | 9.7 ± 0.5 | 10.8 ± 1.0 | | | |
| $C_6H_5COCH_3$, 0.388 M, and $NaBH_4$, 0.097 M, in $Me_2CHOH$ at 22.0 °C | | | | | |
| *P*, MPa | 0.1 | 33.3 | 66.7 | 100 | 133 |
| $k \times 10^4$, $M^{-1} s^{-1}$ | 8.8 ± 0.2 | 9.3 | 11.8 | 13.0 | 13.0 |
| $C_6H_5CHO$ Cannizzaro Reaction (See Text) at 100.0 °C | | | | | |
| *P*, MPa | 0.1 | 33.3 | 66.7 | 100 | |
| $k \times 10^4$, $M^{-2} s^{-1}$ | 2.20 | 3.20 | 4.05 | 5.13 | |
| $C_6H_5CH_2CO_2Et$ and 0.005 N $CH_3ONa$ at 24.3 °C (Ester Interchange) | | | | | |
| *P*, MPa | 0.1 | 33.3 | 66.7 | 113 | |
| $k \times 10^4$, $s^{-1}$ | 1.78 ± 0.06 | 2.11 | 2.39 | 3.33 | |

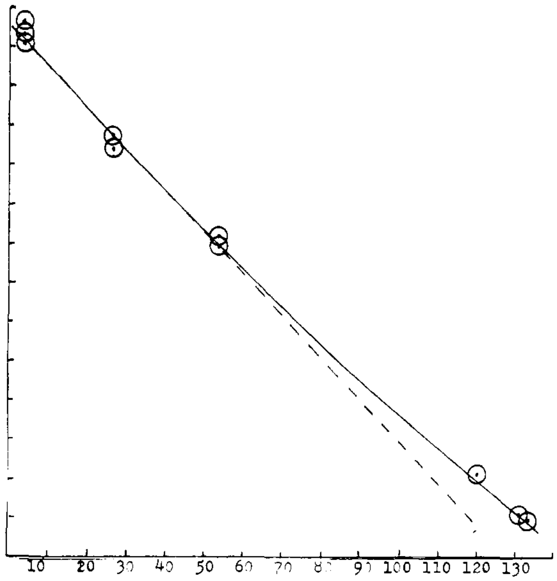

**Figure 3.** Plot of $-\ln k$ ($min^{-1}$) vs. *P* (MPa) for $PhC_2D$.

of $PhC_2D$ in 3 mL of 60% aqueous methanol which was 0.0051 N in Tris and 0.0038 N in HCl. The temperature was 27.0 °C and times ranged from 80 to 200 min. Partially dedeuterated phenylacetylene was isolated for mass spectral analysis by ether extraction as in the case of aqueous acetophenone. A plot of ln *k* vs. *P* is shown in Figure 3 and is fairly typical of other graphs obtained in this study except for the curvature. The uncertainty in the graphical extrapolation of the slope to zero pressure is not susceptible to theoretical analysis at present. The apparent activation volume of −28 mL which was calculated from $-RT(\delta \ln k/\delta P)_T$ contains the volume of ionization of the solvent. Solutions of 0.1 N NaOH and HCl in 60/40 methanol/water were allowed to mix in a dilatometer after thermal equilibration, and the volume change was −25 ± 1 mL/mol. It seems reasonable that the value should be slightly more negative than the widely accepted value of −21 mL for pure water. Subtraction of the volume of ionization from the apparent activation volume gives a net of −1 ± 2 mL/mol.

**Diphenylmethane.** A mixture of 1 g of diphenylmethane, 1 mL of 1.5 N $CH_3ONa$ in $CH_3OD$, and 1 mL of $CD_3SOCD_3$ was maintained at 130 °C for 30 h. After partition between water and ether, the layer containing diphenylmethane was dried and distilled. The mass spectrum indicated 64% replacement of $\alpha$-hydrogen. Reaction mixtures contained 100 mg of deuterated diphenylmethane in 1 mL of 1 N $CH_3OK$ in 75/25 methanol/$Me_2SO$ mixture. The temperature was 109.0 °C and times ranged from 8 to 16 h. Workup and analysis resembled that of acetophenone.

**Borohydride Reduction of Acetophenone.** The reaction rate was determined by the method of Brown.[26] The reaction mixtures contained a stoichiometric quantity of acetophenone (0.242 mL) in 5 mL of 0.103 M $NaBH_4$ in isopropyl alcohol. The reaction time was about 1 h at 22.0 °C.

**Cannizzaro Reaction of Benzaldehyde.** The reaction rate was determined by the method of Wiberg.[27] A polyethylene bell was substituted for the glass bell used in most experiments in order to prevent etching by the hot solution of alkali in aqueous methanol. The reaction time was 3-5 h at 100.0 °C.

**High-Pressure Apparatus.** An Aminco Micro Series reactor and hand-operated hydraulic pump were used. The temperature was stabilized by a 200-lb aluminum ingot which has been bored to fit the reactor snugly. The temperature was controlled to 0.05 °C. For most experiments the outer tube shown in Figure 2 had a closed end rather than a rubber septum.

**Calculation of Activation Volumes.** The logarithm of the rate constant was plotted against pressure as shown in Figure 3, and the best straight line was drawn through the origin and other points. Figure 3 is atypical in that it shows a curvature at the higher pressures. The slope is used in the calculation of activation volume according to the equation.

$$-RT(\delta \ln k/\delta P)_T = \Delta V^*$$

A summary of reaction rate constants is given in Table III.

**Errors of Measurement.** Typically, measurements of reaction rate are accurate to about 3%. The range of deviations from the mean in this study is 1-9% as shown in Table III. In a number of cases we replicated measurements at the highest and lowest pressures because these points have the greatest weight in determining the slope of ln *k* vs. *P*. An error of 3% in *k* over a pressure range of 100 MPa leads to a maximum error of 1 mL provided that there is no apparent curvature. For all compounds except phenylacetylene the curvature was much less than in Figure 3. In applying the activation volume to the characterization of transition states there is at present little value in reducing the error below 1 mL because structural isomers often differ by 1 mL in molar volume.

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# Effect of Aryl Substituents, Solvent, and Steric Effects on the Efficiency of Excited-State Carbonyl Production from 1,2-Dioxetanes

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**Abstract:** The efficiency of triplet carbonyl production was measured for a series of eight variously substituted 1,2-dioxetanes by using stimulated emission from 9,10-dibromoanthracene (DBA). Triplet efficiencies for some of the dioxetanes were also determined by isomerization of *trans*-stilbene. In some instances, singlet ($S_1$) efficiencies were measured by stimulated light emission from 9,10-diphenylanthracene (DPA). In agreement with most previous reports, high triplet/singlet ($S_1$) efficiencies were observed. The effect of solvent on the triplet efficiency was pursued with bis(*p*-anisyl)-1,2-dioxetane (DAD). Here, a change from benzene to methanol solvent decreased the triplet efficiency by 440-fold. The results of the efficiency study were interpreted in terms of a biradical mechanism. The variations in efficiency with changes in dioxetane structure and solvent are explained in terms of partitioning the singlet biradical ($S_R$) between singlet carbonyl products and the triplet biradical ($T_R$). An increase in the rate of production of $T_R$ is expected to increase the triplet efficiency. In general, triplet efficiencies for most dioxetanes are decreased with strongly electron-releasing groups, while triplet efficiencies are increased with increased steric effects. An approximate empirical correlation was noted between the activation energy for thermolysis of dioxetanes and the triplet efficiency ($\alpha_{T_1}$): % $\alpha_{T_1} = 7.24E_a - 156$, where $S_{yx}$ (the standard error estimate of $\alpha_{T_1}$ on $E_a$) is ±8.4%. From an analysis of the solvent effect on $\alpha_{T_1}$ for DAD, *a minimum value of* $\Delta G^{\ddagger} = 4$ kcal/mol *could be set for the decomposition of the singlet* biradical to ground-state carbonyl products in benzene solvent.

A select few classes of molecules possess the ability to produce electronically excited state products in a chemical reaction.[1] Dioxetanes are one class of molecules that can accomplish this feat in the course of thermal decomposition. Of added interest is the observation that ground-state singlet dioxetanes produce excited-state carbonyls that are largely in the triplet state.[1j] Understandably, the thermolyses of 1,2-dioxetanes have recently been an active area of investigation with the hope of unraveling the mechanism whereby triplet products result from a ground-state reactant.

A large portion of our previous work in this area has dealt with a kinetic analysis of various substituted dioxetanes, with the goal of gaining some insight to the mechanism of the thermolysis.[2] We now report the measurements of efficiencies of excited carbonyl production from the thermolysis of these substituted dioxetanes. Our intention was to see how structural modification of dioxetanes affected the efficiency of excited-state carbonyl formation and if these effects could be rationally correlated with our previous mechanistic studies. We have also used solvent variation as a probe to determine the interrelationship between the mechanism of dioxetane thermolysis and excited-state carbonyl production. Some tentative conclusions have been made, but it is clear that this is just a step in understanding the factors that govern the efficiency of excited-state carbonyl production from dioxetanes.

## Results

Preparation of the substituted 1,2-dioxetanes that were used in this study was previously reported.[2] The primary method of determining efficiencies of excited-state carbonyl products, formed from the dioxetanes, was by light emission methods. These methods have been employed in other laboratories and are probably the most convenient method of determining efficiencies.[3,4] In addition, the methods employing 9,10-dibromoanthracene (DBA) and 9,10-diphenylanthracene (DPA) as acceptors provide a unique method of counting triplet and singlet excited-state alkyl carbonyl products.[4]

With DBA as the excited-state energy acceptor in the thermolysis of a dioxetane, the apparent quantum yield ($\Phi_{App}$)

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