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EQUILIBRIUM ACIDITIES OF CARBON ACIDS

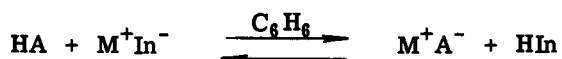
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Abstract - A scale of absolute equilibrium acidities for organic acids in dimethyl sulfoxide solution is presented, and these acidities are compared with: (a) apparent acidities in solvents of low dielectric constant, (b) absolute acidities in water, and (c) relative acidities in the gas phase. In dimethyl sulfoxide the carbon acid acetophenone is weaker than its oxygen analog, benzoic acid, by almost fourteen orders of magnitude, but the Hammett ρ for acetophenones is only one order of magnitude greater than for benzoic acids. This shows that large changes in the stabilities of ions in side chains may be accompanied by relatively small changes in ρ , and that the success of the Hammett equation rests, in part, on its relative insensitivity to energy changes.

INTRODUCTION

For the past 40 years organic chemists have been using a scale developed by McEwen as a guide to the relative acidities of weak acids and the relative stabilities of anions derived therefrom (1). Following a method developed by Conant and Wheland in ether (2), McEwen constructed his scale by determining, in a semiquantitative manner, the position of equilibrium in benzene solution between two weak acids, HA and HIn, one of which forms a colored (indicator) anion, In^- .



In a solvent of low dielectric constant, such as benzene, the metallic salts, M^+In^- and M^+A^- , exist as ion pairs or ion aggregates, and the relative stabilities of these ion pairs or clusters, as well as the relative acidities of the acids, HA and HIn, determine the position of the equilibrium. In other words, the apparent acidity of HA will depend on the nature of the reference base, M^+In^- , with which it is compared. Another disadvantage of the McEwen scale is that it is based on an arbitrary reference standard, the pK of methanol in methanol, which was taken as 16. The choice is arbitrary because, of course, the acidity of MeOH in benzene, if it could be measured free of ion pair effects, would be far less than that in methanol. The McEwen scale was brought up to date by Cram in 1965 in his MSAD scale by adding "pK's" determined by other investigators using similar methods in ether, cyclohexylamine, and the like (3). The relative acidities in the McEwen and MSAD scales are not really pK's, of course, since they are not on an absolute scale, and because the values are subject to change, depending on the reference bases chosen. As a result of work carried out in our laboratory during the past five years it is now possible to replace the McEwen and MSAD scales with an absolute acidity scale that is independent of the reference bases used to construct the scale. This absolute equilibrium acidity scale will be presented in this paper and used to examine a number of structure-reactivity relationships.

ABSOLUTE ACIDITY SCALE IN DIMETHYL SULFOXIDE

The absolute equilibrium acidity scale was constructed by adapting the Conant-Wheland-McEwen method to a solvent, dimethyl sulfoxide, which has solvation and dielectric properties such that, in dilute solution, ion pairing is avoided. The scale was anchored on absolute acidities in the 7 to 12 pK range that had been determined by potentiometric and spectroscopic methods. It was expanded to the 12 through 32 pK region by overlapping of about 20 standard acids having colored anions (indicators) and about 20 standard acids having colorless anions (4). Two different indicators (or standard acids)

were used for each pK determination. Determinations with different indicators were generally within ± 0.05 pK unit of one another, and the overall accuracy in the pK region 7 to 32 is believed to be ± 0.1 pK unit. The method can be applied to any acid within this region that forms an anion that is stable for a matter of minutes. The method has been applied to over 400 compounds of various structural types. A representative list is given in Table 1.

TABLE 1. Acidities of organic compounds in dimethyl sulfoxide

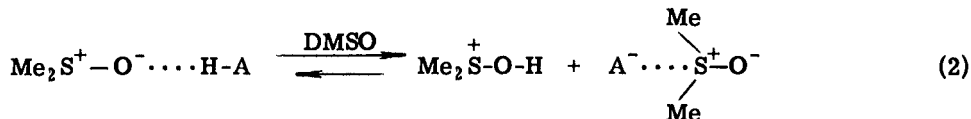
| Acid | pK | Acid | pK |
|---|------------------|---|-------------------|
| PhSO ₂ CH ₂ NO ₂ | 7.1 ₅ | p-PhCOC ₆ H ₄ NH ₂ | 24.4 |
| O ₂ NCH ₂ CO ₂ Et | 9.2 | PhCOCH ₃ | 24.7 |
| 9-CO ₂ Me-fluorene | 10.3 | CH ₃ CONH ₂ | 25.5 |
| 3-Nitropropene | 11.1 | Cyclohexanone | 26.4 |
| (PhSO ₂) ₂ CH ₂ | 12.1 | CH ₃ COCH ₃ | 26.5 |
| CH ₂ (COCH ₃) ₂ | 13.4 | c-PrSO ₂ CF ₃ | 26.6 |
| CH ₂ (CO ₂ Me) ₂ | 15.7 | PhCOC ₆ H ₄ CH ₃ | 26.8 |
| CH ₃ NO ₂ | 17.2 | (H ₂ N) ₂ C=O | 26.9 ₅ |
| CH ₃ SO ₂ NH ₂ | 17.5 | PhCH ₂ SOPh | 27.2 |
| 9-Ph-fluorene | 17.9 | PhC≡CH | 28.8 |
| Cyclopentadiene | 18.0 | PhSO ₂ CH ₃ | 29.0 |
| Indene | 20.1 | Xanthene | 30.0 |
| p-NO ₂ C ₆ H ₄ CH ₃ | 20.5 | Ph ₃ CH | 30.6 |
| Indole | 20.8 | Aniline | 30.7 |
| PhSCH ₂ CN | 20.8 | (PhS) ₂ CH ₂ | 30.8 |
| p-NO ₂ C ₆ H ₄ NH ₂ | 21.0 | 9-Methylantracene | 31.1 |
| (H ₂ N) ₂ C=S | 21.1 | CH ₃ SO ₂ CH ₃ | 31.1 |
| i-PrSO ₂ CF ₃ | 21.8 | CH ₃ CN | 31.3 |
| PhCH ₂ CN | 21.9 | Ph ₂ CH ₂ | 32.2 |
| Fluorene | 22.6 | CH ₃ SOCH ₃ | 35.1 |
| F ₃ CCH ₂ OH | 22.8 | NH ₃ | ~40 |
| (PhS) ₃ CH | 22.8 | PhCH ₃ | ~44 |
| Pyrrrole | 23.0 | PhSCH ₃ | ~49 |
| HCONH ₂ | 23.5 | CH ₄ | >70 |

ACIDITIES IN DMSO COMPARED TO THOSE IN OTHER MEDIA

Acidities in solvents of low dielectric constant

Direct comparisons of the pK values given in Table 1 with "pK's" determined in solvents of low dielectric constant, such as benzene (1), ether (2), diglyme (5), 1,2-dimethoxyethane (6), cyclohexylamine (CHA) (7), etc. are meaningless, since the latter are all relative to some arbitrary standard, often the pK of 9-phenylfluorene, which has been determined to be 18.5 in mixed aqueous solvents by the H₊ method. Nevertheless, there is often surprisingly good agreement between the relative "pK's" determined in these solvents and those determined in DMSO. This agreement has been established only for hydrocarbons, however, and breaks down even with these unless the two hydrocarbons being compared both form anions wherein the negative charge is highly delocalized. Thus, comparison of phenylacetylene with fluorenes gives widely differing results, depending on the solvent. Phenylacetylene forms an anion wherein the negative charge is essentially localized. Its absolute acidity in DMSO is 6 pK units lower than that of fluorene (Table 1). This contrasts sharply with the results in CHA, where the apparent

Examination of Table 2 shows that the acidities of strong inorganic acids are leveled in DMSO, just as they are in water. Despite the greater basicity of DMSO, the strong inorganic acids are not completely dissociated in this solvent, as they are in water. This must be due in part to the lower dielectric constant of DMSO (49 at 20° C vs. 80 for H₂O), but the ability of DMSO to stabilize the undissociated acid by acting as a strong H-bond acceptor, as contrasted with its inability to stabilize the conjugate base of the acid by acting as an H-bond donor, is no doubt of greater importance (equation 2).



Water is a unique solvent in being capable of forming strong H-bonds when acting in either a donor or acceptor capacity. Its ability to act as a strong H-bond donor, whereas DMSO cannot, accounts for the much greater acidity in water of acids that dissociate to given anions in which the negative charge can be delocalized to oxygen (sulfonic acids, sulfonamides, carboxylic acids, nitroalkanes, ketones, etc.). This effect can also be used to explain the greater acidity in water of acids in which the negative charge resides on nitrogen or sulfur (Table 2). For acids dissociating to give anions in which the negative charge resides to an appreciable extent on carbon, H-bonding is much weaker. For such acids stabilization of the anion by the (stronger) dipole and polarizability properties of DMSO may balance the superior H-bonding properties of water. As a result, hydrocarbons, sulfones, sulfoxides, nitriles, and the like may be nearly as acidic in DMSO as in water, or more so (Table 2).

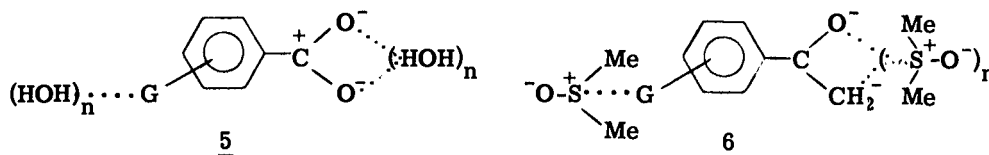
Acidities in the gas phase and in DMSO

Substituent effects in *m*- and *p*-substituted benzoic acids are severely attenuated in water or DMSO, relative to the gas phase. (The Hammett ρ 's are 1.0, 2.5, and ~ 10 , respectively.) This suggests that very strong, specific solvation forces are being exerted at the carboxylic acid group in solution and that the polar and resonance effects of the ring substituents are small by comparison. On the other hand, in several series of carbon acids, such as CH₂(CN)₂, PhCH₂CN, CH₃CN, a plot of relative gas phase acidities versus relative DMSO acidities is roughly linear with a slope near one. It would appear that, when the negative charge is distributed over a substantial part of the anion, as is true for CH(CN)₂⁻, PhCHCN⁻, and CH₂CN⁻ anions, solvation by DMSO is nonspecific and relatively constant (9). In such instances the structural effects on relative acidities in DMSO approach those in the gas phase in size. Additional correlations of this type have been made between enthalpies of deprotonation of weak acids (which are linearly related to DMSO acidities) and gas phase acidities (10).

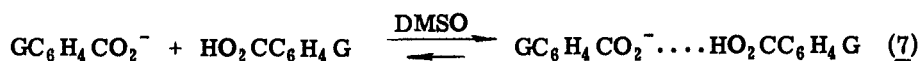
REMOTE SUBSTITUENT EFFECTS

Hammett correlations

There are literally thousands of successful correlations between the effects of *m*- and *p*-substituents on the equilibrium acidities of benzoic acids in water (or 50% EtOH-H₂O) and equilibrium or rate data in other like-substituted benzene systems. The success of these Hammett relationships is remarkable when one considers that the sigma "constants" derived from equilibrium data in water are being related to rate, as well as equilibrium data, for reactions carried out in all types of solvents, as well as in the gas phase. In an earlier section we observed large differences in the abilities of water and DMSO in stabilizing anions (Table 2). We know, for example, that in water benzoate ions and acetophenone enolate ions are strongly H-bonded, whereas in DMSO they are not. The difference in solvent stabilization, as judged by pK differences (Table 2) is of the order of 10 kcal/mole. In addition, we can expect differences in solvation of H-bond acceptor groups, G, when such groups (e.g., MeO, Me₂N, C=O, S=O, NO₂, etc.) are present in the *m*- or *p*-positions of the benzene rings in such anions. These solvation effects in H₂O and DMSO are illustrated in structures 5 and 6.



The importance of H-bonding effects in stabilizing anions is demonstrated further by the observation that the anions of oxygen acids, such as carboxylic acids, phenols, and alcohols, interact with their conjugate acids to form complexes (e.g. 7), even in dilute DMSO solution (11).



Acetophenone, the carbon analog of benzoic acid, is a weaker acid than benzoic acid in DMSO by nearly 14 pK units. (The acidity of benzoic acid in water is higher still by another 6.8 pK units.) One might then expect the acidities of acetophenones in DMSO to be much more sensitive to aryl substituent effects than is true for benzoic acids in water (or DMSO). Also, considerable variation in substituent effects between the two systems would be expected because of the variation of solvation of the individual substituents (compare 5, 6, and 7). In other words, according to this reasoning, the ρ value for acidities of acetophenones in DMSO should be large compared to that for benzoic acids in water (or DMSO), and correlation with Hammett σ constants should be poor. Instead, we find (12) that ρ for acetophenones is not particularly large ($\rho = 3.60$, as compared to 2.5 for benzoic acids in DMSO) and that the Hammett plot is good ($r = 0.992$). We conclude that the negative charge in enolate ion side chain of 6 is so strongly stabilized by DMSO molecules that the negative charge in the benzene ring remains relatively small. For this reason the acidities of acetophenones in DMSO are surprisingly insensitive to changes in the polar nature of G, and even less sensitive to changes in solvation of G. Some idea of the magnitude of the solvation effects stabilizing the enolate ions (6) can be obtained from estimates of the single ion solvation enthalpies in going from the gas phase to water or DMSO solutions. For chloride ion these are 86.8 and 81.7 kcal/mole, respectively (13). Judging from these data, the energies of solvation of the enolate ions (6) in DMSO are large, although not as large as the energies of solvation of the benzoate ions (5) in water. These large solvation forces will be concentrated in each instance around the negatively charged atoms in the side chain. Stabilization of the CO_2^- and ArCOCH_2^- functions by the polar effect of G in 5 or 6 turns out to be small compared to these large solvation effects. For example, the acidifying effect on benzoic acid in water by the "powerful" p-CN group amounts to only 0.9 kcal/mole; the acidifying effect of p-CN on acetophenone in DMSO amounts to 3.7 kcal/mole. It is understandable, then, why the even smaller changes in solvent stabilizing (or destabilizing) effects on G caused by a change in solvent from H_2O to DMSO are not noticeable. We see that even though the PhCOCH_2^- ion in DMSO is less stable by ca. 19 kcal/mole than is the PhCO_2^- ion in water (judging from pK data) the solvation forces on the enolate ion function are still so large that stabilization by the polar effect of m- or p-G remains small by comparison. This must be a general phenomenon, and we conclude that one of the reasons for the remarkable success of the Hammett equation is that the small differences in the electrostatic effects of meta and para substituents are generally submerged in a large sea of solvent effects operating at the reaction site. The result is to level out differences in substituent effects, making the Hammett equation a relatively insensitive probe for changes occurring at the reaction site. When acidities of carbon acid systems in which the charge in the anion is on a carbon atom directly attached to the ring, as in ArCH_2EWG , are examined in DMSO, the sensitivity to substituent effects is found to increase by ca. 2 orders of magnitude. For example, ρ for the ArCH_2CN system in DMSO is 5.5 (14) as compared to 3.6 for ArCOCH_3 . The negative charge in the ArCHCN^- ions apparently still remains largely in the side chain, however, and the leveling effect of the solvent is still enormous. It is only when the electron-withdrawing group (EWG) is replaced by hydrogen, i.e., in m- and p-substituted toluenes, $\text{GC}_6\text{H}_4\text{CH}_3$, that the negative charge becomes extensively delocalized into the benzene ring. Now solvation by DMSO changes from specific to general, and the full force of the electrostatic effect of G is brought into play. The result is an increase in ρ by 10 orders of magnitude for ArCH_3 , relative to ArCH_2CN . It seems likely that the ρ observed for the acidities of toluenes in DMSO solution ($\rho \approx 15$) will rival that for the gas phase acidities.

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MICELLAR CATALYSIS AND INHIBITION

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Abstract - Micelles of non-functional surfactants (detergents) can catalyze bimolecular reactions by bringing reactants together in an environment conducive to reaction and they inhibit reactions by keeping reactants apart but they affect rates of unimolecular reactions by providing a submicroscopic medium. The relation between rate and surfactant concentration can be explained in terms of the distribution of reactants between the aqueous and micellar pseudophases which can also be perturbed by added solutes. Catalysis depends upon the charge type of the reaction and reactant hydrophobicity. Functional micelles are often highly effective as nucleophilic or general base catalysts and can give chiral recognition. Substrate micellization can control reaction stereochemistry.

INTRODUCTION

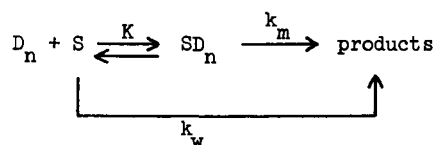
Micelles are submicroscopic aggregates of surfactants (detergents, amphiphiles) which have a hydrophobic residue and an ionic, zwitterionic or polar head group (Ref. 1). Typical ionic surfactants are: cationic, hexadecyltrimethylammonium bromide (CTABr), $n\text{-C}_{16}\text{H}_{33}\text{NMe}_3\text{Br}$; and anionic, sodium dodecylsulfate (NaLS, SDDS), $n\text{-C}_{12}\text{H}_{25}\text{OSO}_3\text{Na}$. Many commercial nonionic surfactants, e.g., Brij, Igepal and Triton are polyethylene oxides with a hydrophobic end group. In dilute aqueous solution ionic surfactants are strong electrolytes, but at the critical micelle concentration (cmc) there are sharp changes in such bulk properties as conductivity and surface tension, and light scattering shows that aggregates form. The cmc decreases with increasing length of the n -alkyl group, e.g., from 7×10^{-2} M for $\text{C}_{10}\text{H}_{21}\text{NMe}_3\text{Br}$ to 9×10^{-4} M for $\text{C}_{16}\text{H}_{33}\text{NMe}_3\text{Br}$ (Ref. 2), and is consistently lower for nonionic than for ionic surfactants, but for ionic surfactants it is relatively insensitive to the sign of the charge on the head group. In water micelles generally contain more than 50 monomer units and the aggregation numbers are larger for nonionic than for ionic micelles where coulombic repulsions oppose the hydrophobic and van der Waals interactions which hold the micelles together. Addition of salts and nonionic hydrophobic solutes increases micellar size and reduces the cmc by reducing interionic head group repulsions and introducing favorable hydrophobic interactions.

At relatively low surfactant concentration micelles are spheroidal, but they grow and elongate at higher surfactant concentration, especially in the presence of hydrophobic solutes (Ref. 1 & 3). Most kinetic studies have used conditions in which the micelles are approximately spheroidal and increase in micellar size, of itself, does not seem to affect the reaction rates (Ref. 4), although they are affected by added salts which change the surface charge of the micelle.

An idealized model of a (spherical) ionic micelle has a hydrocarbon-like interior which is surrounded by the so-called Stern layer containing the ionic head groups and bound counterions. There is then the broader Gouy-Chapman layer into which counterions are attracted (Ref. 1). It is generally assumed that counterions in the Stern layer are closely associated with the micelle, but there is generally a rapid exchange between solutes in the micelle and in bulk solvent and between monomeric and micellized surfactant, so that our definition of the micellar boundary is an arbitrary one, and it has been suggested that the micellar boundary should be defined in terms of the region of electric neutrality between micelle and bulk solvent rather than in terms of the boundary of the Stern layer (Ref. 5). Although the present discussion is concerned only with the normal micelles which form in water and in some other highly associated solvents (Ref. 6), reversed micelles, with the ionic or polar head group in the micellar interior, form in many nonpolar solvents. These micelles are often very effective catalysts and their chemical and physical properties are exciting considerable interest (Ref. 7). With both these systems, as with polyelectrolytes, we are studying reactions at the surfaces of submicroscopic aggregates, which in some respects model interfaces in biological systems.

Hydrophobic solutes and counterions will be attracted to the micelle so that a cationic micelle should assist reaction between neutral molecules and anions, whereas an anionic micelle will inhibit such a reaction (Ref. 8 - 11). Micelles may affect the rates of spontaneous, unimolecular reactions by attracting the substrate and providing an environment which is more or less favorable to reaction than the bulk solvent. Micellar effects on ionic equilibria were initially interpreted by Hartley (Ref. 12) in terms of micellar charge and reaction charge type, and his concepts have been successfully applied to rates, with the prediction that cationic micelles will catalyze, and anionic micelles inhibit, reaction between a neutral substrate and an anion. This coulombic role tells us nothing about the effects of non-ionic micelles, but they sometimes inhibit reactions of hydrophobic substrates which enter the micellar interior where they are protected from hydrophobic reagents (Ref. 13). There are also many examples of reactions of sparingly water soluble compounds being run effectively on a preparative scale using such adducts as quaternary ammonium ions or cationic or non-ionic surfactants (Ref. 14 & 15), but in many of these systems the important factors are phase transfer (Ref. 15), or dispersion of the insoluble reactant (Ref. 16).

The simplest model for micellar catalysis or inhibition is:



where S is the substrate and D the surfactant (detergent), and D_n the micelle. Provided that we assume that only one substrate molecule is incorporated into n each micelle, that the reactants do not change the micellar properties, and that k_w is unaffected by added surfactant we can write (Ref. 9 & 10):

$$k_\psi = (k_w + k_m K C_m) / (1 + K C_m) \quad (1)$$

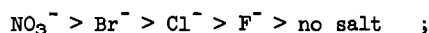
where the concentration of micelles, $C_m = (C_D - cmc)/N$, and N is the aggregation number of the micelles. These assumptions require that the surfactant be in large excess over the substrate, and most experiments have been done under these conditions. For this reason most workers use substrates whose reactions can be followed by a sensitive analytical technique, e.g., spectrophotometry, so that nitrophenyl derivatives are very popular substrates.

Equation 1 is akin to the well known Michaelis-Menten equation and is usually rearranged into the reciprocal form (Ref. 17), which is analogous to the Lineweaver-Burk equation as applied to enzymic reactions:

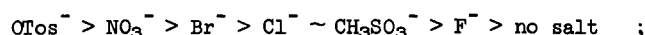
$$\frac{1}{k_\psi} = \frac{1}{k_w - k_m} + \frac{1}{(k_w - k_m)} \frac{N}{K(C_D - cmc)} \quad (2)$$

Equations 1 and 2 are successful in treating micellar inhibition and micellar catalysis of unimolecular reactions where rate constants increase with increasing surfactant concentration above the cmc to plateau values when all the substrate is in the micelles (Ref. 4, 9, 10 & 17). But many bimolecular reactions give rate maxima because equations 1 and 2 do not take into account the distribution of both reagents (Ref. 8 - 10, 18 & 19). Qualitatively we can assume that the rate will increase as both reactants are brought together in the micelle, but once one of the reactants is almost wholly in the micelles a further increase in surfactant concentration will "dilute" the reactants in the micellar pseudophase. There are, however, some bimolecular reactions which give rate-surfactant plateaux, and they appear to involve hydrophobic reactants of structures such that incorporation of one reactant into the micelle assists incorporation of the other. Some examples are: aromatic nucleophilic substitution by PhS^- and reactions of triarylmethyl carbocations with OH^- or BH_4^- catalyzed by cationic micelles. Association constants, K , have been determined directly, e.g., by gel filtration or solubility, and by kinetic analysis. They are as large as 10^8 for hydrophobic substrates.

Before considering further the failure of the quantitative treatment as applied to many bimolecular reactions it will be useful to consider qualitatively the decrease of micellar catalysis brought about by added salts, as shown below by the following sequences of inhibition. For the reaction of OH^- with carboxylic esters in cationic micelles the inhibition follows the anion order:

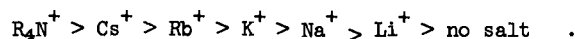


and for the corresponding reactions of halonitrobenzenes and triaryl phosphates it is:



but for the acid hydrolysis of trimethylorthoobenzoate in anionic micelles inhibition follows

the cation order:



The salt inhibition clearly depends on the nature of the added ion of opposite charge to the micelle. For univalent ions the large effects are given by low charge density, hydrophobic, ions which interact strongly with the micelle and compete for it with ionic reagents (Ref. 20). The salt orders of inhibition depend little upon the nature of reactions of the same charge type, except for a few unimolecular reactions where the salt effects are anomalous (Ref. 21). These anomalies can be understood in terms of changes in the structure of the micelle, and in general counterions reduce micellar catalysis by excluding ionic reagents from the micelle. These negative salt effects show very clearly that reaction actually occurs on the micelles and that one ion can displace another at the micellar surface so that even in the absence of added electrolyte we must consider the distribution of reagents between micelles and bulk solvent.

This problem of the distribution of more than one reagent between micelles and bulk solvent, which complicates the simple quantitative treatment, has been treated by several groups. (a) One approach is to use electrochemical methods to determine the distribution of an ionic reagent between water and the micelles. (The distribution of nonionic reagents can often be determined directly.) For example we can assume that pH will measure only the concentration of hydrogen ions in water, and for a specific hydrogen ion catalyzed reaction in the presence of anionic micelles we can calculate the number of hydrogen ions bound to the micelle, and therefore the second order rate constant with respect to the concentration of both reagents in the micelles. This approach has been applied to acetal hydrolysis in NaLS, and the corrected second order rate constants do not vary appreciably over a range of concentrations of acid and surfactant (Ref. 19). (b) A somewhat similar approach has been to use relatively hydrophobic reagents whose concentrations in the micelle can be determined directly (Ref. 22). This method has been applied to a number of nucleophilic additions and substitutions by Berezin and his coworkers who used solubility to determine the distribution of hydrophobic reagents between micelles and bulk solvent, for such reactions as ester deacylation by aldoximes, and aromatic nucleophilic substitution (Ref. 18 & 23). (c) A third approach is to treat distribution constants between water and the micelle as disposable parameters, and so evaluate rate constant-surfactant profiles which fit the observed profiles (Ref. 24). This approach also treats negative salt effects in terms of a competition for the micelle between a reacting ion and an inhibiting ion.

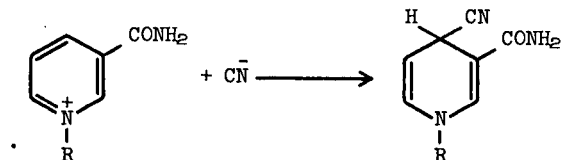
All these methods show that in bimolecular micellar catalyzed reactions we must consider the distribution of both reagents between the micelles and bulk solvent. Each method introduces its own uncertainties, for example added surfactants may alter the properties of a glass electrode or liquid junction (Ref. 19), and the distribution constants of two hydrophobic solutes between water and micelles may not be mutually independent, because either may alter the micellar properties and so affect the incorporation of the other. (The effect of added thiophenoxide ion on the interaction of CTABr with a fatty acid is discussed in Ref. 25.) However in principle these methods allow us to measure rate constants in the micellar phase. Unfortunately different investigators have measured the concentrations in different ways. The concentration of aqueous solutes is generally measured in molarities, and for dilute solution this measure gives the relative numbers of solute and solvent molecules or ions. The concentration of solutes in the micellar pseudophase can also be measured in terms of moles per unit volume, but then we have to choose our volume element. If we use the total volume of the micelle we have the problem that the solute is not distributed uniformly throughout the micelle (Ref. 18 & 23), because polar or ionic solutes will be located in the Stern layer at the micellar surface, and alternatively we can estimate the volume of the Stern layer and use this as our volume element (Ref. 24). Another approach is to ignore micellar volumes and to calculate concentrations in terms of mole fractions, and to compare the number of solute molecules per micellar head group with the number per solvent molecule (Ref. 19).

Thus our comparison of second order rate constants in water and in the micelle depends on our arbitrary choice of volume element, but despite this problem the results suggest that for many bimolecular reactions the second order rate constants are little larger, and may even be smaller, than in water, showing that micellar catalysis is often due largely to the increased reagent concentrations in the micelles as compared with bulk solvent (Ref. 18, 19, 23 & 24). It has been pointed out by a number of workers that the formation of bimolecular transition states involves considerable loss of translational, and sometimes, rotational entropy, and bringing reagents into a small volume element, prior to transition state formation, is a powerful mode of catalysis. This is the principle of the so-called intramolecular catalysis (Ref. 26), and it can also apply to catalysis at other submicroscopic surfaces e.g., enzymes or polyelectrolytes, where we should also consider the distribution of reagents, e.g., hydrogen ions, between reaction site and bulk solvent.

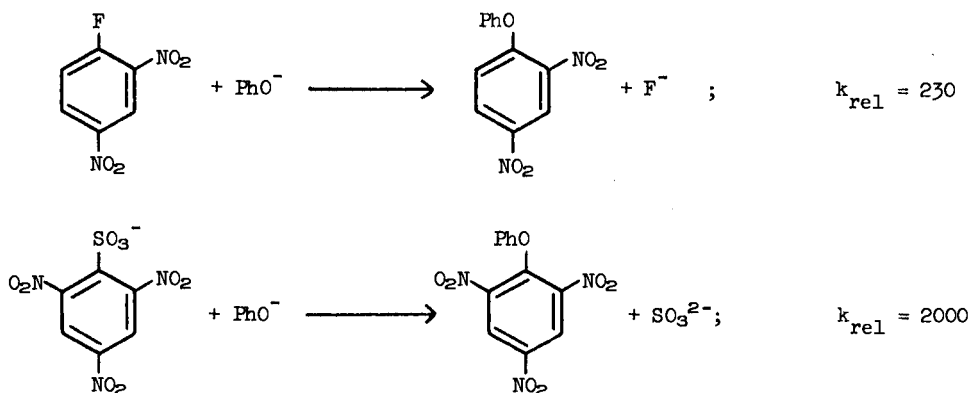
We should not assume that only this concentration effect is important in micellar catalysis. It plays no part in the catalysis of unimolecular reactions, for example cationic micelles effectively catalyze unimolecular anionic decarboxylations (Ref. 21), and the unimolecular elimination of PO_3^- from dinitrophenyl phosphate dianions (Ref. 4 & 17), and typically S_N1

reactions are inhibited by micelles (Ref. 21b and 27). In these reactions the micelle behaves as a submicroscopic solvent which can either assist or inhibit reaction.

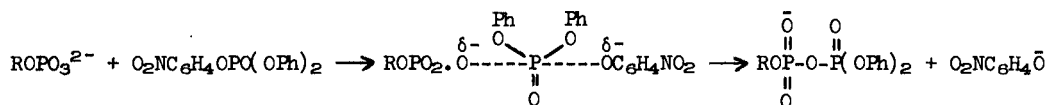
For some bimolecular reactions the variation of overall reaction rate with substrate seems to depend upon both the second order rate constants and reactant concentration in the micellar pseudophase. The cationic micellar catalysis of addition of cyanide ions to N-alkyl pyridinium ions increases with increasing length of the alkyl group (Ref. 28), possibly because this group draws the reaction center more deeply into the Stern layer of the cationic micelle and creates an unfavorable initial state coulombic interaction which is lost in forming the transition state:



A similar pattern is shown by the reactions of phenoxide ion with 2,4-dinitrofluorobenzene and 2,4,6-trinitrobenzenesulfonate in CTABr, because all the reagents should interact strongly with the micelle.

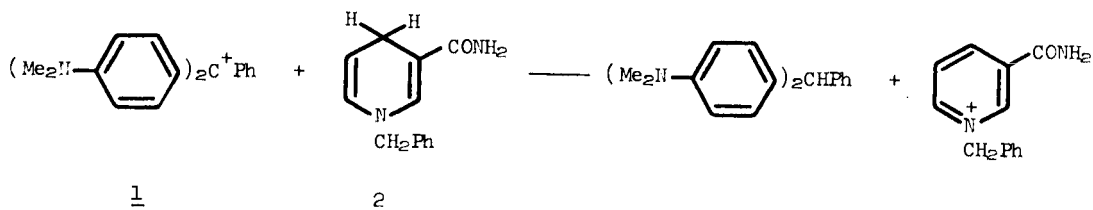


Another example of the micelle apparently acting as a submicroscopic medium in a bimolecular reaction comes from phosphorylation:



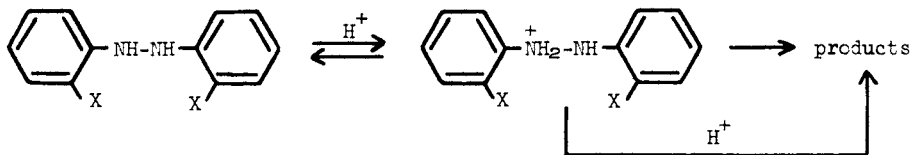
This reaction is catalyzed by cationic micelles, for example with R=H-; C₆H₅-; n-C₁₀H₂₁-; n-C₁₂H₂₅-, and the catalysis increases with increasing hydrophobicity of R (Ref. 29 & 30). Instead of using a cationic micelle we can make R sufficiently hydrophobic for the alkyl phosphate dianion itself to micellize, but although these anionic micelles should take up the hydrophobic substrate and bring it into close proximity with the nucleophile, they are poor catalysts, suggesting that the anionic transition state is best stabilized by cationic centers

Micellar effects upon reactions of carbocations with nucleophiles have been extensively studied (Ref. 31 & 32), and provide other examples in which micellar catalysis depends not merely upon the bringing together of the reagents but upon the interaction between the head groups and the reactive centers. Reactions of triarylmethyl dye cations, e.g., Malachite Green (1) with hydroxide and borohydride ions are catalyzed by cationic and inhibited by anionic micelles (Ref. 31 & 33). The reaction with 1-benzylidihydronicotinamide (2) is catalyzed by anionic micelles but cationic micelles have almost no effect, even though they should take up both reactants, probably because of unfavorable interactions between the cationic head groups and the developing pyridinium ions.



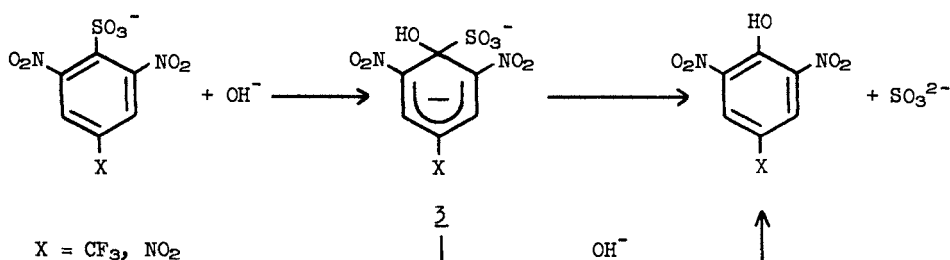
The catalysis of the reaction of borohydride ion (300-fold) is much greater than that of hydroxide ion (15-fold), illustrating the importance of hydrophobicity of an ionic reagent.

The conclusion that concentration of the reagents into the Stern layer of a micelle is one of the key ingredients in catalysis suggests that for similar substrates the catalysis should increase with increasing reaction order. The benzidine rearrangement is a good candidate for this test, because both one and two proton rearrangements can be observed using structurally similar substrates; e. g.,



When $X = \text{H, Me, OMe}$, the products are diaminobiphenyls, and the two proton rearrangements are powerfully catalyzed by anionic micelles of NaLS by up to 5000-fold, but for a one proton rearrangement ($X = \text{OMe}$), the catalysis is only ca. 50-fold (Ref. 34).

However generalizations are dangerous, because a different pattern is followed for the reaction of hydroxide ion with activated arenesulfonates, which involves addition followed by spontaneous and base catalyzed decomposition of an addition complex.

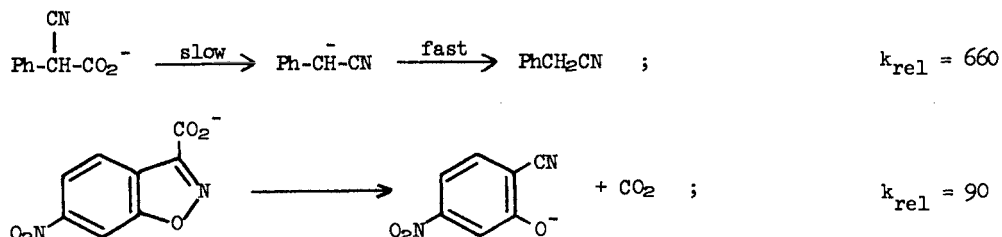


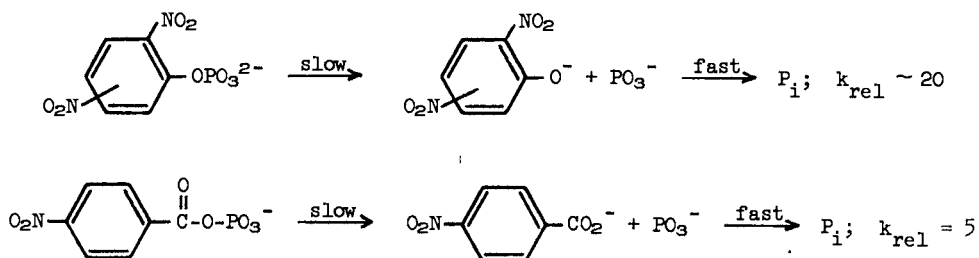
In dilute hydroxide ion the reaction is catalyzed by cationic micelles of CTABr (Ref. 35), as is typical of aromatic nucleophilic substitutions (Ref. 36), but the micellar catalysis decreases with increasing hydroxide ion concentration, showing that the micelle provides an environment which is unfavorable to the hydroxide ion catalyzed decomposition of the intermediate (3).

RELATION BETWEEN MICELLAR CATALYSIS AND SUBSTRATE STRUCTURE

Incorporation of reactants into the micelle is essential and increases with increasing reactant hydrophobicity. Its importance can be seen very clearly by comparing micellar catalysis for a series of similar reactions involving different nucleophiles, for example in nucleophilic aromatic substitution the maximum catalysis by CTABr of reactions of 2,4-dinitrofluorobenzene with hydroxide, phenoxide and thiophenoxide are 60, 230 and 1100 respectively (Ref. 36). It appears that reactant structure influences not only distribution of reactants between solvent and micelles, but also the relative free energies of reactants and transition state in the micelles, i. e., the specific reaction rate in the micelles.

Pearson's concept of hard and soft reagents (Ref. 37), provides a useful rationalization of micellar catalysis. For example a quaternary ammonium ion is a very soft reagent, which should interact more readily with a soft low charge density anion than with a hard anion. For unimolecular reactions having anionic transition states micellar catalysis should be greatest when a hard anion in the initial state is converted with a soft, low charge density, transition state; and this generalization is shown very clearly by considering some spontaneous unimolecular decarboxylations (Ref. 21), and dephosphorylations (Ref. 17 & 38):





In the decarboxylations transition states have considerable carbanionic character, and the catalyses are large. In reactions of the dinitrophenyl phosphate dianions the transition state is akin to a phenoxide ion, with much of the negative charge on oxygen, and the micellar catalysis is smaller, and in reaction of an acyl phosphate dianion the leaving carboxylate ion has all its charge on oxygen, and the micellar catalysis is even smaller (Ref. 38). In these unimolecular reactions there is a clear relation between the rate enhancements by a cationic micelle and the dispersion of negative charge in the transition state, i.e., the softness of the transition state.

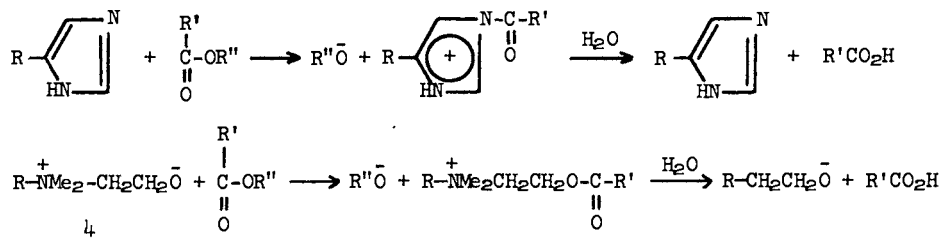
It is not so simple to test this hypothesis for bimolecular reactions where more than one reactant is taken up by the micelles, but for reactions involving hydroxide ion as a nucleophile micellar catalyses appear to be larger for nucleophilic aromatic substitution where the transition state is carbanion like than for deacylations of esters and related compounds where the negative charges in the transition state are on oxygen. These differences should not be due to differences in the hydrophobicities of the substrate, for example 2,4-dinitrochlorobenzene with a 60-fold catalysis in CTABr (Ref. 36a) should be no more hydrophobic than p-nitrophenyldiphenyl phosphate with an 11-fold catalysis (Ref. 13), and for some deacylations, e.g., that of p-nitrobenzoyl phosphate dianion by hydroxide ion (Ref. 38), the catalysis is only by a factor of 9 in CTABr, even though the cationic micelle should bring two anions together by coulombic attraction.

In this context I note that there are strong interactions between aromatic moieties and quaternary ammonium ions in both micellar and nonmicellar systems (Ref. 39), so that reactions in which negative charge is delocalized into an aryl group are generally effectively catalyzed by cationic micelles.

CATALYSIS BY FUNCTIONAL MICELLES

The phenomenon of "intramolecular catalysis" or "neighboring group participation" is well recognized in physical organic chemistry (Ref. 26), and analogies between it and micellar catalysis of a bimolecular reaction become even closer if one of the reactants is chemically bound to the micelle. There are now many examples of reactions in which a micelle of a functional surfactant is a very effective reagent (Ref. 40). Typically the functional group is a nucleophile or a general base, for example amino, thio or hydroxy, and because of the role of imidazole at the active site of many proteolytic enzymes many workers have used imidazole derivatives. The substrates have usually been carboxylic esters, although aryl carbonates and phosphates and activated aryl halides have also been used.

In most of these reactions the nucleophilic functional group attacks the reaction center giving a covalent intermediate, e.g., an acyl imidazole, and in a few cases formation of a covalent intermediate has been detected kinetically or spectrophotometrically (Ref. 41).



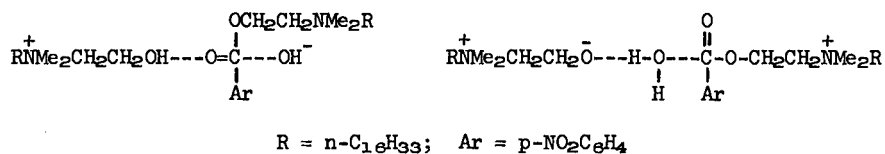
If the functional group acts as a base, e.g., if it activates a water molecule, it will not become bound in a covalent intermediate, so that detection of such an intermediate immediately demonstrates the mode of catalysis. This test is similar to the "burst" experiments often used to study the initial steps in enzymic reactions (Ref. 42), and it has been used to demonstrate initial acylation in reactions of carboxylic esters catalyzed by both imidazole (Ref. 41) and hydroxyethyl (Ref. 43) derived surfactants, where there is an initial

"burst" of *p*-nitrophenoxide ion, followed by a slower deacylation turnover step. A problem is that these experiments require the substrate to be in large excess over the functional surfactant, so that the micelles may be drastically affected by the substrate, e.g., their structures may be those of micellized substrate containing small amounts of the functional surfactant.

Another approach is to use the typical conditions of micellar catalysis, where the concentration of substrate is much less than that of surfactant, and to detect the covalent intermediate physically, e.g., spectrophotometrically. This method has been applied to the hydrolysis of 2,4-dinitrohalobenzenes catalyzed by the hydroxyethyl derived surfactant (4, R = C₁₆H₃₃).

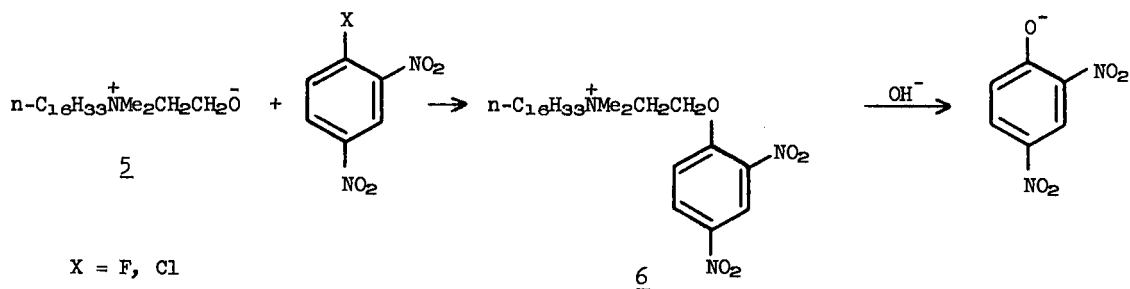
Evidence can also be obtained by choosing a system in which intermediate formation gives no chemical change. Micelles of hydroxyethyl derived surfactants (4) are effective catalysts of deacylation and of the hydrolysis of di- and trisubstituted aryl phosphates, and of S_N reactions of alkyl halides and addition of triarylmethyl carbocations (Ref. 44 - 46). For the dephosphorylations there is evidence that the first step is attack upon the phosphoryl group by the alkoxide moiety, and from the variation of reaction rate with pH a pK_a value of 12.4 (Ref. 44) has been estimated for micellized 4. (This value is lower than that of choline, pK_a = 13.9 (Ref. 47), because micellization increases acid strength.)

The catalyzed hydrolysis of carboxylic esters could, in principle, follow two routes: (i) nucleophilic attack giving an acyl intermediate (Ref. 43), or (ii) the hydroxy group of 4 could hydrogen bond to the ester, and activate it towards nucleophilic attack by hydroxide ion, or (iii) the alkoxide moiety could act as a general base and activate a water molecule. Transition state models for these general or acid base catalyzed reactions are shown for an ester in which nucleophilic attack would lead to no chemical change.



Thus if the hydroxyethyl-derived surfactant acted as a general acid or base it would always be a better catalyst than an otherwise similar nonfunctional micelle of, for example, CTABr. But if it acted as a nucleophilic catalyst it would, as it does, speed the hydrolysis of *p*-nitrophenyl esters, but not the reactions shown above. For these reactions it is an ineffective catalyst, suggesting that it always acts as a nucleophilic and never as a general acid-base (Ref. 48).

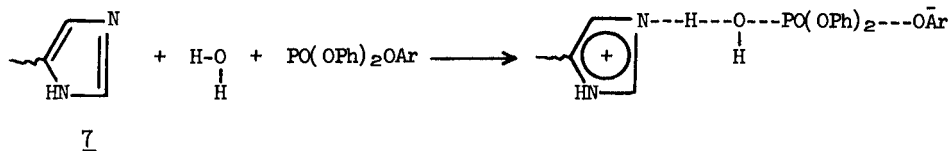
I noted earlier that for both uni- and bimolecular reactions catalysis by cationic micelles increases as we go to reactions in which there is extensive delocalization of charge in the transition state. The same pattern is shown for reactions in micelles of the hydroxyethyl surfactant (4) which involve the zwitterion (5). The first step of hydrolysis of fluoro- and chloro-2,4-dinitrobenzene catalyzed by 4 is formation of the ether (6) which then decomposes to products (Ref. 49).



The rate enhancements can be illustrated by considering the (hypothetical) molarity of hydroxide ion in water which would be required to give the same rate as 1M micellized zwitterion (5). This comparison is often used to illustrate the magnitude of intramolecular catalysis (Ref. 26). The molarities are: for 2,4-dinitrochlorobenzene, 410 M; for 2,4-dinitrofluorobenzene, 170 M; for *p*-nitrophenyldiphenyl phosphate, 8 M; for ethyl *p*-nitrophenyl phosphate monoanion, 3.5 M; and for *p*-nitrobenzoyl phosphate dianion, 4 M. We cannot make a direct comparison with reactions of carboxylic esters because of the different experimental conditions (Ref. 45 & 50), but here the rate enhancements seem to be of the same order of magnitude as those for the aryl and acyl phosphates and much lower than for aromatic nucleophilic substitution.

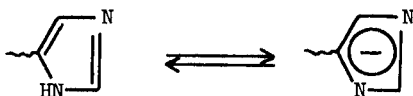
There are a few examples of general base catalysis by a functional micelle. The chiral surfactant (7) is a stereospecific catalyst in carboxylic ester hydrolysis, where reaction

almost certainly involves initial acylation of the imidazole moiety (Ref. 51). But **7** is also an effective catalyst for the hydrolysis of *p*-nitrophenyldiphenyl phosphate (Ref. 52), and the kinetic deuterium solvent isotope effects ($k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}} = 2.5-2.8$) are in the range typical of general base catalysis. (The isotope effects for reactions of carboxylic esters are $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}} \sim 1.4$ in the range typical of nucleophilic catalysis). In addition there is no evidence for build-up of a covalent intermediate, e.g., a phosphorylated imidazole, when reaction is done using a comicelle of **7** and the nonionic surfactant, Brij, and an excess of *p*-nitrophenyldiphenyl phosphate over **7**.



I know of no evidence for general base catalysis of carboxylic ester hydrolysis by a functional micelle, for example Moss and his coworkers have prepared micelles of functional surfactants which contain imidazole and hydroxyethyl moieties, and are effective catalysts, but less so than the imidazole derivatives, but they see no evidence for any reaction other than acylation of the imidazole (Ref. 53).

Rates of deacylation in the presence of functional surfactants containing an imidazole moiety generally increase with increasing pH above 8, because of deprotonation of the imidazole moiety to the highly reactive anion (Ref. 40 & 54).

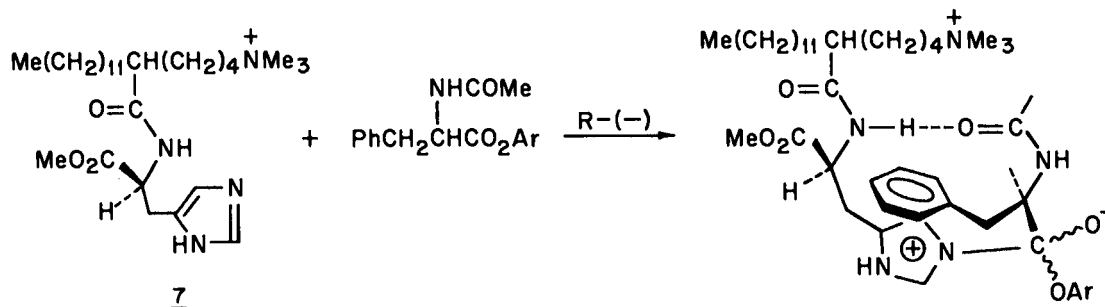


At pH < 6 the rate increases as protonated imidazole is deprotonated; there is then a plateau region at pH ~ 7 in which an imidazole moiety is the reagent, and the rate then increases with formation of the imidazole anion. For hydrolysis of *p*-nitrophenyldiphenyl phosphate in micelles of **7**, which we believe to be general base catalyzed, the rate increases only slightly with increasing pH, suggesting that under these conditions the imidazole anion is not a particularly effective kinetic base although it is an excellent nucleophile.

STEREOCHEMICAL CONSEQUENCES OF MICELLIZATION

There have been a number of attempts to use micelles in chiral recognition, and to control the stereochemical course of reactions by micellization, and a limited degree of success has been obtained using both approaches.

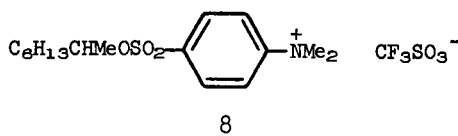
The use of micelles of nonfunctional chiral surfactants as catalysts leads to little or no chiral recognition (Ref. 55). But micelles of the chiral surfactant (**7**) derived from L-histidine give a 3-fold specificity in the catalyzed hydrolyses of the enantiomers of *p*-nitrophenyl *N*-acetylphenylalanine (Ref. 51).



However only a small chiral recognition was found in the hydrolysis of *p*-nitrophenyl-2-phenylpropionate and it was suggested that chiral recognition depended on hydrogen bonding between amide moieties which leads to unfavorable phenyl-imidazole interactions in reaction of the R(-) ester but not of the S(+) ester. Formation of the tetrahedral intermediate from the R(-) ester forces an unfavorable interaction between the imidazole group and the phenyl group of the ester. There appears to be no chiral recognition in the binding of the enantiomeric substrates to the chiral micelle.

There are also several systems in which substrate micellization controls the stereochemical course of reactions. The nitrous acid deamination of chiral primary amines generally involves extensive racemization with partial inversion of the product alcohol. However if the alkyl group of the amine is sufficiently hydrophobic for substrate micellization the product has a partially retained configuration, because micellization causes the intermediate carbocation, or ion pair, to suffer predominantly front side attack by water molecules of the solvent (Ref. 56). The stereochemical course of the reaction is also very sensitive to added salts whose anions cluster around the micellized alkylammonium ion and so affect attack of water.

The other examples involve stereochemical control in S_N1 solvolyses. Comicellization of 8 with NaLS changes the stereochemical course of the reaction from complete inversion in water



to 56% inversion with approximately 1:1 substrate:surfactant (Ref. 57). However substrate micellization or comicellization with CTABr has little effect on either rate or stereochemistry. These results can be rationalized on the assumption that strong head group interactions between 8 and NaLS force water molecules away from the reaction center, but head group repulsions in the cationic micelles allow water molecules to enter the Stern layer and orient around the reaction center. Slightly different results were obtained for the S_N1 solvolysis of 1-methylheptyltrifluoromethane sulfonate which is strongly inhibited by micelles of either NaLS or CTABr and both anionic and cationic micelles change the stereochemical course of reaction from net inversion in aqueous solvents to net retention (Ref. 58).

PREPARATIVE APPLICATIONS

Mechanistic work on micellar effects is typically done using low reactant concentrations, much below those required for useful preparations. However surfactants are used in emulsion polymerization (Ref. 59), where the micelles control chain initiation and growth, and in some organic reactions (Ref. 16). The use of surfactants in phase transfer catalysis is well established (Ref. 14 & 15), although micellization may not be important here. Unfortunately surfactants often complicate product isolation, and therefore the use of immobilized reagents is attractive, cf. Ref. 60. We have found that the histidine derived surfactant 7 binds well to sulfonate ion resin and then effectively catalyzes hydrolysis of p-nitrophenyldiphenyl phosphate (Ref. 61), and in this system the catalyst can be reused after recovery by filtration with little loss of activity.

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QUANTUM CHEMICAL STUDIES OF CO, CS AND RELATED DOUBLE BONDS

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Abstract - After a critical examination of current quantum chemical ab initio methods and their use for the study of chemical problems a classification of the different types of double bonds and a qualitative discussion of their properties is given. Then the results of some recent computations on small molecules that involve CO, CS or related double bonds are reviewed. This review includes ground state properties such as molecular geometries, dipole moments, force fields and vibrational frequencies, further ionization potentials, UV spectra and properties of excited states, intermolecular and intramolecular interactions (mainly proton affinities and hydrogen bonding), and finally chemical reactions, both involving the ground state and excited states.

1. APPRECIATION OF AB INITIO CALCULATIONS APPLIED TO CHEMICAL PROBLEMS

In 1966 an excellent review on the theory of the CO double bond by Berthier and Serre was published (1). As far as our qualitative understanding of the CO double bond is concerned this article is still quite up to date. On the other hand the era of ab-initio calculations of organic molecules had just started when that review was written and a wealth of calculations on carbonyl bonds has been published since then. The tendency in these calculations has been to concentrate on (hopefully) sufficiently accurate calculations of small prototype systems rather than on poor calculations of large molecules. For theoreticians in the past decade the carbonyl bond has mainly, but not exclusively been the one in formaldehyde. We limit ourselves to a discussion of the ab-initio studies, since in this field the progress was most striking within the last ten years.

It is not easy to assess to which extent ab-initio calculations have contributed to a better understanding of our present topic, the CO, CS and related double bonds, or of chemistry in general. For an observer from outside the philosophy of quantum chemical calculations seems to be the following one. The theoretician starts by choosing a particular molecule, then tries to get a sufficiently good approximate solution of the many-electron Schrödinger equation and, from this, numerical values of certain physical properties of the molecule, e.g. equilibrium geometry, dipole moments, ionization potentials etc.. And he is proud when he has reproduced the values known for this molecule from experiment.

If one is using quantum chemistry in this way one has to face the criticism, that one only tests the Schrödinger equation, which is beyond doubt anyway. However, the attempt to reproduce experimental quantities from theory is actually not a test of the Schrödinger equation but rather of a particular approximation scheme. Such tests are necessary since so far we have no fully reliable intrinsic criteria to judge the quality of a quantum chemical method. To be sure, such a test should not be an end in itself. Methods that have been tested should be used to get information that is not, not yet or not easily obtained from experiment.

Quantum chemical papers are often hard to appreciate for a non-initiated reader. One of the reasons is that it is usually not stated explicitly in the paper how good the methods used are for the particular problems studied. For historical reasons theoreticians may have some tendency to present their methods as better than they really are. There is a rather unpleasant inflation of terms like 'exact', 'accurate', 'rigorous', 'improved' etc. in the quantum chemical literature. A standardized nomenclature of the quality of ab-initio papers might be useful and there are some trends in this direction. This was recognized long ago by Mulliken (2). The big merit of Pople (3), who joined the ab-initio field rather late when it was already well developed, is that he has proceeded in an extremely standardized way. In Table 1 we have tried to present a hierarchy of quantum chemical ab-initio methods with increasing sophistication from the top to the bottom and we have indicated applications for which the different approaches are either appropriate or unreliable. This table is, of course, incomplete, but it covers the most widely used approaches. Furthermore our classification is oversimplified in particular, where basis sets are concerned.

TABLE 1. Classification of current quantum chemical ab-initio methods

| Type | Basis set | Properties, or classes of compounds for which the method is satisfactory | fails |
|--|---|---|--|
| self-consistent field (SCF) ¹⁾ | minimal basis ²⁾ e.g. ST0-3G | molecular geometries, orbital energies (to correlate with PE spectra) | dissociation energies, force constants, negative ions |
| | double zeta ³⁾ quality | isomerization energies, conformations | cyclic vs. linear molecules, negative ions |
| | double zeta plus 'diffuse' functions ⁴⁾ | negative ions, excited states | |
| | double zeta plus polarization functions ⁵⁾ | hydrogenation and protonation energies, dipole moments, cyclic vs. linear molecules, inversion barriers | dissociation energies, classical vs. non-classical ions |
| limited configuration interaction (CI) ⁶⁾ | double zeta ³⁾ plus 'diffuse' functions ⁴⁾ | spectral transitions | accurate properties of the states involved in the transition |
| extended CI ⁶⁾ coupled electron pair approximation ⁷⁾ (CEPA) | double zeta ⁴⁾ plus polarization functions ⁵⁾ | spectroscopic constants, dissociation energies, all static properties | |
| MC-SCF ⁸⁾ etc. | large basis sets plus additional techniques | van der Waals minima, spin densities, magnetic susceptibilities | |

- 1) In the SCF approach the wave function is a single Slater determinant.
- 2) A minimum basis for H_2CO consists of one 1s AO for each H and 1s, 2s, 2p_x, 2p_y, 2p_z for C and O, i.e. one function for each hydrogen and five functions for each 1st or 2nd row element.
- 3) Double zeta quality means each basis function of the minimal basis is replaced by at least two functions.
- 4) Diffuse functions have small orbital exponents to represent 3s, 3p etc. type spectroscopic AOs.
- 5) Polarization functions are at least p for H and d for first and second row elements.
- 6) In a CI approach the wave function is a linear combination of Slater determinants.
- 7) The coupled electron pair approximation is equivalent to a CI with all doubly substituted configurations with respect to a leading Slater determinant, plus an approximate treatment for certain four fold (and higher) substitutions (so called 'unlinked clusters').
- 8) In a multiconfiguration self-consistent field (MC-SCF) approximation the wave function is a linear combination of a limited number of Slater determinants, unlike in CI not only the expansion coefficient but also the orbitals are optimized.

The notations single zeta, double zeta etc. originally introduced for Slater type (ST0) basis sets (2) can with some care also be applied to basis sets of contracted gaussians. However, we think that it does not make too much sense to distinguish between double and triple (or higher) zeta basis sets. To characterize basis sets between just double zeta quality augmented by polarization functions and basis sets that are good for 'Hartree-Fock-limit' results one has to indicate the size of the basis of primitive gaussians (usually those proposed by

Huzinaga (4)) and the contraction. It should further be mentioned that basis sets of the same size may be of different quality for different classes of molecules. While the (7,3) basis (consisting of 7 primitive s- and 3 primitive p type gaussians) contracted to double zeta quality and augmented by one set of d-functions is excellent for carbon in hydrocarbons, heteroatoms like oxygen require larger basis sets. In formaldehyde a (9,5) basis is necessary for comparable quality.

One feature of many papers on quantum chemical ab initio studies is that results obtained with different methods or different basis sets are collected. There are several justifications for this (comparison of methods, use of cheaper methods for most calculations and more expensive ones for selected calculations, investigation of convergence behaviour, etc.), but a non-initiated reader may, however, get confused and wonder which calculated values are the 'good ones'. In many cases the computed total energy is one (though however not the only significant) measure of the quality of the calculation (so far as it is variational). Usually the lower (i.e. the larger in absolute value) the total energy the better the calculation. Even this test must be carefully applied since, e.g. augmenting the basis for the inner shells has a significant effect on the total energy, without improving the properties associated with the valence shell. In a way it is more important that the basis is 'balanced' rather than that it is large. And it requires some experience to judge whether a basis is balanced (2).

Agreement of certain computed properties with their experimental counterparts is as such no criterion for the quality of a calculation.

2. COMPLEMENTARITY OF THEORY AND EXPERIMENT

Although calculations on a known molecule have to be performed in order to test the methods, it is much more interesting to study theoretically molecules which are inaccessible to experimental investigations, e.g. because they are unstable. Examples of molecules that are better known from theory than from experiment are the ion CH_5^+ (5) and unsubstituted cyclobutadiene (6). Transition states of molecular rearrangements like, e.g., the eclipsed form of ethane (7) or of chemical reactions (e.g. for nucleophilic substitutions on saturated carbon (8)), which correspond to saddle points rather than local minima of the potential hypersurface are also more easily studied theoretically. Thioformaldehyde is an unstable species for which theory and experiment are competitive.

It is often forgotten that few molecular properties are determined 'directly' in experiments. Usually some theory has to be used to extract the 'experimental values' from the quantities that were really measured. These theories may be quite straightforward e.g., those that lead from the microwave spectrum to the molecular geometry, or rather tricky like when going from measured dielectric constants to dipole moments.

Furthermore one should realize that in theory one always considers 'one molecule in space' whereas in experiment one usually deals with a molecule that interacts with other molecules of the same or different kind, with a solvent or even with an 'inert' matrix. The different environments make the comparison of theoretical and experimental values somewhat more difficult. On the other hand one may take advantage of this difference and use theory for the study of isolated molecules and rely on experiments for the molecules in their surroundings. We must admit that quantum chemical calculations are usually not accurate enough to allow direct deductions about solvent effects by comparison of theoretical and measured quantities. Nevertheless there are striking examples where the solvent effects are so large that they dominate the difference between experimental and theoretical quantities. This is e.g. the case for proton affinities which for a chemist are usually understood as those in (mostly aqueous) solution while a theoretician rather computes proton affinities in the gas phase. As it is well known the order of basicities can be different in solution and in the gas phase (3). The difference between theoretical (gas phase) values that can be obtained rather accurately by simple methods (10) and experimental basicities in solution are due to solvent effects.

There is another more subtle point concerning the comparison of theoretical and experimental quantities. Theoretical equilibrium properties of a molecule always refer to the geometry for which the energy has its minimum, measured properties on the other hand, are always averaged at least over the zero point vibrations, often also over a Boltzmann distribution of vibrational levels. These differences are usually small, but for XH bond lengths r_e and r_0 differ by 0.01 Å which is larger than the error of the best quantum chemical calculations (see Table 2) (11).

Another difference between theoretical and experimental values arises in the study of force constants. Theoretically both the diagonal and the off-diagonal harmonic force constants are directly accessible (though much more refined methods are necessary than for getting bond distances with the same accuracy) whereas experimentally there are problems to acquire enough data for uniquely determining the complete force field matrix, and with the 'harmonization' of the measured force constants.

TABLE 2. Ground state equilibrium geometry, dipole moment and symmetric diagonal force constants (i.e. those for the A_1 symmetry species) of formaldehyde^a

| Method | r_{CO} | r_{CH} | \angle_{HCH} | Dipole moment | k_{CO}^S | k_{CH}^S | k_{HCH}^S |
|---------------------------|----------|----------|-----------------------|---------------|------------|------------|-------------|
| Minimal Basis | | | | | | | |
| STO-3G SCF b) | 1.217 | 1.101 | 114.5 ⁰ | | 17.8 | 6.9 | 0.92 |
| 4-31G SCF c) | 1.206 | 1.081 | 116.4 ⁰ | | | | |
| 4-31G MCSCF d) | 1.24 | 1.084 | 118 ⁰ | | 11.9 | 6.1 | 0.54 |
| Double zeta SCF e) | 1.220 | (1.120) | (118 ⁰) | 3.46 | 14.34 | | |
| Double zeta SCF f) | (1.210) | (1.120) | (118 ⁰) | 3.10 | | | |
| Double zeta limited CI e) | 1.243 | (1.120) | (118 ⁰) | 2.94 | 11.76 | | |
| Double zeta limited CI f) | (1.210) | (1.120) | (118 ⁰) | 2.59 | | | |
| (7,3,1/3,1)SCF g) | 1.177 | 1.103 | 114.3 ⁰ | 2.33 | 16.72 | 5.40 | 0.69 |
| (9,5,1/5,1)SCF g) | 1.176 | 1.092 | 116.3 ⁰ | 2.69 | | | |
| Hartree-Fock limit h) | (1.208) | (1.116) | (116.5 ⁰) | 2.86 | | | |
| (7,3,1/3,1)CEPA g) | 1.199 | 1.116 | 114.0 ⁰ | | 14.75 | 4.85 | 0.63 |
| (9,5,1/5,1)CEPA g) | 1.202 | 1.104 | (116.3 ⁰) | | | | |
| i) j) | | | | | 13.91 | 5.00 | 0.65 |
| exp. r_e k) | 1.202 | 1.100 | 116.3 ⁰ | 2.32 | 12.90 | 4.96 | 0.57 |
| exp. r_o k) | 1.207 | 1.117 | 116.2 ⁰ | | | | |

a) all distances in Å, dipole moments in Debye, force constants in $\text{mdyn}/\text{Å}$ or $\text{mdyn}\cdot\text{Å}/\text{rad}^2$, values in parentheses are assumed rather than optimized.

b) M.D. Newton, W.A. Lathan, W.J. Hehre, and J.A. Pople, *J.Chem.Phys.* **52**, 4064-4072 (1970).

c) R. Ditchfield, W.J. Hehre, and J.A. Pople, *J.Chem. Phys.* **54**, 724-728 (1971).

d) R.L. Jaffe and K. Morokuma, *J.Chem.Phys.* **54**, 4881-4886 (1976).

e) R.J. Buenker, and S.D. Peyerimhoff, *J.Chem.Phys.* **53**, 1368-1384 (1970), only r_{CO} was varied.

f) L.B. Harding, and W.A. Goddard III, *J.Am.Chem.Soc.* **97**, 6293-6299 (1975)

g) R. Jaquet, Diplomarbeit Ruhr-Universität Bochum 1976, for the basis contraction see table 6.

h) B.J. Garrison, H.F. Schaefer III, and W.A. Lester, *J.Chem.Phys.* **61**, 3039-3042 (1974).

i) for classification of this method see the present paper, sec. 4.

j) W. Meyer, and P. Pulay, *Theor.Chim.Acta* **32**, 253-264 (1974).

k) J.L. Duncan, *Mol.Phys.* **28**, 1177-1191 (1974).

3. THE INTERPRETATION OF QUANTUM MECHANICAL RESULTS AND THE USE OF NON-OBSERVABLES

One must admit that the interpretation of quantum chemical results in term of simple models or mechanistic arguments is not very popular nowadays, but an understanding of the electronic structure and related phenomena is only possible in terms of non-observable quantities. Typical questions arising in this context are: 'What is the d-orbital contribution to the PO bond in a phosphine oxide?' or 'How localized are the π -orbitals in glyoxal?' or 'How polar is the C=O bond?' or 'Why is the CO bond in a carbonyl fluoride stronger than that in a formaldehyde?' etc.. These questions cannot be answered in a very precise way but the answers are usually precise enough to decide whether a certain model of the binding situation is appropriate and can be used for more complicated molecules of the same class. When we claim that d-AO's on phosphorous lower the binding energy of the PO bond in phosphineoxide by -40 kcal/mol this means that we performed one calculation with and one without d-AO's on P in otherwise the same basis (12). This result is surely not independent of the kind of 'd-free' basis used (in fact it can be changed strongly if the 'd-free' basis is unbalanced, as, e.g., in (13)), but the comparison with an amine oxide (where the d-AO's on N contribute only -3 kcal/mol to the binding energy) is qualitatively significant

concerning the role of d-AO's in amine oxide and phosphine oxide compounds. Another question to be answered easily in the same way is that of hyperconjugation in the classical ethyl cation $H_3C-CH_2^+$, where one can perform one calculation in which there is a $p\pi$ -AO on the carbon of the CH_2^+ group and one where it is not present (14). The effect of this $p\pi$ -AO and hence of hyperconjugation on the binding energy is 11 kcal/mol and on the C-C bond distance is a reduction by 0.10 Å. It should be mentioned that standard ab-initio calculations automatically take care of hyperconjugation (and conjugation) and that one has to introduce some artefact into the calculation, if one wants to eliminate hyperconjugation. In a somewhat analogous way one can also eliminate conjugation (15).

In interpreting quantum chemical results one is very much interested in associating certain properties with the individual atoms and with the different bonds. We know that this attempt is bound to fail when we want to do it in a rigorous way. However, the Mulliken population analysis (16), when applied to calculations with well-balanced basis sets is a fairly good practical tool for discussing the ionicity and covalency of the bonds in a molecule. A preferable scheme for a population analysis, which leads to results that are nearly basis-independent, has recently been proposed by Ahlrichs and Heinzmann (17) but there have not been very many applications so far.

In Table 3 we compare the Mulliken gross and overlap populations for formaldehyde, thioformaldehyde (18), amine oxide and phosphine oxide (12) with basis sets of comparable quality. Although none of the figures should be taken literally the differences are quite instructive.

TABLE 3A. Partial and total gross populations

| H_2CO | | | | | H_2CS | | | | |
|---------|------|------|------|------|---------|------|-------|------|-------|
| | s | p | d | sum | | s | p | d | sum |
| C | 3.13 | 2.47 | 0.11 | 5.70 | C | 3.27 | 2.84 | 0.05 | 6.16 |
| O | 3.83 | 4.51 | 0.02 | 8.36 | S | 5.87 | 10.13 | 0.08 | 16.07 |
| H | 0.94 | 0.03 | - | 0.97 | H | 0.85 | 0.03 | - | 0.88 |
| H_3NO | | | | | H_3PO | | | | |
| N | 3.38 | 3.42 | 0.04 | 6.84 | P | 5.14 | 8.23 | 0.30 | 13.67 |
| O | 3.96 | 4.58 | 0.03 | 8.57 | O | 3.95 | 4.97 | 0.05 | 8.97 |
| H | 0.79 | 0.07 | - | 0.86 | H | 1.09 | 0.03 | - | 1.12 |

TABLE 3B. Overlap Populations

| H_2CO | | | | H_2CS | | | | | |
|--------------------------|------|-------|-------|--------------------------|-------|-------|-------|-------|-------|
| | C | O | H_1 | | C | S | H_1 | | |
| O | 1.19 | | | S | 0.94 | | | | |
| H_1 | 0.78 | -0.08 | | H_1 | 0.81 | -0.09 | | | |
| H_2 | 0.78 | -0.08 | -0.16 | H_2 | 0.81 | -0.09 | -0.07 | | |
| H_3NO (with d-AO's) | | | | H_3PO (with d-AO's) | | | | | |
| | N | O | H_1 | H_2 | | P | O | H_1 | H_2 |
| O | 0.31 | | | | O | 0.71 | | | |
| H_1 | 0.76 | -0.07 | | | H_1 | 0.75 | -0.07 | | |
| H_2 | 0.76 | -0.07 | -0.07 | | H_2 | 0.75 | -0.07 | -0.11 | |
| H_3 | 0.76 | -0.07 | -0.07 | -0.07 | H_3 | 0.75 | -0.07 | -0.11 | -0.11 |
| H_3NO (without d-AO's) | | | | H_3PO (without d-AO's) | | | | | |
| | N | O | H_1 | H_2 | | P | O | H_1 | H_2 |
| O | 0.12 | | | | O | 0.20 | | | |
| H_1 | 0.71 | -0.07 | | | H_1 | 0.63 | -0.06 | | |
| H_2 | 0.71 | -0.07 | -0.08 | | H_2 | 0.63 | -0.06 | -0.13 | |
| H_3 | 0.71 | -0.07 | -0.08 | -0.08 | H_3 | 0.63 | -0.06 | -0.13 | -0.13 |

One sees that the CS bond in thioformaldehyde is nearly unpolar whereas there is an appreciable charge transfer from C to O in formaldehyde. In formaldehyde and thioformaldehyde the contribution of d-AO's is very small as it is in amine oxide, whereas in phosphine oxide the d-AO contribution on P (which is responsible for back bonding) is significant. The d-AO's have little effect on the overlap population in formaldehyde and thioformaldehyde but influence the overlap populations in amine oxide and phosphine oxide to a large extent. Part of this influence is indirect in the case of phosphine oxide where the equilibrium bond distance is smaller by 0.2 Å in the calculations with d-functions than in the ones without (12).

4. DIFFERENT TYPES OF DOUBLE BONDS

What in chemical formulae is simply written as a double bond may correspond to quite different bonding situations from the quantum chemical point of view.

In Table 4 different types of double bonds are illustrated. We note that the double bond in O_2 (and similarly SO, S_2) consists of a σ -bond plus two "half- π " bonds (one electron π -bonds) perpendicular to each other, whereas the double bond in C_2 consists of two full perpendicular π -bonds and no σ -bond at all. The conventional double bond of organic chemistry as it is present in e.g. ethylene, and as it was first understood quantum mechanically by E. Hückel (19) is built up from one σ -bond and one π -bond perpendicular to the molecular plane. One has to note that the term π -bond has a somewhat different meaning in linear and in planar molecules (20). We further remind the reader that O_2 has an open-shell configuration and hence, in conformity with Hund's rule a triplet ground state, whereas both C_2 and C_2H_4 have closed-shell configurations and hence singlet ground states.

TABLE 4. Different types of double bonds

| | $\sigma(z)$ | | $\pi(x)$ | | $\pi(y)$ | |
|------------|-------------|----------------------|----------|----------------------|----------------------|----------------------|
| O_2 | O | $\uparrow\downarrow$ | O | $\uparrow\downarrow$ | O | $\uparrow\downarrow$ |
| C_2 | C | | C | $\uparrow\downarrow$ | C | $\uparrow\downarrow$ |
| C_2H_4 | H_2C | $\uparrow\downarrow$ | CH_2 | $\uparrow\downarrow$ | CH_2 | |
| CaO | Ca^{2+} | | O^{2-} | | | |
| BF | B | $\uparrow\downarrow$ | F | B..... | $\uparrow\downarrow$ | F |
| R_3NO | R_3N | $\uparrow\downarrow$ | | O | | |
| R_3PO | R_3P | $\uparrow\downarrow$ | | O | R_3P | |
| R_3PCH_2 | R_3P | $\uparrow\downarrow$ | | CH_2 | R_3P | |

While the three types of double bonds just discussed are covalent, we have, of course, also to consider ionic double bonds like, e.g., in the CaO molecule, although pure ionic double bonds are even rarer than pure ionic single bonds, i.e. they have always a significant covalent contribution. Then there are the so-called semipolar bonds like in $R_3N^+-O^-$ where within the simplest model approach one has one covalent bond and one ionic bond. Actually, the name 'ylid' proposed by Wittig for bonds of this kind (yl stand for the covalent and id for the ionic bond) alludes to this kind of double bond.

In the valence-isoelectronic phosphine oxides one nowadays assumes that there is a covalent double bond with a σ and a π -component, the latter involving d-AO's of the P atom. Although this ideal bonding situation is not fully realized in phosphine oxides we must point out that the definition of σ and π -orbitals in molecules like phosphine oxides is much closer to that in linear than in planar molecules. In particular there are two potential PO π -bonding-MO's perpendicular to each other (whereas in formaldehyde there is just one C-O π -bonding MO). If there is really a double bond in phosphine oxides this bond is closer to that in O_2 (with two half π -bonds) than to that in ethylene. (A better and simpler model for the bonding situation in phosphine oxide may be BF, where there is a single B-F σ bond and back-bonding from the lone pairs of F into the empty $p\pi$ -AO's of B to such an extent that there is no triple bond as in N_2 or CO but rather something like a double bond. This model example shows better that the bond in phosphine oxide is somewhere between single and triple and that only by chance it may happen to be a double bond.

The PO bond in phosphine oxide is slightly different from the PC bond in methylenephosphorane H_3PCH_2 (21) where only a π -bond in one direction (antisymmetric with respect to the CH_2 plane) is possible. Even in methylenephosphorane the 'double bond' is very different from that in ethylene, as can be deduced directly from the difference in the barriers for internal rotation (60 kcal/mol in ethylene and <1 kcal/mol (21) in methylenephosphorane). Only the ethylene-type double bond is sterically rigid.

We finally must mention some bonds that are conventionally written as double bonds though they mean bonds of higher order. An example is the C=O bond in carbon dioxide $\text{O}=\text{C}=\text{O}$ where two localized C-O σ -bonds and two 3-center 4-electron π -bonds are present such that each CO bond is roughly a 2.5 fold bond, a statement which, of course must not be taken too literally. The bond lengths in CO and CO_2 are 1.13 Å and 1.16 Å. The bonds lengths in CS and CS_2 , namely 1.54 Å and 1.56 Å, differ similarly from the value of 1.61 Å for a 'genuine' CS bond. The bonding situation in ketene $\text{H}_2\text{C}=\text{C}=\text{O}$, where one has one localized CO- π -bond and, perpendicular to it one 3-center-4-electron π -bond, is similar whereas in allene $\text{H}_2\text{C}=\text{C}=\text{CH}_2$ the situation is best described by two isolated double bonds, the π -contributions of which are perpendicular to each other. This indicates that the isoelectronic replacement of CH_2 by O may change the bonding situation appreciably.

In non-symmetric double bonds the polarities of the σ and the π -bond may be in the same or opposite directions. Opposite polarity occurs in back-bonding situations like in B=F or in phosphine oxides. The bond in carbon monoxide $\text{C}\equiv\text{O}$ is best described as a triple bond whereas in metal carbonyls the CO bond is between a double and a triple bond. Only bridge CO units between two transition metal ions show a bonding situation like in formaldehyde.

In this section we have assumed tacitly that a double bond is a well defined entity in a molecule, at least as far as isolated double bonds are concerned. This is supported by quantum chemical calculations as in these systems a transformation of the canonical orbitals to localized ones is usually possible (22). A straightforward application of either of the standard localization criteria (22) does not lead to a σ plus a π bonding orbital for ethylene type double bonds but rather to two banana type orbitals. Localized σ and π bonding orbitals can be obtained in planar molecules if one maintains the σ - π separation and localizes σ and π orbitals separately. For ethylene type double bonds the two descriptions are equivalent.

In carbonyl compounds the standard localization procedures lead to two equivalent lone pair orbitals, which together with the two banana bond orbitals are directed tetrahedrally from the O atom (like the four localized orbitals in the water molecule). Nevertheless, the lone pairs which play a role in the PE and uv spectra are not these localized ones but rather canonical (delocalized) orbitals. However, these canonical orbitals are usually energetically the highest ones of their symmetry and rather well localized. These semilocalized orbitals are to a good approximation the + and - linear combination of the localized lone-pair orbitals.

For the P-O 'double-bond' one gets very different localized orbitals, namely (at least if one uses a large basis) 3 'bananas' between P and O, localized closer to O (and hence with some lone-pair character) and a genuine lone pair pointing away from the P-O bond. The fact that the localization scheme can be basis dependent and is often not even unique, is a hint that localized orbitals should not be overinterpreted.

5. SPECIAL CHARACTERISTICS OF CO, CS AND OTHER DOUBLE BONDS

CO, CN, CS etc. double bonds differ from CC double bonds in several respects.

- 1) They are polar; the C atom has a partial positive and the heteroatom a partial negative charge. Some idea about this polarity can be obtained from the population analysis of formaldehyde and thioformaldehyde (as given in table 3).
- 2) These bonds are stronger than CC double bonds, like generally an AB bond is stronger than the mean of an AA and a BB bond. This increased bond strength is manifested in shorter bond distances and larger force constants (compared to those of a CC bond).
- 3) The heteroatoms carry lone pairs and many properties, like proton affinity (basicity), ability to form complexes, chemical reactivity as well as some aspects of their uv spectra are directly based on these lone pairs.
- 4) They differ from CC double bonds as far as delocalization (resonance) is concerned. This difference is mainly due to the fact that C=O or C=S double bonds can only be at the end of a conjugated system and cannot participate in cyclic conjugation, but that they can more easily be part of an allylic or carbonate type conjugated system. For hydrocarbons, allyl cations or anions exist in reactive intermediates whereas carboxylic acids and their derivatives show allylic conjugation even as neutral molecules. The conjugation in carboxylic acids the $-\text{SO}_3\text{H}$ groups is often pointed out. Properties of the CO bond so much that these compounds are usually treated as a separate class rather than as carbonyl compounds.

The analogy between the $-\text{CO}_2\text{H}$ and the $-\text{SO}_3\text{H}$ groups is often pointed out. However, only in $-\text{CO}_2\text{H}$ is a double bond (though conjugated with the π -type lone pairs of OH) present, whereas the SO bonds in $-\text{SO}_3\text{H}$ are semipolar and get some multiple bond character only through participation of the d- AO 's on sulphur, much like the PO bond in phosphine oxide.

It is not yet clear whether there is also a direct difference in the extent of conjugation between C=O or C=C bonds in conjugated systems of similar kind, say glyoxal vs. butadiene. In this context we note that the N=N bond does differ from the C=C bond. As is wellknown, benzene C_6H_6 is a very stable compound whereas its hexaaza derivative N_6 is unknown. Nevertheless if one calculated N_6 in D_{6h} symmetry one gets the minimum of the energy for the very 'reasonable' N-N distance of 1.33 Å. When the radius of the circle that goes through the N atoms is than kept fixed and one allows for bond alternation one finds a new (deeper) minimum for alternate bond lengths of 1.20 Å and 1.45 Å which rather nicely indicates alternate single and double bonds (23). The N=N double bonds do not want to 'resonate'. If one relaxes all symmetry restrictions N_6 dissociates into three nitrogen molecules. N_6 is not even a metastable compound.

6. GROUND STATE PROPERTIES OF MOLECULES WITH CO AND RELATED DOUBLE BONDS

In Table 2 we compare the computed bond lengths, bond angles, dipole moments and harmonic diagonal force constants of formaldehyde with the corresponding experimental values. As far as the latter are concerned one must note the difference between the average values $r_0 = \langle r \rangle$ directly accessible from experiment (to be precise, one gets $\langle r^{-2} \rangle^{-1/2}$ rather than $\langle r \rangle$ from microwave experiments) and the equilibrium value r_e obtained only indirectly. Theory gives directly equilibrium values.

One sees that all computed geometrical parameters agree with the experimental ones within a few %. Looking more closely one realizes that the minimal basis (STO-3G) yields r_{CO} somewhat too large whereas the SCF calculations with double zeta quality plus polarization functions lead to r_{CO} values which are too small. There is a general trend of this kind. Lathan et al. (24) have compared 69 bond lengths in various H_mABH_m molecules and found a mean discrepancy of 0.03 Å between experimental and STO-3G values, with the computed values mostly too long (except for the CH bond where they come out rather close to the experimental values). Bond lengths obtained at the near Hartree-Fock level are usually too short while the inclusion of electron correlation e.g. with the CEPA-PNO method (25,26) move them to practically the experimental r_e values. Meyer and Rosmus (27) have shown that for all first and second row diatomic hydrides the CEPA bond lengths are accurate to within 0.003 Å. We realize that by a choice of the basis somewhere between minimal and Hartree-Fock limit one may by chance reproduce some bond lengths quite accurately, but that bond lengths with a systematic error of much less than 1% can only be obtained after inclusion of electron correlation. (This is, e.g., necessary if one wants to decide whether some absorption lines observed in interstellar space correspond to the rotational spectrum of some particular unknown molecule).

Figure 1 is a qualitative, somewhat exaggerated illustration of why near Hartree-Fock equilibrium distances are too small and minimal basis SCF distances too large. The SCF curve behaves incorrectly for large distances - it increases too steeply for distances larger than the equilibrium. This leads to a minimum at a too short distance. Minimal basis set SCF calculations show the same wrong behaviour, but they are less capable of bonding, so that the repulsion dominates and the whole curve is shifted to longer distances.

In the case of formaldehyde we also note a difference between the geometries obtained with a (7,3,1) and (9,5,1) basis, both of which are of at least double zeta quality plus polarization. Only the somewhat larger (9,5,1) basis leads to reliable geometry predictions (for hydrocarbons the (7,3,1) basis is usually sufficient (7,15)).

Dipole moments are expectation values of one-electron operators and one would hope that SCF calculations are good enough for obtaining them. However, dipole moments of formaldehyde computed at the SCF level with most basis sets are too large. Garrison, Schaefer and Lester (28) claim that their results are close to the Hartree-Fock limit (i.e. to the best possible SCF results). If this is so, one has to conclude that electron correlation should reduce the dipole moment by about 0.5 Debye. No calculations exist so far which have accounted for this correlation effect directly, but the results for the CO molecule (29) where correlation changes the dipole moment by 0.5 Debye as well as the reduction of the dipole moment of formaldehyde through CI observed by various authors (see Table 2) are not in conflict with a correlation effect of this magnitude. As to the ab initio calculation of dipole moments in general see ref. (30).

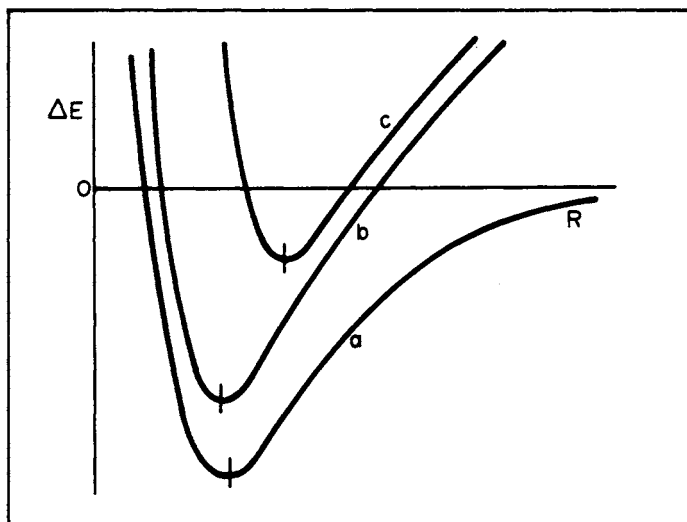


Fig. 1. Typical potential curve of a diatomic molecule a) exact b) SCF (close to the Hartree-Fock limit c) minimal basis SCF.

Other expectation values of one-electron operators like the components of the quadrupole moment, field gradient, etc., at near Hartree-Fock level at the experimental average geometry have been published by Garrison et al. (28). These are supposed to be less affected by correlation than the dipole moments (see also ref. 37).

Force constants are obtained together with the equilibrium geometry from the potential hypersurface in the neighbourhood of its minimum. However, force constants are much more sensitive to the quality of the calculation than are the geometrical parameters. The Hartree-Fock limit diagonal force constants are much too large and the inclusion of electron correlation brings them close to the experimental values. The present status of our experience is that XH-force constants can be obtained very accurately in the CEPA scheme (Meyer and Rosmus (27) find an agreement within 1% for monohydrides), but that the force constants for double bonds still pose problems. Even with CEPA the CO force constant in formaldehyde comes out (about 10-15%) too large (18) (as in the CO (18) and CO₂ molecules (31)). This problem will probably be settled within the next few years and we do not want to speculate on it now. (In the calculations we refer to singly substituted configurations have not been included). It has been found (18) that linear correlation effects, i.e. the first derivatives of the correlation energy with respect to the internal coordinates are more important than second order effects and that these first order effects on the force constants can be taken care of if one calculates the second derivatives of the SCF energy at the CEPA minimum. This explains the success of the method of Pulay (32) who calculates SCF force constants at the experimental geometry rather than at the geometry of the SCF minimum.

Calculated and experimental harmonic vibration frequencies of formaldehyde are compared in Table 5.

The influence of substituents R on the CO bond lengths in aldehydes and ketones has been studied by Del Bene et al. (33), in an SCF approach with minimal (STO-3G) basis sets. While the experimental bond lengths vary between 1.174 Å (F₂CO) and 1.243 Å (HCONH₂) the computed bond lengths only vary between 1.209 Å (F₂CO) and 1.218 Å (HCONH₂). A method (SCF with STO-3G) that is only capable of reproducing bond lengths to within 0.03 Å is obviously not accurate enough to account correctly for bond length variations that are smaller than this. Del Bene et al. account in their calculations for the change in the polarity of the C=O bond which are according to Walsh (34) responsible for the change in the C=O bond lengths. But it is disappointing that they do not account well enough for the variation of the bond lengths. From the population analysis given by Del Bene et al. (33) all substituents are σ -electron withdrawing (in the order CH₃<<OH<NH₂<F) and π -donating (in the order CH₃<<F<OH<NH₂) such that the σ -withdrawing effect dominates, so the change of polarity is (except for CH₃) qualitatively such as suggested by Walsh. As far as theoretical investigations of substituent effects on vibration frequencies is concerned the old semi-empirical study of Bratoz and Besnainou (35) in the framework of the PPP method is still interesting especially since they differentiate between electronic and vibrational coupling effects.

Other ground state properties of interest are the so-called second order properties like polarizabilities, susceptibilities and chemical shifts. They are not calculated as expectation

TABLE 5. Harmonic vibration frequencies of formaldehyde^{a)}

| symmetry | assignment | SCF _{bc)} | SCF _{de)} | CEPA _{de)} | exp.f) |
|----------------|-----------------------|--------------------|--------------------|---------------------|--------|
| A ₁ | ν_{CH} | 2954 | 3066 | 2906 | 2944 |
| A ₁ | ν_{CO} | 1849 | 2059 | 1893 | 1764 |
| A ₁ | δ_{HCH} | 1625 | 1687 | 1617 | 1562 |
| B ₁ | γ_{HCH} | 1326 | 1316 | 1215 | 1191 |
| B ₂ | ν_{CH} | 3037 | 3115 | 3008 | 3009 |
| B ₂ | δ_{HCH} | 1349 | 1376 | 1315 | 1288 |

- a) all frequencies in cm^{-1} , all basis sets are of double zeta + polarization functions quality.
 b) W. Meyer and P. Pulay, *Theor.Chim.Acta* 32, 253-264 (1974).
 c) SCF force constants calculated at the experimental geometry.
 d) force constants calculated at the respective theoretical minimum of the potential surface.
 e) R. Jaquet, Diplomarbeit, Ruhr-Universität Bochum 1976.
 f) J.L. Duncan, *Mol. Phys.* 28, 1177 (1974).

values of some operator but require the application of perturbation theory or the computation of a molecule in an electric or magnetic field. The results available for formaldehyde at present are still quite unsatisfactory, especially for the magnetic susceptibility, of which only the so-called diamagnetic (or low frequency) part can be calculated accurately. The results for the chemical shifts σ are better. Experimentally, absolute values of σ are unknown (here theory is probably better) so that one can only compare differences. The chemical shift of ^{13}C in formaldehyde relative to methane is experimentally - 197 ppm (36,39) whereas theoretical values are - 179 ppm (38), - 189 ppm (39) and - 200 ppm (40). The results for the chemical shifts of hydrogen are less satisfactory.

Thioformaldehyde has been the subject of fewer calculations (18,41,42) and experimental studies (43). For the geometry, fair agreement was obtained (see Table 6). The vibrational spectrum has only been observed in the region of the CH vibration and there are no ab-initio calculations that are accurate enough to predict the full vibrational spectrum of this unstable molecule.

TABLE 6. Ground state equilibrium geometry, dipole moment and symmetric diagonal force constants of thioformaldehyde^{a)}

| Method | | r_{CS} | r_{CH} | \angle_{HCH} | Dipole moment | k_{CS}^s | k_{CH}^s | k_{HCH}^s |
|---------------------------------|----|-----------------|-----------------|-----------------------|---------------|-------------------|-------------------|--------------------|
| Minimal Basis | | | | | | | | |
| STO-3G | b) | 1.631 | 1.090 | 114.6 ^o | 1.58 | | | |
| Double zeta SCF | c) | 1.635 | (1.093) | (116.9 ^o) | | 7.00 | | |
| Double zeta + polarization SCF | d) | 1.594 | 1.087 | 115.2 ^o | 1.98 | 8.49 | 5.94 | 0.54 |
| Double zeta limited CI | c) | 1.672 | (1.093) | (116.9 ^o) | | 6.46 | | |
| Double zeta + polarization CEPA | d) | 1.613 | (1.087) | (115.2 ^o) | | 7.46 | | |
| exp. r_0 | e) | 1.611 | 1.093 | 116.9 ^o | 1.65 | | | |
| exp. | c) | | | | | 6.0 - 6.8 | | |

- a) all distances in Å, dipole moments in Debye, force constants in $\text{mdyn}/\text{Å}$ or $\text{mdyn}\cdot\text{Å}/\text{rad}^2$, values in parentheses are assumed rather than optimized.
 b) N.C. Baird and J.R. Swenson, *J.Phys. Chem.* 77, 277-280 (1973).
 c) P.J. Bruna, S.D. Peyerimhoff, R.J. Buenker and P. Rosmus, *Chem.Phys.* 3, 35-53 (1974)
 d) R. Jaquet, Diplomarbeit, Ruhr-Universität Bochum 1976.
 e) D.R. Johnson, F.X. Powell and W.H. Kirchhoff, *J.Mol.Spectr.* 39, 136-145 (1971).

The simplest dialdehyde, namely glyoxal (HCHO)₂ has recently been investigated theoretically by several research groups (44-48). In all the studies the trans isomer was found to have the lower energy (by ~5 kcal/mol) compared to the cisform (the experimental value for this difference is ~3 kcal/mol). The cis-trans isomerization barrier has also been studied.

As far as PO or SO 'double bonds' are concerned we only want to point out that the PO and SO bond lengths are much more sensitive to substituent effects than e.g. the CO double bonds, mainly because the nature of this double bond is different (see sec. 4) and since the d-participation in backbonding depends more on the effective charge of the P (or S atom). Theory gives the correct magnitude of these bond length variations (12).

7. IONIZATION POTENTIALS AND PROPERTIES OF IONIZED STATES

A wealth of data on ionization potentials of carbonyl compounds has been accumulated from photoelectron spectra (49). Most theoretical attempts to calculate these spectra were based on the use of Koopmans' theorem (50) either in an ab-initio or in a semiempirical framework, i.e. the negative Hartree-Fock-orbital energies were regarded as approximations to the ionization potentials. Usually there is no direct agreement between the orbital energies and the measured ionization potentials (as it should be if Koopmans' theorem were strictly valid) but there is often a very good linear correlation. This means that a comparison of the measured ionization potentials and the orbital energies (which are, by the way not very sensitive to the quality of the basis, see Table 7) helps in the assignment of the PE spectra. There are, however, some cases where Koopmans' theorem breaks down in the sense that the order of the orbital energies does not correspond to the order of the ionization potentials of the respective symmetry classification. In order to be on the safe side one then has to perform independent and rather accurate calculations of the ground state of the neutral molecule and

TABLE 7. Orbital energies and ionization potentials of formaldehyde.

| | | MO Energies negative (in eV) | | | | total energy (a.u.) |
|--------------------------------------|----|------------------------------|-----------------------------|-----------------------------|-----------------------------|------------------------|
| | | 2b ₂ (n) | 1b ₂ (π) | 5a ₁ | 1b ₂ | |
| Minimal basis | a) | 10.48 | 12.78 | 15.53 | 18.35 | -113.4496 |
| double zeta basis | b) | 12.03 | 14.57 | 17.52 | 19.10 | -113.8334 |
| double zeta basis | c) | 11.98 | 14.53 | 17.70 | 18.76 | -113.8917 |
| double zeta basis | d) | 11.89 | 14.35 | 17.29 | 19.04 | -113.8094 |
| double zeta plus polarization | e) | 12.03 | 14.60 | 17.77 | 18.82 | -113.9149 |
| double zeta plus polarization | f) | 12.08 | 14.63 | 17.76 | 18.82 | -113.9012 |
| double zeta plus polarization | g) | 11.95 | 14.66 | 17.77 | 18.84 | -113.8981 |
| double zeta plus polarization | h) | 11.50 | 14.24 | 17.38 | 18.42 | -113.7500 |
| direct perturbative method | f) | 10.84 | 14.29 | 16.36 | 17.13 | |
| experimental ionization potential | i) | 10.9 | 14.5 | 16.2 | 17.0 | |
| experimental assignment | | ² B ₂ | ² B ₁ | ² B ₂ | ² A ₁ | |

- a) M.D. Newton, W.E. Palke, *J.Chem.Phys.* 45, 2329-2330 (1966).
 b) N.W. Winter, T.H. Dunning, and J.H. Letcher, *J.Chem.Phys.* 49, 1871-1877 (1968).
 c) D.B. Neumann, and J.W. Moskowitz, *J.Chem.Phys.* 50, 2216-2236 (1969).
 d) R.J. Buenker, and S.D. Peyerimhoff, *J.Chem.Phys.* 53, 1368-1384 (1970).
 e) B.J. Garrison, H.F. Schaefer III, and W.A. Lester, *J.Chem.Phys.* 61, 3039-3042 (1974).
 f) L.S. Cederbaum, W.Domcke, and W. v.Niessen, *Chem.Phys.Letters* 34, 60-62 (1975).
 g) R. Jaquet, Diplomarbeit Ruhr-Universität Bochum, 1976, calculation with a (9,5) Huzinaga basis in the contraction (5,4x1/3,2x1) plus a d set for C and O and a 5s(3,2x1) basis for H plus one p function.
 h) as g) but with a (7,3) basis in the contraction (4,1,1,1/2,1) for C and O.
 i) D.W. Turner, C. Baker, A.D. Baker, and C.R. Brundle *'Molecular Photoelectron Spectroscopy'*, Wiley, New York (1970).

the respective ion and compute the difference of their energies either vertically or adiabatically to get the correct ionization potential (this has e.g. been done by Meyer (25) for methane); alternatively one can use a 'direct' method for the calculation of energy differences, e.g. one based on perturbation theory in a framework of one-particle Green functions (51). In this approach the orbital energies are the first approximations, which are then improved by higher order contributions. The formaldehyde molecule has been studied in this way by Cederbaum et al. (52). The ground state configuration of formaldehyde is

$1a_1^2 2a_1^2 3a_1^2 4a_1^2 1b_2^2 5a_1^2 1b_1^2 2b_2^2$. Of these orbitals $2b_2$ describes the lone pair in the molecular plane, antisymmetric to the plane bisecting the HCH angle, $1b_1$ is the binding π -MO and $5a_1$ mainly the other (totally symmetric) lone pair. The orbital energies of the 4 highest MO's are compared in Table 7 with the improved theoretical values of Cederbaum et al. (52) and the experimental ionization energies. The assignment could be confirmed definitely by a calculation of the vibrational structure of the different PE bands (52). In this case the order of the orbital energies agrees with that of the corresponding ionization potentials (but disagrees with the original assignment given by Turner (49), based on band shapes and intuitive arguments).

It is an interesting task for theoreticians to study the properties of the radical ions that are produced in photoelectron experiments since they are only to some extent accessible to experimental investigations. A theoretical study of reorganisation upon ionization (as well as excitation) has recently been published by Özkan et al. (53) based on SCF calculation with double zeta and double zeta plus polarization basis sets. For details concerning both the change of the electronic structure and the change of the equilibrium geometry the reader is referred to the original paper (53).

The influence of substituents on the highest orbital energies (and, indirectly, via Koopmans' theorem, on the vibrational ionization potentials) was studied by Del Bene et al. (33). The trends were well reproduced, but, as expected, not the explicit values of the ionization potentials. The semiempirical CNDO/S is also still being used to help in the assignment of the PE spectra of carbonyl compounds (54).

8. UV SPECTRA AND THE PROPERTIES OF EXCITED STATES

Ab initio calculations of uv-absorption spectra are somewhat more difficult than calculations of photoelectron spectra. Nevertheless calculations are available that help to understand, and to assign, better the uv spectra of small molecules. The identification of still unknown molecules from their uv spectra (e.g. from astrophysical measurements) may be possible in the near future. It requires somewhat less effort to calculate just vertical transition frequencies, i.e. differences between the ground state and excited states in the equilibrium geometry of the ground state. A full calculation of the spectra would imply calculations of the potential hypersurfaces of both states near their equilibria, solution of the vibrational Schrödinger equations and calculation of the Franck-Condon factors.

Excited states of different symmetry or spin multiplicity than the ground state can be treated quantum chemically by similar techniques if they are the lowest states of their symmetry and spin multiplicity. An example of such a state is the $^3(n-\pi^*)$ state of formaldehyde or even the $^1(n-\pi^*)$ state as long as one imposes at least C_s symmetry. Other examples are the $^1(\pi-\pi^*)$ and $^3(\pi-\pi^*)$ states of ethylene, while the $^1(\pi-\pi^*)$ state of formaldehyde has the same symmetry as the ground state. For states that are not the lowest ones of their symmetry a configuration interaction (CI) approach is necessary and one has to take the second lowest (or a higher) root of the secular equation. CI is also necessary whenever avoided crossing of potential surfaces occur, and this is much more frequent for excited states than for ground states.

In principle one can get the energies (and wave functions) of the ground and several excited states from a single CI and thus even take care of correlation effects for all these states. CI seems to be the method of choice for the calculation of (spectra). However, in a CI that is satisfactory in all desired respects one has to include an astronomical number of configurations. In order to get the calculations done one has to be modest and to select only those configurations that are supposed to be 'important'. It is not necessary to use a large basis set (polarization functions will usually be a luxury) but basis functions with small orbital exponents (so called 'diffuse functions') have to be included since they are essential for Rydberg-type and Rydberg-like orbitals. Omission of 'diffuse functions' usually leads to acceptable results only for some low-lying excited states. The amount of correlation energy that one can take care of is usually of the order of ~10% and one can only hope that the change of correlation energy between different states are smaller than this.

That in this way one gets surprisingly good spectra is, nevertheless, understandable. Spectral

transition energies are in the order of a few 100 kcal/mol i.e. quite large compared with energy differences that matter in ground state calculations. Moreover the observed bands are usually quite broad and an error of -10 kcal/mol (-0.5 eV) is regarded as small.

Like for PE spectra 'direct methods' for uv-spectra, which yield the energy differences directly and not as a difference between two numbers, are competitive with the more traditional methods like CI. The most successful one of these direct methods is the 'equation of motion' method (EOM) which can be regarded as an improved 'random phase approximation' (RPA). The advantage of EOM as compared to CI is that it requires much less computer time. A disadvantage is the lack of a rigorous theoretical foundation (55,56).

The present state of our understanding of the electronic spectrum of formaldehyde has been reviewed by Moule and Walsh (57), we therefore need not to go into details here. In Table 8

TABLE 8. Electronic transition energies of formaldehyde^{a)}

| Assignment | exp. ^{b)} | exp. ^{c)} | CI ^{d)} | CI without flat functions ^{e)} | CI with flat functions ^{f)} | GVB-CI ^{g)} | MC-SCF ^{h)} | EOM ^{i)j)} |
|--|--------------------|--------------------|------------------|---|--------------------------------------|----------------------|----------------------|---------------------|
| ${}^1A_1 \rightarrow {}^3A_2 ({}^3A''); {}^3(n-\pi^*)$ | 3.12 | 3.5 | 3.38 | 3.01 | 3.41 | 3.62 | | 3.46 |
| $\rightarrow {}^1A_2 ({}^1A''); {}^1(n-\pi^*)$ | 3.50 | 4.1 | 3.80 | 3.43 | 3.81 | 4.09 | | 4.04 |
| $\rightarrow {}^3A_1; {}^3(\pi-\pi^*)$ | | 6.0 | 5.66 | 4.99 | 5.56 | 5.95 | | 5.29 |
| $\rightarrow {}^3B_2; {}^3(n-s)$ | | | | | 7.32 | | | |
| $\rightarrow {}^1B_2; {}^1(n-s)$ | 7.08 | | 7.48 | | 7.38 | | | 7.28 |
| $\rightarrow {}^3A_1; {}^3(n-p)$ | | | | | 8.09 | | | |
| $\rightarrow {}^1A_1; {}^1(n-p)$ | 7.97 | | 8.30 | | 8.11 | | | 8.12 |
| $\rightarrow {}^3B_1; {}^3(\sigma-\pi^*)$ | | | | | 8.14 | | | |
| $\rightarrow {}^1B_1; {}^1(\sigma-\pi^*)$ | | | 9.35 | 8.61 | 9.03 | | | 9.19 |
| $\rightarrow {}^3A_2; {}^3(n-p)$ | | | | | 9.06 | | | |
| $\rightarrow {}^1A_2; {}^1(n-p)$ | 8.47 ^{k)} | | | | 9.07 | | | 8.35 |
| $\rightarrow {}^3B_2; {}^3(n-p)$ | | | | | 8.29 | | | |
| $\rightarrow {}^1B_2; {}^1(n-p)$ | 8.14 ^{k)} | | | | 8.39 | | | 8.15 |
| $\rightarrow {}^1A_1; {}^1(\pi-\pi^*)$ | | (10.5) | 11.31 | 11.72 | 11.41 | 10.77 | 11.2 | 10.10 |

a) energies in eV.

b) G. Herzberg, Molecular spectra and molecular structure. III. Electronic spectra and electronic structure of poly atomic molecules, Princeton, van Nostrand, 1966.

c) L.B. Harding, and W.A. Goddard, J. Am. Chem. Soc. **97**, 6293-6299 (1975)

d) J.L. Whitten, and M. Hackmeyer, J. Chem. Phys. **51**, 5584-5596 (1969)

e) R.J. Buenker, and S.D. Peyerimhoff, J. Chem. Phys. **53**, 1368-1384 (1970)

f) S.D. Peyerimhoff, R.J. Buenker, W.E. Kammer, and H. Hsu, Chem. Phys. Letters **8**, 129-135 (1971)

g) GVB = generalized valence bond

h) S.R. Langhoff, S.T. Elbert, C.F. Jackels, and E.R. Davidson, Chem. Phys. Letters **29**, 247-249 (1974)

i) EOM = equations of motions

j) D.L. Yeager, and V. McKoy, J. Chem. Phys. **60**, 2714-2716 (1974)

k) C.R. Lessard, and D.C. Moule, J. Mol. Spectr. **60**, 343-347 (1976)

we compare theoretical and experimental absorption frequencies of formaldehyde. It becomes clear from Ref. 57 that the ab-initio calculations (58-60) especially those of Buenker and Peyerimhoff (58) and of Whitten and Hackmeyer (59) were very helpful for a better understanding of the spectrum of formaldehyde.

On the long-wave length side of the spectrum one first finds two weak but rather sharp bands with maxima close to 3968 Å (3.12 eV) and 3538 Å (3.50 eV) about the assignment of which as ${}^3(n-\pi^*)$ and ${}^1(n-\pi^*)$ transitions respectively no doubt existed. Next, theory predicts the ${}^3(\pi-\pi^*)$ transition at 5-6 eV. An absorption observed recently (61) near 6 eV in the electron impact spectrum can be identified with this transition. The most unexpected result from the

calculations is that the $^1(\pi-\pi^*)$ transition lies at least at 10 eV (62), probably at 11 eV (63). Some time ago the strong absorption at 1750 Å (7 eV) was assigned as $^1(\pi-\pi)$ transition, but it is now well-established that this band as well as another one at 1556 Å (8 eV) are the first members of Rydberg series.

Concerning the $^1(\pi-\pi^*)$ excited state there has been some discussion as to how 'diffuse' it is (or alternatively 'how much Rydberg character it has'). The distinction between valence and Rydberg states becomes rather meaningless for a state like this one which is energetically so close to its ionization limit (the π -ionization potential is 14.5 eV) since the long range behaviour of a wave function is determined by its ionization potential ϵ through (64)

$$\psi(r) \sim \exp \sqrt{-2\epsilon} r$$

and it has to have a long range if ϵ is small, irrespective of whether it is assigned as a valence or Rydberg excited state.

Two more critical points concerning the $^1(\pi-\pi^*)$ state are a) that it lies above several excited states of the same (1A_1) symmetry that belong to a $^1(n-p)$ Rydberg series, which makes its computation somewhat difficult. b) that it lies above the first ionization potential of formaldehyde, it can hence in principle interact with continuum states of the same symmetry and autoionize. It does not seem that it will be easy to observe this state, namely there are several factors that will make the absorption broad and diffuse (strong change in the geometry as well as possible autoionization); furthermore, in this range of frequencies other transitions may show up.

It is not clear to what extent the change in the assignment of the spectrum has consequences for the assignment of the spectra of other carbonyl compounds. The $^1(\pi-\pi^*)$ state may lie lower in other carbonyls than it does in formaldehyde. Robin et al. (65) present strong arguments for assigning the $^1(\pi-\pi^*)$ band of formamide at ~7.5 eV, however the π -MO in formamide (like in the formate ion (66)) is more an allyl-type non bonding MO (with a strong participation of the lone pair of N) than a bonding π -MO (as in formaldehyde).

For the chemistry of the carbonyl groups the $^1(n-\pi^*)$ and $^3(n-\pi^*)$ excited states are especially important. It has been shown experimentally (67-69) that these states are non-planar, i.e. pyramidal. The geometries deduced from experimental studies are in good agreement with the theoretical ones (see Table 9).

TABLE 9. Equilibrium geometry of the lowest excited triplet state of H_2CO^a

| | SCF ^{a)} STO-3G | SCF ^{b)} double zeta | limited CI double zeta | double zeta + polarization, SCF | near Hartree- Fock ^{e)} | exp. ^{f)} |
|------------------|-----------------------------|-------------------------------------|------------------------------|---------------------------------------|--|--------------------|
| r_{CO} | 1.393 | 1.370 | | 1.33 | | 1.31 |
| r_{CH} | 1.088 | | | | | 1.10 |
| $\angle HCH$ | 117.3 ^o | | | | | 118 ^o |
| $\angle CO/CH_2$ | 37.8 ^o | 32 ^o | | 30 ^o | | 35 ^o |
| dipole moment | | 1.76 1.76 ^{c)} | 1.68 1.59 ^{c)} | | 1.453 | 1.29 |

a) W.A. Lathan, L.A. Curtiss, W.J. Hehre, J.B. Lisle, and J.A. Pople, *Prog.Phys.Org.Chem.* 11, 175-261 (1974)

b) R.J. Buenker, and S.D. Peyerimhoff, *J.Chem. Phys.* 53, 1368-1384 (1970)

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e) B.J. Garrison, H.F. Schaefer III, and W.A. Lester, *J.Chem.Phys.* 61, 3039 (1974)

f) R.N. Dixon, *Mol. Phys.* 12, 83-90 (1967)

The $^1(n-\pi^*)$ and $^3(n-\pi^*)$ states do not differ much in their geometry. This is a consequence of the small energy difference between them and this again is due to the smallness of the exchange integral between n and π^* orbitals - they are localized in different regions of space - which is mainly responsible for the singlet triplet splitting.

Garrison et al. (28) have calculated several expectation values such as dipole moments, quadrupole moments, field gradients etc. of the various excited states. The influence of substituents on the $n-\pi^*$ transition frequencies was studied by Del Bene et al. (33) and by Ha and Keller (70). In spite of the smallness of the basis sets used the agreement with experiment

was satisfactory in both studies. The vertical $n-\pi^*$ -transitions in formaldehyde are symmetry-forbidden for the electric dipole moment but allowed for the magnetic dipole. If, by a slight distortion of the symmetry through substitution, the transition gets dipole-allowed; the condition for high circular dichroism is fulfilled. A recent study of the magnetic circular dichroism of the $n-\pi^*$ -transition in formaldehyde can be found in Ref. 71.

Some theoretical predictions of the spectrum of thioformaldehyde are collected in Table 10. The difference compared to formaldehyde lies mainly in the prediction that the $^1(\pi-\pi^*)$ transition should occur at ~ 8 eV, and hence below the first ionization limit and in the fact that the $(n-\pi^*)$ transition should appear at larger wave lengths, namely in the visible region of the spectrum and thioformaldehyde should hence be a coloured species (probably red to violet).

TABLE 10. Electronic transition energies of thioformaldehyde^{a)}

| Assignment | exp. ^{b)} | PPP ^{c)} | STO-3G SCF ^{d)} | double zeta + diffuse ^{b)} functions, CI |
|--|--------------------|-------------------|-----------------------------|--|
| $^1A_1 \rightarrow ^3A_2; ^3(n-\pi^*)$ | 2.1 | 1.89 | 1.76 | 1.84 |
| $\rightarrow ^1A_2; ^1(n-\pi^*)$ | 2.4 | 2.34 | 2.87 | 2.17 |
| $\rightarrow ^3A_1; ^3(\pi-\pi^*)$ | | | | 3.28 |
| $\rightarrow ^3B_2; ^3(n-s)$ | | | | 5.72 |
| $\rightarrow ^1B_2; ^1(n-s)$ | 5.9 | | | 5.83 |
| $\rightarrow ^3A_1; ^3(n-p)$ | | | | 6.58 |
| $\rightarrow ^1A_1; ^1(n-p)$ | 5.8 | | | 6.62 |
| $\rightarrow ^1A_1; ^1(\pi-\pi)$ | | | | 7.92 |

a) all energies in eV.

b) P.J. Bruna, S.D. Peyerimhoff, R.J. Buenker, and P. Rosmus, *Chem.Phys.* **3**, 35-53 (1974); not all calculated frequencies reported there are reproduced, the experimental values are not from thioformaldehyde but mean values from some other thiones.

c) J. Fabian and A. Mehlhorn, *Z.Chem.* **9**, 271-272 (1969).

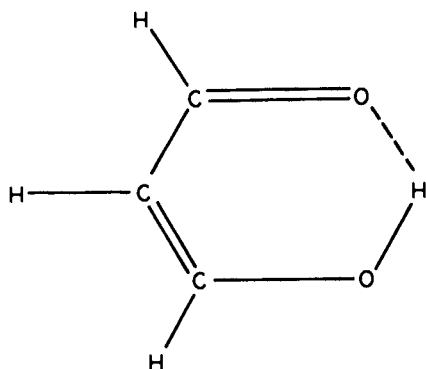
d) N.C. Baird, and J.R. Swenson, *J. Phys.Chem.* **77**, 277-280 (1973).

In none of the papers (43) where studies on thioformaldehyde are reported could information on the colour of this species be found. The more stable thiones are known to be deeply coloured (72).

9. INTERMOLECULAR (AND INTRAMOLECULAR) INTERACTIONS

Carbonyl compounds readily form molecular complexes. They can act both as electron donors and as electron acceptors. In the transition metal complexes of carbonyl compounds the σ -donor and π -acceptor properties are important. The π -acceptor function is also essential in the charge transfer complexes involving carbonyls, while in hydrogen bonded complexes the σ -donor properties are used. The simplest models for complexes where the carbonyl group is a donor are the protonated carbonyls. To calculate protonation energies is one of the easiest tasks in quantum chemistry. SCF calculations are usually sufficient because the correlation energy does not change significantly on protonation. Moreover polarization functions, although important for both the protonated and the unprotonated molecule, have little effect on the energy difference between them.

The 'gas phase' proton affinity of formaldehyde as well as that of many other molecules has been calculated by Lathan et al. (24). They find a proton affinity of 221 kcal/mol for formaldehyde compared to the one for water of 229 kcal/mol with the STO-3G basis, whereas the respective values obtained with the 4-31G basis (that is close to double zeta quality) are 178 and 182 kcal/mol. For both basis sets, but especially the first one, the proton affinities are much too high, (the experimental gas phase values are close to 160 kcal/mol). The result that there is nearly no difference between water and formaldehyde is common to both calculations and the experiment (73). This is a hint that the proton affinity is mainly a property of the lone pair at the oxygen. 4-31G basis sets have also been used in the study of the protonation of formaldehyde and thioformaldehyde by Bernardi et al. (74). They find 180 kcal/mol for formaldehyde and 177 kcal/mol for thioformaldehyde. The optimum geometry of the cations H_2COH^+ and H_2CSH^+ were found to be an all-planar arrangement. The computed geometrical parameters are collected in Table 11.



The most sophisticated SCF calculation of Karlström et al. (81) led to the conclusion that the C_s structure with an asymmetric H bond is stabler by ~ 12 kcal/mol than a C_{2v} structure with a symmetrical H bridge. That this result cannot yet be regarded as fully certain is due a) to the neglect of correlation effect in this study (in the related system $H_5O_2^+$ (82) the correlation energy leads to a significant stabilization of the symmetric structure); b) the fact that not all geometrical parameters have been optimized (this should be less critical in the present case). The conditions under which symmetrical structures occur are still not fully understood (see however ref. 80).

Unfortunately no calculations have been performed either on the trans structure (where no H bond is possible) or on the diketo isomer in order to evaluate the stabilization through enolization (i.e. π -delocalization) of β diketones.

10. CHEMICAL REACTIONS

The most important elementary chemical process that involves carbonyl compounds is the nucleophilic attack on the carbon atom. The simplest nucleophile is H^- , therefore a study of the reaction of formaldehyde with H^- to yield H_3CO^- has some model character. The minimum energy path for this reaction was calculated in the SCF approximation with a small basis of gaussians (between single and double zeta quality, no polarization functions, no flat functions to describe H⁻ appropriately) by Bürgi, Lehn and Wipff (83). As expected, this reaction is highly exoenergetic and has no barrier, the reaction product was found to be ~ 50 kcal/mol lower in energy than the reactants. The change in the various geometrical parameters along this minimum energy path was found to be in good agreement with results deduced from crystal structure determinations on the interaction of amino groups with carbonyls. Depending on the distance between these subunits in different crystals the optimum relaxation of the internal coordinates and the optimum relative orientation could be studied (84).

As long as H^- is far from formaldehyde it approaches the formaldehyde unit in its molecular plane from the side of the H atoms along the line bisecting them. When it is closer it prefers an approach nearly perpendicular to the formaldehyd plane. Only when the H^- starts to get directly bonded to the C-atom the formaldehyd gets slightly deformed until the nearly tetrahedral reaction product H_3CO^- is obtained

A more realistic nucleophilic substitutions reaction was recently studied theoretically by Alagona et al. (85), namely the hydrolysis of formamide by OH^- . The reaction path goes in three steps, (a) addition of OH^- to the nearly tetrahedral complex

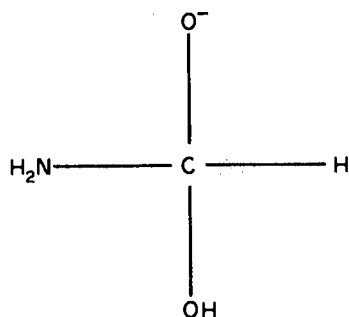


TABLE 11. Geometry of protonated formaldehyde and thioformaldehyde

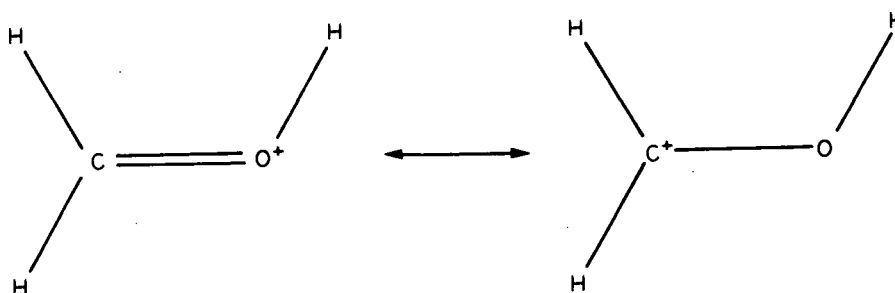
| | H ₂ COH ⁺ b) | H ₂ COH ⁺ c) | H ₂ CSH ⁺ c) |
|-----------------------|------------------------------------|------------------------------------|------------------------------------|
| r(CH) | 1.11 | 1.09 | 1.07 |
| r _{CO,(CS)} | 1.27 | 1.25 | 1.65 |
| r(XH) | 1.00 | 0.96 | 1.36 |
| ∠ _{HCH} | 121° | 122.1° | 117.3° |
| ∠ _{HOC(HSC)} | 114.7° | 124.7° | 100.9° |

a) all distances in Å.

b) W.A. Lathan, L.A. Curtiss, W.J. Hehre, J.B. Lisle and J.A. Pople, *Prog.Phys.Org. Chem.* 11, 175-261 (1974).

c) F. Bernadi, I.G. Csizmadia, H.B. Schlegel, and S. Wolfe, *Canad.J.Chem.* 53, 1144-1153 (1975).

The increase in the CO(CS) bond lengths compared to the parent molecules, indicates that there is some charge delocalization or to use a somewhat old fashioned formulation, a resonance between the mesomeric forms



The partial positive charge makes a nucleophilic attack on the C atom easier than in the unprotonated form.

H₂COH⁺ and H₂CSH⁺ are isoelectronic with methyleneimine, H₂CNH, for which Lehn et al. (75) have studied the possible isomerizations through either inversion or rotation about the double bond. Bernardi et al. (74) found that for H₂COH⁺ like for H₂CNH (75), inversion (involving a C_{2v} transition state with a linear C-O-H bond) is more favourable. A barrier of 14 kcal/mol was found for this process, whereas in H₂CSH⁺ rotation (with a barrier of 37 kcal/mol) is energetically favoured over inversion. It has to be mentioned that Bernardi et al. used a CI procedure for the determination of rotational barriers, since it is well known that closed shell SCF-calculations overestimate rotational barriers about C=C double bonds terribly (for ethylene one finds e.g. 100 instead of 60 kcal/mol). For the two systems considered here, the SCF-error for the barriers is smaller.

There exists, of course, some similarity between the protonation of carbonyls and the formation of hydrogen bonds between a carbonyl and some proton donor. The binding energy of formaldehyde via hydrogen bonding to various proton donors, obtained by Kollman et al. (76) is, on the whole, 1-4 kcal/mol smaller than that of water with the same proton donors. The binding energies of thioformaldehyde are smaller by 1-4 kcal/mol and are practically the same as those for hydrogen sulfide. For the interaction with, e.g., HF the following values (in kcal/mol) were computed: H₂O:13.4; H₂CO:10.0; H₂S:5.8; H₂CS:6.1. Some recent theoretical studies on the hydrogen bonds involving carbonyl compounds are those of Ottersen (77) and Paoloni (78).

Of the hydrogen bonds involving carbonyl groups the ones in the adenine-cytosine base pair (79) are probably the most studied. One particular hydrogen bond involving a carbonyl group has recently received the theoreticians interest, namely, the internal H bond in the enol form of malondialdehyde (80,81)

(b) the migration of an H atom from O to N and (c) the abstraction of NH_3 . The first step is geometrically very similar to the addition of H^- to Cl_2O as studied by Bürgi et al. (83).

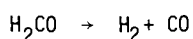
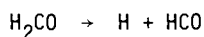
All these theoretical studies have to be regarded as preliminary, not so much because they deal with gas phase reactions, but rather due to the small basis sets used. There is a special problem with negative ions which has been realized for quite a while but which is still ignored in most current theoretical studies, namely, the AO basis for the neutral atoms are not the appropriate ones for the ions (86,87). This leads to unrealistically high energies of negative ions (unless one includes diffuse functions as for calculations of spectra) and spurious stabilization of larger ions with delocalized charges. Polarization functions as well as correlation effects are probably less important.

Another question is whether it is really appropriate to formulate nucleophilic substitution reactions in solution in terms of free negative ions as intermediates (92). The proton-catalyzed hydrolysis of formamide was studied theoretically by Hopkins and Czismadia (88).

For carbonyl compounds like formaldehyde photochemical reactions are nearly as important as reactions that start from the ground state. The first step of any photochemical reaction of formaldehyde is the excitation to the $^1(n-\pi^*)$ state. There are then three possible reaction paths:

- a) reaction on the surface of the $^1(n-\pi^*)$ state;
- b) intersystem crossing to the $^3(n-\pi^*)$ state which is highly probable in formaldehyde because of the small singlet triplet splitting - followed by a reaction on the triplet surface;
- c) radiationless transition to a vibrationally excited state of the electronic ground state and reaction on this surface.

One can further think of a transition between these branches during the course of the reaction. The simplest unimolecular photochemical decompositions of formaldehyde



were studied by Morokuma (89) with minimal basis SCF and CI calculations and recently with MC-SCF and 4-31G basis sets. For both types of reactions the three potential surfaces of the ground state and the lowest excited singlet and triplet states were computed. Unambiguous conclusions concerning the reaction paths are not yet possible, for the first reaction only path a) could be ruled out whereas for the second reaction path c) seems to be most likely, although there is a 1 eV discrepancy in the computed and experimental thresholds.

The addition of $(n-\pi^*)$ -formaldehyde to electron-rich ketones (90) or inverse processes like the thermal dissociation of (tetramethyl)dioxetane which leads to acetone in the $^3(n-\pi^*)$ state (91) are somewhat more complicated. The theoretical study of photochemical reactions will probably be one of the most interesting quantum chemical topics in the near future.

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Notes added after submission of the manuscript

Thioformaldehyde has meanwhile been prepared in pure form by thermal decomposition of methyl-sulfenylchloride (93).

Prior to the synthesis, the PE spectrum of thioformaldehyde had been calculated by P. Rosmus on the basis of PNO-CI calculations for the neutral molecule and various states of the radical cation. The PE spectrum served to identify thioformaldehyde and to obtain it free from contaminations. This is one of the most impressive examples when ab-initio calculations had an important part in the planning of a synthesis.

The PE spectrum of thioformaldehyde was also studied independently using the Green's function method (94). The agreement between the two sets of calculations and experiments is nearly perfect, whereas the Koopmans energies differ by 1 to 2 eV, except for the two first ionization potentials where the agreement is better (this is quite similar to what one finds for formaldehyde, see table 7).

Additional information on the theoretical PE spectrum of formaldehyde can be found in Ref. 95 where also the fifth ionization potential is given (exp. 21.60 eV, calc. 21.57 eV).

Concerning experimental information on the UV spectrum of thioformaldehyde, ref. 96, 97 and 98 may be consulted.

A comparative theoretical study of the UV spectra of some simple carbonyl and thio-carbonyl compounds has been performed by P.J. Bruna (to be published).

SOME MECHANISTIC STUDIES ON THE HYDROLYSIS OF ACETALS AND
HEMIACETALS

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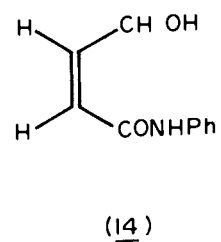
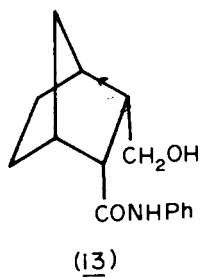
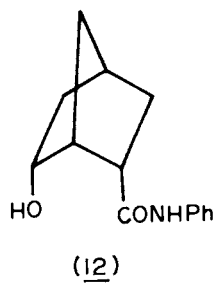
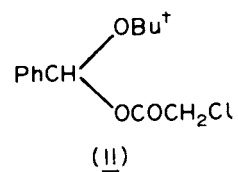
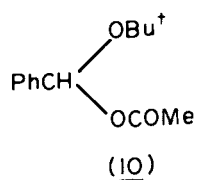
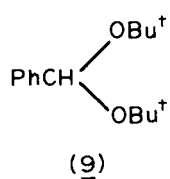
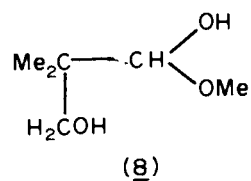
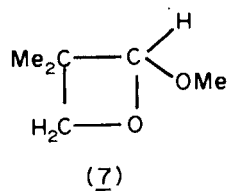
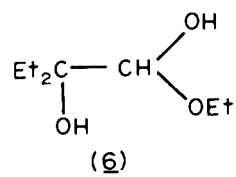
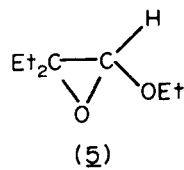
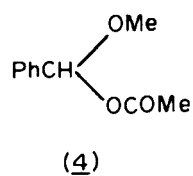
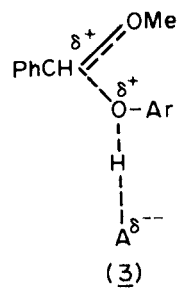
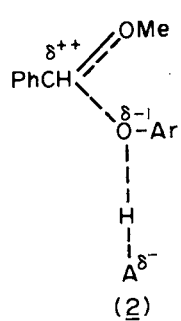
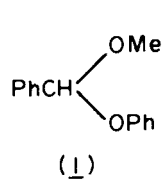
Abstract - The general-acid catalysed hydrolysis of acetals is discussed. It is shown that under certain conditions the rate-limiting step in the hydrolysis of α -acetoxy- α -methoxy-toluene and benzaldehyde di-*t*-butylacetal is decomposition of the hemiacetal. Attempts to study the decomposition of tetrahedral intermediates at the oxidation level of carboxylic acids are described.

The work that I am going to describe today was started about ten years ago and continues until last week. This means that in the early part of my lecture I shall be describing work that is already published or in the course of publication and on which our ideas are reasonably clear, whereas in the second half I shall be describing very recent work upon which our ideas are less clear and for which we have not completed all the experiments we should have liked to have done.

About ten years ago one of my students, Dr. E. Anderson, and I decided that we would try to find an acetal whose hydrolysis was general-acid catalysed, intermolecularly. We had discovered previously examples of intramolecular general-acid catalysis (1) and wondered if it was possible by suitable choice of acetal to observe intermolecular general-acid catalysis. It had been shown by Brønsted and Wynne-Jones that the hydrolysis of diethyl acetal was specific-acid catalysed (2). This has usually been interpreted as indicating that the proton transfer occurs in a rapid and reversible step and is followed by a rate-limiting decomposition of the conjugate acid to give a carbonium-oxonium ion. We considered the free-energy reaction coordinate diagram for such a mechanism and asked the question (3): "what structural changes would be necessary to cause a change to general-acid catalysis?". For the reaction to be general-acid catalysed it would be necessary for the proton transfer step to be rate-limiting and we considered that it would be possible to achieve this by making the conjugate acid less stable and/or the carbonium-oxonium ion more stable. We therefore studied the hydrolysis of benzaldehyde methyl phenyl acetal (1) and found this reaction to be general-acid catalysed. This work was published in 1969 (3), shortly after Fife and Jao's report of the first well authenticated example of general-acid catalysis in the hydrolysis of an acetal, *p*-nitrophenoxy-tetrahydropyran (4).

Another way of looking at this change from specific- to general-acid catalysis on going from diethyl acetal to benzaldehyde methyl phenyl acetal is that with the former compound complete proton transfer is necessary for bond cleavage to occur, whereas with the latter partial proton transfer is sufficient.

After this work Dr. Anderson departed for California to continue his work on acetals very successfully in Professor Fife's laboratory and the investigation was continued in our laboratory by Dr. Nimmo. Dr. Nimmo studied the effect of substituents on the rate constants for the general-acid catalysed hydrolysis of benzaldehyde methyl phenyl acetal. His most interesting result was that both electron-withdrawing and electron-releasing substituents in the phenoxy group caused an increase in catalytic constants for hydrolysis when the catalyst was a carboxylic acid. This result puzzled us for a long time but eventually we hit on what we think is the correct explanation (5). The general-acid catalysed hydrolysis of benzaldehyde methyl phenyl acetal is an electrophilic substitution on oxygen which involves breaking of a carbon-oxygen bond and formation of a hydrogen-oxygen bond. If the former runs ahead of the latter the oxygen upon which the substitution takes place will carry a net negative



charge (2) whereas if the latter runs ahead of the former it will carry a net positive charge (3). Thus the experimental observations could be explained if compounds with electron-withdrawing substituents in the phenoxy group had a transition state of type (2) whereas compounds with electron-releasing substituents had a transition state of type (3). That this is reasonable is seen by consideration of the contour diagram of the type introduced by Dr. More O'Ferrall (6) and used widely by Professor Jencks (7). In this diagram (Fig.1) proton transfer is plotted on the x-axis and C-O bond breaking on the y-axis. If the transition state saddle point lies above the positively sloping diagonal there is more C-O bond breaking than O-H bond forming and increasing the electron-withdrawing power of the substituent would cause the transition state to move towards the left and top of the diagram and its energy to decrease. Conversely increasing the electron-releasing power of the substituent will cause the transition state to move towards the right and bottom of the diagram and increase until the diagonal is passed. The saddle point then lies below the diagonal with more O-H bond forming than C-O bond breaking and while increasing the electron-releasing ability of the substituent still causes the saddle point to move to the right and bottom of the diagram, it now causes a decrease in the energy of the transition state, because the oxygen now carries a net positive charge.

This behaviour is not found in the hydronium-ion catalysed reaction for which electron-releasing substituents are rate enhancing and electron-withdrawing substituents rate decreasing. This suggests that the transition state saddle point always lies below the positively sloping diagonal when the hydronium ion is the catalyst and that O-H bond forming always runs ahead of C-O bond breaking.

We were interested to note that a similar effect appeared to be occurring in the decomposition of the addition compounds of alcohols with the N,Q-tri-methylene phthalimidium ion studied by Gravitz and Jencks (8).

Before completing his Ph.D. Dr. Nimmo carried out a brief investigation of the hydrolysis of α -acetoxy- α -methoxy-toluene (4). This compound was originally made in our laboratory by Dr. Anderson but he did not have time to carry out a kinetic investigation. We were interested in studying this compound because on going from benzaldehyde dimethyl acetal to benzaldehyde methyl phenyl acetal the hydrolysis changes from being specific-acid catalysed to general-acid catalysed and we wondered what the effect would be of having a still better leaving group, acetoxy, instead of phenoxy.

Would the reaction still be general-acid catalysed or would we get a reaction that follows the pathway of the left-hand side and the top of the More O'Ferrall-Jencks diagram (Fig.1)? Now of course we know on the basis of Jencks' rule (9) that the latter is what would be expected for catalysis by carboxylic acids because there would be no thermodynamic advantage for the transfer of a proton from a catalyst to the leaving group. Dr. Nimmo just carried out a series of reactions in several carboxylic-acid buffers but only used one buffer ratio for each acid. He followed the formation of benzaldehyde spectrophotometrically (280 nm) and observed catalysis by the components of the buffer. We assumed that by analogy to benzaldehyde methyl phenyl acetal that general-acid catalysis was occurring and calculated catalytic constants on this basis. These showed very little variation with structure of the carboxylic acid. This result was subsequently confirmed by Mr. Gordon Reid and although we were able to find an explanation for this result we were not entirely happy with it and checked to see if the reaction was also general base catalysed. This was found to be so in acetate buffers and we obtained catalytic constants $k(\text{HOAc}) = 0.0771 \text{ l/mole/s}$ and $k(\text{AcO}^-) = 0.180 \text{ l/mole/s}$ at 15° . The value of $k(\text{HOAc})$ was not unreasonable but that of $k(\text{AcO}^-)$ was very much larger than $k(\text{AcO}^-)$ for the hydrolysis of *p*-nitrophenyl acetate which is $5.64 \times 10^{-6} \text{ l/mole/s}$ at 25° . It seemed to us that this catalysis could not be nucleophilic or general-base catalysis of a reaction at the acetoxy group of the starting material since *p*-nitrophenoxy should be a much better leaving group than α -methoxy- α -phenoxy-methoxy. It is also difficult to see how a catalytic constant of this magnitude could arise from attack at the pro-acyl carbon. After quite a long time we realised what must be happening. The acetoxy-group is such a good leaving group that the step in which it leaves is not the rate determining step which has become decomposition of the hemiacetal. Hemiacetal decomposition is similar to the dehydration of aldehyde hydrates (11) and the mutarotation of glucose (12) both of which show general-acid and general-base catalysis. To test whether decomposition of the hemiacetal were rate-determining we studied the hydrolysis of α -chloroacetoxy- α -methoxy-toluene

since if a reaction of the starting material were rate-determining different rate constants would be expected for the α -acetoxy and α -chloroacetoxy compounds whereas if the decomposition of the hemiacetal were rate-determining, the rate constants should be identical within experimental error. The experimental results show that the latter is occurring. Further evidence that decomposition of the hemiacetal was slower than its formation was obtained by following the reaction in an acetate buffer (0.1M NaOAc, 0.1M DOAc) in a mixture of deuterated dimethyl sulphoxide and deuterium oxide (1:1 v/v) at 2° by NMR spectroscopy (Varian HA 100). The chemical shift of the signal of the pro-acyl CH proton of the starting material was determined about one minute after dissolving to be $\delta=6.48$ ppm downfield from internal sodium 2,2-dimethyl-2-silapentane-5-sulphonate. In this spectrum there was a very small signal at $\delta=5.44$ ppm which was ascribed to the pro-acyl CH proton of the hemiacetal since its chemical shift was close to that of the CH proton of benzaldehyde dimethyl acetal for which $\delta=5.35$ ppm. This signal increased in intensity as the signal at $\delta=6.48$ decreased and after about 14 minutes the two signals were of approximately equal intensities. In this spectrum there was also a small signal at $\delta=9.88$ ppm which is the chemical shift of the acyl CH proton of benzaldehyde. After two hours the signals at $\delta=6.48$ and 5.44 ppm had disappeared and only the signal at $\delta=9.88$ remained. Thus under these conditions formation of the hemiacetal is faster than its decomposition to benzaldehyde.

There have been relatively few previous investigations of the decomposition of hemiacetals (13, 14, 15, 16) and to our knowledge none of those derived from aromatic aldehydes. In the hydrolysis of acetals the decomposition of the hemiacetal is normally a fast step (17) and for aromatic aldehydes the equilibrium constant for the formation of hemiacetals is normally unfavourable unless electron-withdrawing substituents are present (18). The generation of hemiacetals of aromatic aldehydes as intermediates in the hydrolysis of their *O*-acetates therefore provides for the first time a general method for studying their decomposition. In the pH-range 3.69 to 6.27 there is no indication of a change in the rate-determining step to formation of the hemiacetal but this may occur at higher pHs.

This work indicates that if one had a very reactive acetal there is a possibility that decomposition of the hemiacetal might be the rate-limiting step. In recent years two examples of this type of behaviour have been discovered (15, 16). Thus Schaleger and his co-workers found that at low pHs decomposition of the hemiacetal (6) was rate-limiting in the hydrolysis of acetal (5) and Atkinson and Bruce found that decomposition of hemiacetal (8) was rate-limiting in the hydrolysis of acetal (7). The rate-limiting step changed to formation of the hemiacetal at high pHs with both compounds. We wondered if there were any further examples of this type of behaviour that had not been recognised and remembered the hydrolysis of benzaldehyde di-*t*-butyl acetal (2). It had been shown by Cawley and Westheimer that bond fission occurs between the pro-acyl carbon and the oxygen and not between the *t*-butyl group and the oxygen (19) and Anderson and Fife reported that it was hydrolysed rapidly with general-acid catalysis (20). This was considered to arise from the sterically crowded ground state which caused the acetal bond to be broken easily. It seemed to us that a similar rate enhancement would not be expected with the hemiacetal as it is much less sterically crowded and hence there might be a change in the rate-limiting step to decomposition of the hemiacetal. Mr. Duncan Grieve in our laboratory has studied the hydrolysis of compounds (9), (10) and (11). At pH 4.6 the rate constants of formation of benzaldehyde were identical from all three compounds. At pH 7.5 the rate constants for the formation of benzaldehyde from compounds (10) and (11) were identical and about 35 times greater than the rate constant for the formation of benzaldehyde from (9). At intermediate pHs the formation of benzaldehyde from (9) no longer followed the first-order rate law but that from (10) and (11) did. At some pHs a definite induction period could be seen in the formation of benzaldehyde from (9) while at others the non-first order behaviour was indicated by the first, second and third half lives not being equal. This behaviour is very similar to that reported by Atkinson and Bruce (16) for the hydrolysis of (7). We interpret these results to indicate that under our conditions, with the buffer concentration less than 0.025M, the rate-limiting step is decomposition of the hemiacetal at pHs less than 4.6 and formation of the hemiacetal at pHs greater than about 7. At intermediate pHs formation and decomposition of the hemiacetal occur at comparable rates. Anderson and Fife (20) used higher buffer concentrations and we are not sure at present whether this conclusion applies to these conditions as well.

We next asked ourselves if it would be possible to go to a higher oxidation level and generate the tetrahedral intermediate of an acyl-transfer reaction by hydrolysis of its O-acetate. Several tetrahedral intermediates at the oxidation level of a carboxylic acid have been prepared or detected spectroscopically (21) and two fairly detailed kinetic investigations have been reported (22). All these compounds have fairly complex structures however and there has been no kinetic investigation of the decomposition of a tetrahedral intermediate formed from a simple formate, acetate, or benzoate.

There have recently been some very interesting calculations by Guthrie on the stability of this type of tetrahedral intermediate (23). On the basis of these one can calculate that the tetrahedral intermediate in the hydrolysis of methyl formate, $\text{HC}(\text{OH})_2(\text{OMe})$, would be most stable in aqueous solution at pH ca 5 and at this pH would decompose mainly through its monoanion with a half life of 1 to 5 seconds at 25°. We are currently trying to generate the very similar tetrahedral intermediate $\text{HC}(\text{OH})(\text{OMe})_2$ by hydrolysis of $\text{HC}(\text{OAc})(\text{OMe})_2$.

Finally I should like to turn to the question of whether any carboxylic acid derivative reacts through a detectable concentration of a tetrahedral intermediate. Dr. Cleland studied the hydrolysis of amides (12), (13) and (14) in aqueous perchloric acid of concentration greater than 0.1M. He followed the decrease in absorbance at 242 nm at which wave length the extinction coefficient of the anilinium ion is much smaller than that of the amide. He found that the variation of absorbance with time did not follow the first-order rate law but consisted of two phases, one fast and one slow. We checked the purity of the starting materials and the reaction products and considered that this behaviour could not be from the starting material being impure or from it undergoing two reactions. We also considered the possibility that it arose from a slow cis-trans isomerisation of the starting amide, but the reaction appears to be too slow for this to be happening. In 0.01M perchloric acid and in imidazole buffers the hydrolyses of these compounds shows simple first-order behaviour. This behaviour was checked for compound (12) by Mr. I. McCaffer. The most reasonable explanation seems to be that there is accumulation of an appreciable concentration of a tetrahedral intermediate. We have analysed the kinetics of hydrolysis of compound (12) on the basis of Scheme 1 on the assumption that the extinction coefficient at 242 nm of the protonated tetrahedral intermediate (15) would be similar to that of the anilinium ion, i.e. small compared to that of the starting amide. The value of k_2 , the rate constant for decomposition of the tetrahedral intermediate decreases with increasing acid concentration. This behaviour is similar to that found for the decomposition of a carbinolamine derived from a Schiff base (24). The rate constants k_1 and k_{-1} increase with increasing acid concentration up to about 4M and then decrease at higher concentrations.

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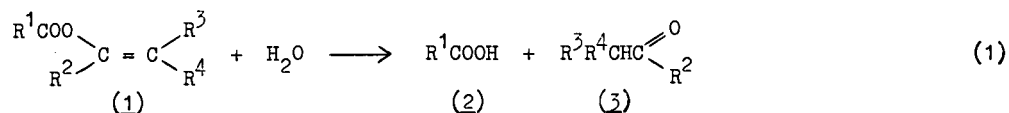
MECHANISMS AND CATALYSIS IN VINYL ESTER HYDROLYSIS

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Abstract - A critical survey of literature concerning the catalysis, mechanisms, and kinetics in vinyl ester hydrolysis is presented together with new results. The relatively fast alkaline and acid-catalysed hydrolyses usually take place with acyl-oxygen fission. General base and nucleophilic catalyses are known. Appreciable neutral ester hydrolysis by general base catalysis of water occurs generally. The unsymmetrically acid-catalysed partition of the tetrahedral intermediate formed in the neutral hydrolysis has been found to lead to acid catalysis if the ester has electronegative substituents. Vinyl esters differ from other esters by the possible electrophilic addition to the double bond. Thus mercury(II) and thallium(III) ions catalyse the reaction, and acid catalysis takes place by AS_E2 mechanism at high acidities or when the formed carbenium ion is structurally stabilized.

INTRODUCTION



Vinyl esters (1) are of importance as raw material for polymers. The following discussion is, however, limited to monomeric esters. The term vinyl ester is used for all kinds of 1-alkenyl or enol esters excluding, however, phenyl esters and similar compounds in which the double bond belongs to an aromatic system. The first hydrolysis products of vinyl esters are the carboxylic acid (2) and an aldehyde, a ketone, or even an acid halide (3) depending on whether R^2 is hydrogen, an alkyl or aryl group, or halogen. As far as I am aware, there is only one extensive review of the kinetics and mechanisms in vinyl ester hydrolysis. It is written in Russian by Rekasheva (1) and it deals also with vinyl ethers. The subject is considered in general reviews of ester hydrolysis (Ref. 2 & 3).

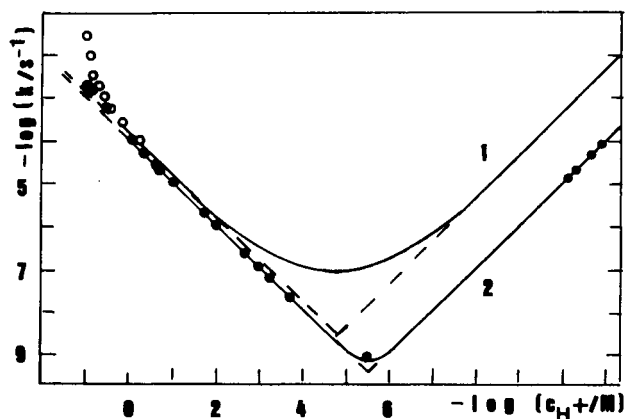


Fig. 1. The logarithm of the experimental rate coefficient in water at 25 °C for the hydrolysis of vinyl acetate (1, Ref. 4-7) and ethyl acetate (2, Ref. 2) as a function of the logarithm of hydrogen ion concentration.

Typical of the hydrolysis of ordinary esters is that the rate is proportional to the oxonium or hydroxide ion concentration over wide pH ranges in the absence of other catalysts with a minimum at the acid side as shown in Fig. 1 for ethyl acetate. Vinyl esters differ from the corresponding saturated esters as follows: (i) the acid-catalysed hydrolysis is slightly faster, (ii) the alkaline hydrolysis is considerably faster, (iii) they have a significant pH-independent or neutral hydrolysis, (iv) electrophilic addition to the double bond occurs.

The well-known Ingold's classification of ester hydrolysis mechanisms (Ref. 2 & 8) is used in this review. The only Ingold's mechanisms for which there is evidence in the case of vinyl esters are the $B_{AC}2$, $A_{AC}2$, and $A_{AC}1$ mechanisms. Vinyl esters can hydrolyse also by the $AS_{AC}2$ mechanism. For the nucleophilic and general base catalyses the notations $B_{AC}N$ and $B_{AC}3$, respectively, are proposed by myself (Ref. 9) to distinguish them from the alkaline hydrolysis, $B_{AC}2$. The acid catalysis due to unsymmetrically catalysed partition of the intermediate formed in the $B_{AC}3$ reaction also needs a special notation. I propose the symbol $A-B_{AC}3$ for it.

ALKALINE HYDROLYSIS ($B_{AC}2$)

Surprisingly few reliable kinetic data are available for the alkaline hydrolysis of vinyl esters. This is certainly caused by the high reaction rates and also by the tendency of vinyl esters to polymerize in alkaline solutions. Many published data are erroneous. In some cases buffer solutions were employed, when general base catalysis by buffer is possible. That probably was the case in the first kinetic study of vinyl esters performed by Skrabal and Zahorka (4) in 1927. The alkaline hydrolysis of vinyl acetate was followed in a borate buffer, and the value obtained for the rate coefficient seems to be too high by a factor of 2 or 3. This is noticed if their value, $10.3 \text{ M}^{-1} \text{ s}^{-1}$ in water at 25°C , is compared with the more recent values 2.34 and 2.6 at 27°C by Sharma and Sharma (10), 4.30 (?) by Rostovskii *et al.* (11), and 3.28 at 20°C by DePuy and Mahoney (7). Another reason for erroneous results may be the common use of alcoholic solutions with low water content in kinetic determinations. Alcoholysis which accompanies the hydrolysis may lead to the formation of the corresponding alkyl ester, the hydrolysis of which is then followed if the liberated acid is determined. This can be the explanation, why in a study (Ref. 11) performed in 95.5% aqueous ethanol almost identical values were obtained for the rate coefficients of vinyl and ethyl acetates. In another case (Ref. 12) the esters were employed as methanol solutions, where methanolysis could have occurred as similar values (6.22 and $6.59 \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$, respectively) were obtained for vinyl and ethyl acetate in 60% aqueous methanol. At least in one case (Ref. 13) evidently the rate of solution rather than that of reaction was followed.

In spite of the paucity of data and of the above-mentioned shortcomings, several generalizations can be made. (i) The reaction follows second-order kinetics. (ii) The rate is 13-45 times higher for a vinyl ester than for the corresponding saturated ester under the same conditions. Experimental results include the following data: $k(\text{vinyl acetate})/k(\text{ethyl acetate}) = 44$ in water at 25°C (Ref. 7 & 2) and 38 in 70 vol.% acetone-water at 24.8°C (Ref. 15), $k(\text{isopropenyl acetate})/k(\text{isopropyl acetate}) = 15$ in water at 25°C (Ref. 10 & 2), $k(1\text{-cyclopentenyl acetate})/k(\text{cyclopentyl acetate}) = 32$ in water at 40°C (Ref. 7), $k(1\text{-phenylvinyl acetate})/k(1\text{-phenylethyl acetate}) = 13$ (Ref. 16). (iii) The corresponding values of activation parameters for vinyl esters ($\Delta H^\ddagger = 40\text{-}50 \text{ kJ/mol}$, $\Delta S^\ddagger = -80 - (-150) \text{ J/(mol K)}$, Ref. 7, 15 & 17) and ethyl esters (Ref. 2) are similar. (iv) Structural effects are similar for vinyl and corresponding saturated esters. Electronegative substituents increase the rate similarly in both cases (Ref. 14, 18 & 2). Hammett's equation is followed in the case of substituted benzoates, the reaction constant ρ being similar for vinyl ($\rho = 2.48$ in 13 M water in ethanol at 25°C , Ref. 14) and ethyl esters ($\rho = 2.43$ in 88% ethanol-water at 25°C , Ref. 2). (v) Vinyl acetate hydrolyses about 10 times faster than isopropenyl acetate: $k(\text{vinyl acetate})/k(\text{isopropenyl acetate}) = 11$ in water at 20°C (Ref. 7) and 6 in water at 10°C (Ref. 10), and 12 in 70 vol.% acetone-water at 25°C (Ref. 15). (vi) Electronegative substituents in the vinyl group increase the rate ($\rho = 0.47$ for substituted 1-phenylvinyl acetates in 5 vol.% ethanol-water at 29.9°C , Ref. 16).

All of the above-mentioned facts are in accordance with the $B_{AC}2$ mechanism. Some inconsistent results were obtained when the site of bond fission was determined by the oxygen-18 method. Kiprianova and Rekasheva hydrolysed vinyl acetate and benzoate in alkaline aqueous solutions containing oxygen-18 (Ref. 19) and several vinyl esters having an excess of oxygen-18 in the ethereal oxygen or in both oxygen atoms (Ref. 14). The results were interpreted by assuming that both vinyl-oxygen and acyl-oxygen fissions take place (Ref. 14 & 19) or that intramolecular vinyl shift occurs in the formed tetrahedral intermediate (Ref. 1). To clarify this controversy we redetermined the site of the bond fission by a slightly modified oxygen-18 method (Ref. 20). The results obtained for both vinyl and ethyl acetate were very similar: The ratio $m(46)/m(44)$ was found to be 2.31 or 2.38 in carbon dioxide obtained from the acetate ion formed in the hydrolysis of vinyl acetate. The corresponding ratio was 2.24 or 2.28 for ethyl acetate. The calculated values were 2.35 for acyl-oxygen fission and 0.41 for alkyl-oxygen fission. These results are in accordance with the kinetic data and indicate that the alkaline hydrolysis of vinyl acetate takes place by the normal $B_{AC}2$ mechanism with acyl-oxygen fission.

GENERAL BASE CATALYSIS (B_{AC})

The first kinetic measurements of the hydrolysis of vinyl acetate by Skrabal and Zahorka (4) already include data that show that acetate ion catalyses the reaction, although the authors supposed that the rate increase was an electrolyte effect. The only case where general base catalysis has been claimed to take place in vinyl ester hydrolysis is the above-mentioned study by Briody and Satchell (24), when chloroacetate, acetate, and acetoacetate ions were concluded to function as general bases when catalysing the hydrolysis of diketene.

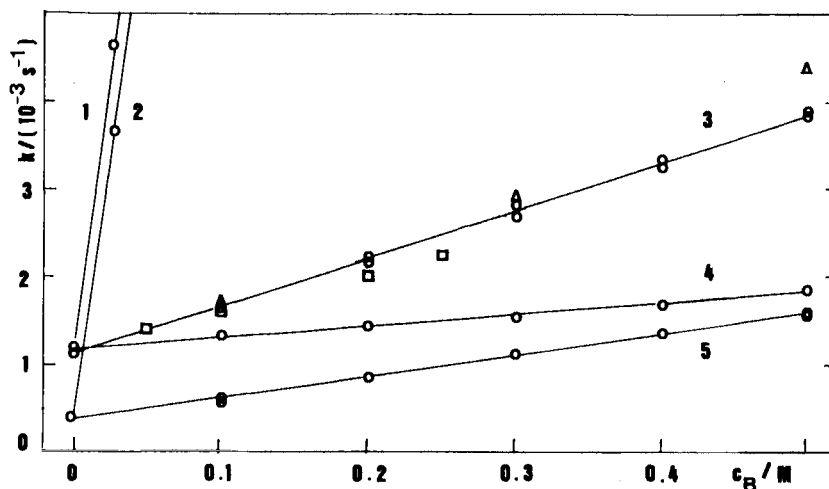


Fig. 2. plots of the experimental rate coefficients against the base concentration for the hydrolysis of 2,2-dichlorovinyl chloroacetate in aqueous buffer solutions with ionic strength 0.5 M at 25 °C. The buffer ratio was 1:1 (circles) except for some acetate buffers where $\frac{c(\text{AcO}^-)}{c(\text{AcOH})}$ was 5:1 (triangles) or 1:2 (squares). Buffer bases: hydrogen phosphate ion in ordinary water (1), hydrogen phosphate ion in deuterium oxide (2), acetate ion in ordinary water (3), chloroacetate ion (4), and acetate ion in deuterium oxide (5).

We have recently performed a study of general base catalysis in the hydrolysis of 2,2-dichlorovinyl chloroacetate (Ref. 26). The spectrophotometrically determined rates were found to depend almost linearly on the base concentration (Fig. 2). A slight increase was sometimes found at the highest concentrations employed and when the acid-base ratio of the buffer was decreased. A constant buffer ratio (1:1) was used in actual determinations. An appreciable neutral hydrolysis was always observed. The results obtained for the base catalysis are collected in Table 2. The data are in general agreement with those earlier found for general base-catalysed ester hydrolysis (Ref. 9 & 27). Especially characteristic are the values for the solvent isotope effect of the neutral and acetate ion-catalysed hydrolysis, the low values of activation enthalpy, and the highly negative values of activation entropy. The solvent isotope effect for the hydrogen phosphate ion-catalysed hydrolysis is exceptional. The rate of the imidazole-catalysed reaction was found to depend on the wave length used, which may be due to the formation of some intermediate. These observations together with the high rates (see below) can be indications of nucleophilic catalysis by the two last-mentioned bases although it was not studied closer.

TABLE 1. Catalytic data of the hydrolysis of 2,2-dichlorovinyl chloroacetate in aqueous solution with the ionic strength of 0.5 M (NaClO_4 or LiClO_4) at 25 °C.

| Base | pK_B | $\frac{k_B}{10^{-3} \text{ M}^{-1} \text{ s}^{-1}}$ | $\frac{k_B(\text{H}_2\text{O})}{k_B(\text{D}_2\text{O})}$ | $\frac{\Delta H^\ddagger}{\text{kJ mol}^{-1}}$ | $\frac{\Delta S^\ddagger}{\text{J mol}^{-1} \text{ K}^{-1}}$ |
|---------------------------------------|---------------|---|---|--|--|
| H_2O | 15.73 | 0.0213 | 2.97 | 49.7 ± 0.9 | -135 ± 3 |
| $\text{CH}_2\text{ClCO}_2^-$ | 11.15 | 1.30 | | | |
| HCO_2^- | 10.25 | 3.68 | | | |
| CH_3CO_2^- | 9.24 | 5.51 | 2.25 | 51.6 ± 2.5 | -115 ± 8 |
| $\text{CH}_3\text{CH}_2\text{CO}_2^-$ | 9.12 | 5.33 | | | |
| HPO_4^{2-} | 6.79 | 120 | 1.10 | | |
| imidazole | 7.05 | 400-1000 | | | |

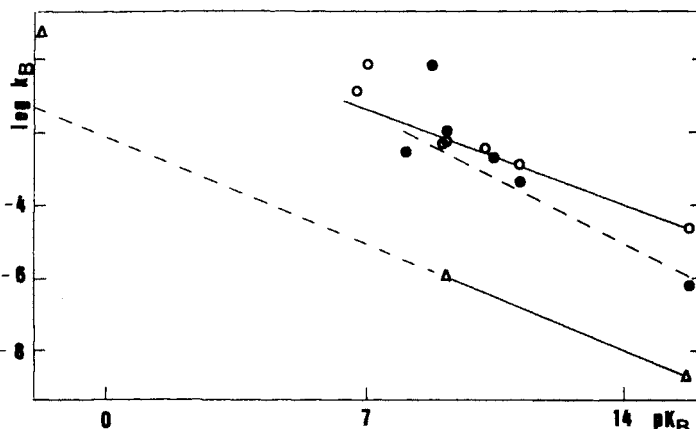


Fig. 3. Brønsted plots for 2,2-dichlorovinyl chloroacetate (o) and vinyl acetate (Δ , Ref. 4) in water and diketene (\bullet , Ref. 24) in 40 % dioxane-water at 25 °C.

The Brønsted plots for the above data are shown in Fig. 3. No statistical corrections were made. The points for 2,2-dichlorovinyl chloroacetate satisfactorily obey the Brønsted relationship, with the exceptional point for imidazole and possibly also for the hydrogen phosphate ion. The other points give for the Brønsted coefficient the value 0.37, which is in agreement with the earlier values 0.47 for ethyl dichloroacetate (Ref. 27), 0.39 for chloromethyl chloroacetate (Ref. 9), and 0.40 for substituted 2,2-dimethyl-1,3-dioxane-4,6-diones (Ref. 28). It is to be noted that the point for water falls on the same line indicating that the mechanisms of neutral ester hydrolysis and the reaction catalysed by carboxylate anions are the same.

From Fig. 3 it is also seen that the two points calculated for water and the acetate ion from Skrabal and Zahorka's (4) data for vinyl acetate give a parallel line. The point for the alkaline hydrolysis of vinyl acetate lies clearly above the Brønsted's line as is found also in other cases (Ref. 9 & 27). A direct nucleophilic attack of the hydroxide ion evidently takes place without catalysis. Figure 3 further includes the data for the hydrolysis of diketene measured by Briody and Satchell (24). Although the points are more scattered, they seem to confirm their conclusion that the chloroacetate and acetoacetate ions and evidently also 2,4-lutidine act as general bases and pyridine as a nucleophile in this reaction. In the case of the acetate ion general base catalysis is accompanied by other reactions.

The mechanism for general base-catalysed ester hydrolysis (Ref. 29) is included in the reaction scheme presented in the chapter for the acid catalysis due to unsymmetrically catalysed decomposition of the tetrahedral intermediate in neutral ester hydrolysis. The notation $B_{AC}3$ was proposed for it to distinguish it from the mechanism of alkaline hydrolysis and to indicate that three molecules, ester, water, and the base, are in the transition state (Ref. 9). The same notation should be used for neutral ester hydrolysis.

NEUTRAL ESTER HYDROLYSIS

Only few data for the neutral hydrolysis of vinyl esters can be found in the literature; Skrabal and Zahorka (4) determined the rate coefficient for vinyl acetate and Yrjänä (30) for vinyl chloroacetate in water. Yrjänä also found that the values of activation enthalpy and entropy for the last-mentioned ester are of the same magnitudes as the values for other esters reacting by the $B_{AC}3$ mechanism (Ref. 2). Briody and Satchell (24) found that diketene has a pH-independent hydrolysis in the region of 1-8 and concluded on the basis of the low value of activation energy that acyl-oxygen fission occurs. More extensive measurements have been performed in our laboratory (Ref. 26, 31 & 32) in connexion with our studies on neutral ester hydrolysis in general. The choice of the esters and solvents was based on the possibility to obtain the most accurate results by the conductometric and spectrophotometric methods employed. This sometimes limited severely the range of conditions where investigations could be made.

Data illustrating structural effects in the neutral hydrolysis of vinyl esters are collected in Table 2. It is seen that electronegative substituents increase the rate greatly, as is usually found in neutral ester hydrolysis in accordance with the proposed mechanism (Ref. 2). More quantitative consideration of these structural effects is not possible because of the paucity of data under comparable conditions.

TABLE 2. Absolute and relative rate coefficients for the neutral hydrolysis of vinyl esters in p "% acetonitrile-water solutions at 25 °C.

| Ester | p | $k/(10^{-4} \text{ s}^{-1})$ | $k_{\text{rel.}}$ | Ref. |
|---|-----|------------------------------|---------------------|---------|
| $\text{CH}_3\text{COOCH}=\text{CH}_2$ | 0 | 0.00113 | 1 | 4 |
| $\text{CH}_2\text{ClCOOCH}=\text{CH}_2$ | 0 | 0.591 | 523 | 30 |
| $\text{CH}_3\text{COOCH}=\text{CCl}_2$ | 0 | 0.0427 | 38 | 1/410 |
| $\text{CH}_2\text{ClCOOCH}=\text{CCl}_2$ | 0 | 17.5 | 15,000 | 1 |
| $\text{CH}_2\text{ClCOOCH}=\text{CCl}_2$ | 40 | 1.22 | 1 | 31 |
| $\text{CHCl}_2\text{COOCH}=\text{CCl}_2$ | 40 | 142 | 116 | 31 |
| $\text{CHCl}_2\text{COOCH}=\text{CCl}_2$ | 64 | 38.2 | | 1 31 |
| $\text{CCl}_3\text{COOCH}=\text{CCl}_2$ | 64 | 2440 | | 64 26 |
| $\text{CHCl}_2\text{COOCCl}=\text{CCl}_2$ | 64 | 661 | | 17 32 |
| $\text{CCl}_3\text{COOCH}=\text{CH}_2$ | 64 | 36.8 | (1.7×10^6) | 0.96 26 |
| $\text{CF}_3\text{COOCH}=\text{CH}_2$ | 64 | 562 | (27×10^6) | 15 26 |

Solvent effects in the neutral hydrolysis of vinyl esters are seen from Fig. 4. The plots are of the same general type as usually found for the reaction. The slopes of the curves, sometimes called the apparent order of reaction in respect to water, vary between 5 and 7 in acetonitrile solutions rich in water and diminish to a value below two in solutions containing about 25 per cent of water.

The activation enthalpy is plotted as a function of the mole fraction of water for the neutral hydrolysis of vinyl esters in acetonitrile-water solutions in Fig. 5. It is seen that the values of activation enthalpy are low, around 40 kJ/mol. All of the curves have similar forms. There is a minimum at the mole fraction of about 0.95 followed by a maximum at $x(\text{water})$ of ca. 0.7. The detailed form of the curves depends on the structure of the ester, probably mostly on that of its alkyl component. For methyl trifluoroacetate the curves are very shallow around the extreme values, which become clearer for chloromethyl dichloroacetate and are most pronounced for the vinyl esters.

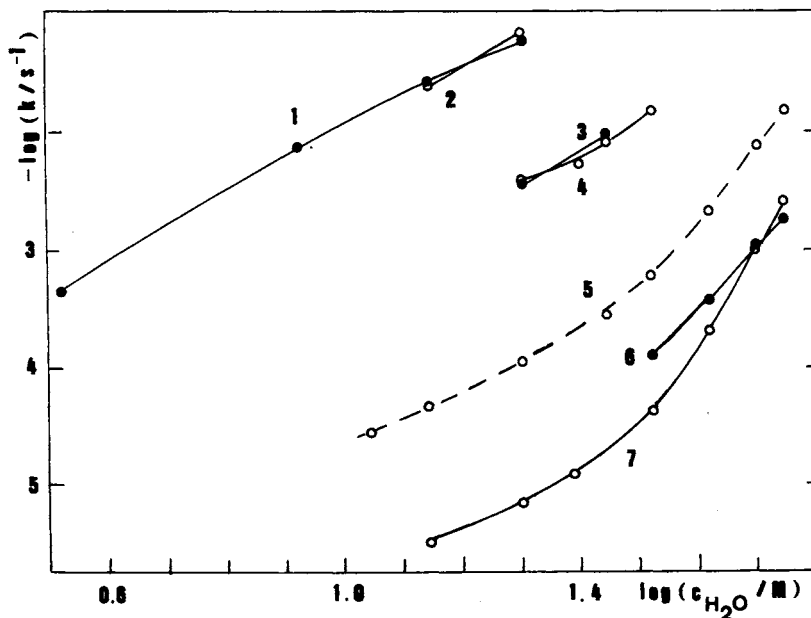


Fig. 4. Plots of the logarithm of the rate coefficient against the concentration of water in acetonitrile-water solutions at 25 °C for the neutral hydrolysis of vinyl trifluoroacetate (1), 1,2,2-trichlorovinyl dichloroacetate (2), vinyl trichloroacetate (3), 2,2-dichlorovinyl dichloroacetate (4), 2,2-dichlorovinyl chloroacetate (6), and E-1,2-dichloro-1-propenyl 2-chloropropionate (7). The broken line is for chloromethyl dichloroacetate (5, Ref. 33).

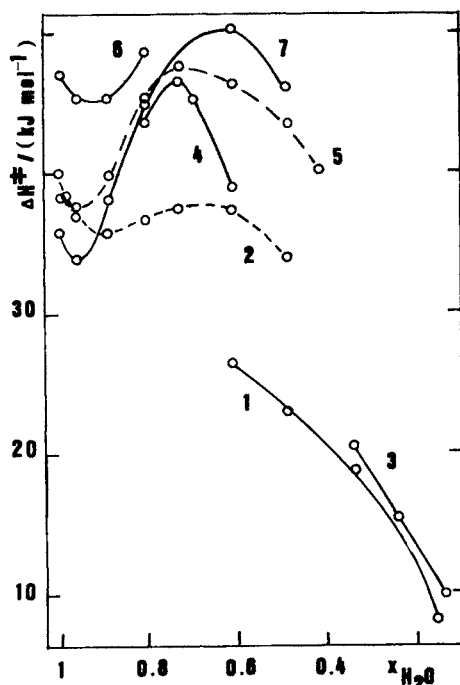


Fig. 5.

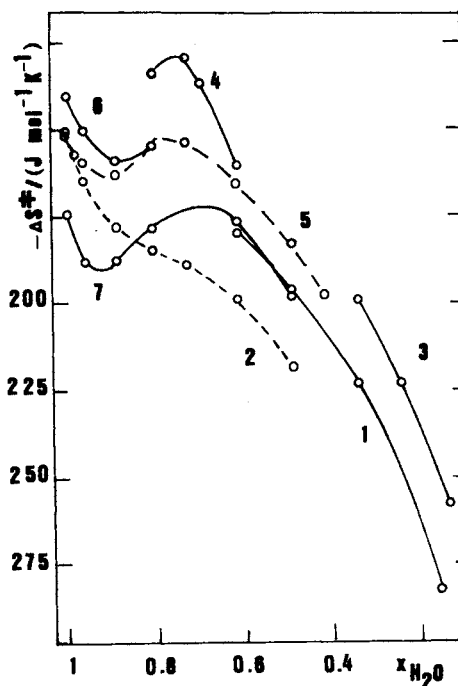


Fig. 6.

Variation of activation enthalpy (Fig. 5) and entropy (Fig. 6) as a function of the mole fraction of water in acetonitrile-water mixtures at 25 °C for the neutral hydrolysis of vinyl trifluoroacetate (1), 2,2-dichlorovinyl trichloroacetate (3), 2,2-dichlorovinyl dichloroacetate (4), 2,2-dichlorovinyl chloroacetate (6), and E-1,2-dichloro-1-propenyl 2-chloropropionate (7). Curves of comparison: Chloromethyl dichloroacetate (5, broken line, Ref. 33) and methyl trifluoroacetate (2, dotted line, Ref. 34).

The curves for activation entropy (Fig. 6) show similar trends as those for activation enthalpy. The values are highly negative, around $-200 \text{ J}/(\text{mol K})$. Methyl trifluoroacetate exhibits no extreme values at all, but chloromethyl dichloroacetate and the vinyl esters have maxima and minima, which are located at almost the same water contents as the extreme values for activation enthalpy. Hence the same factors, probably changes in solvent structure, influence activation enthalpy and entropy. Because they depend on temperature, their dependence on the composition of solvent is different at different temperatures.

TABLE 3. Values of the heat capacity of activation, $\Delta C_p^\ddagger = \partial(\Delta H^\ddagger)/\partial T$, for the neutral hydrolysis of vinyl esters in *p* % acetonitrile-water (AN) and dimethylsulfoxide-water (DMSO) solutions.

| Ester | <i>p</i> | Temperature interval/°C | ΔC_p^\ddagger | Ref. |
|--|----------|-------------------------|-----------------------------------|------|
| | | | $\text{J mol}^{-1} \text{K}^{-1}$ | |
| $\text{CF}_3\text{COOCH}=\text{CH}_2$ | 64 AN | 0-25 | -656 ± 10 | 26 |
| | 75 AN | -3-25 | -540 ± 8 | 26 |
| | 85 AN | 0-65 | -297 ± 13 | 26 |
| | 94 AN | 0-65 | -182 ± 16 | 26 |
| | 94 DMSO | 7-55 | -477 ± 46 | 26 |
| | 97 DMSO | 15-85 | -176 ± 38 | 26 |
| 99 DMSO | 18-85 | -138 ± 59 | 26 | |
| $\text{CCl}_3\text{COOCH}=\text{CH}_2$ | 50 AN | 0-40 | -423 ± 4 | 26 |
| | 64 AN | 0-45 | -384 ± 4 | 26 |
| E- $\text{CH}_3\text{CHClCOOCCl}=\text{CClCH}_3$ | 0 | | -225 ± 21 | 32 |
| | 10 AN | | -46 ± 8 | 32 |
| $\text{CHCl}_2\text{COOCCl}=\text{CCl}_2$ | 64 AN | | -619 ± 50 | 26 |
| | 75 AN | | -305 ± 71 | 26 |

We have directed much attention to the temperature dependence of the rate of neutral ester hydrolysis, especially to structural and solvent effects on the heat capacity of activation. Neutral ester hydrolysis is a suitable reaction for studying these effects because of the low activation energy. Data for vinyl esters are given in Table 3. All the values of the heat capacity of activation are negative, as generally found in reactions where transition state is more polar than initial state (Ref. 29, 33, 34 & 35). The large variation of the values depends mainly on strong solvent effects. Cleve's (33 & 34) thorough investigations have shown that the values of the heat capacity of activation for the neutral hydrolysis of methyl trifluoroacetate and chloromethyl dichloroacetate in acetonitrile-water solutions have a maximum at a mole fraction of water of about 0.85 and a minimum at ca. 0.7. It was found that the height of the maximum and the depth of the minimum are more profound for the last-mentioned ester. The data for the vinyl esters studied seem to exhibit similar behaviour but with still higher maxima and much lower minima. Negative values of the heat capacity of activation are explained to be due to the necessity of breaking the solvation shell around the reaction centre in activation. Therefore the heat capacity of activation should be an important parameter when kinetic solvent effects are studied. The structure of the ester and especially of its alkyl component seems to be of importance in this respect. The data for vinyl esters are, however, too few for any detailed discussion.

TABLE 4. Kinetic data for the neutral hydrolysis of isomeric 1,2-dichloro-1-propenyl 2-chloropropionates, $\text{CH}_2\text{CHClCOOCCl}=\text{CClCH}_3$, in 10% acetonitrile-water at 25 °C (Ref. 32).

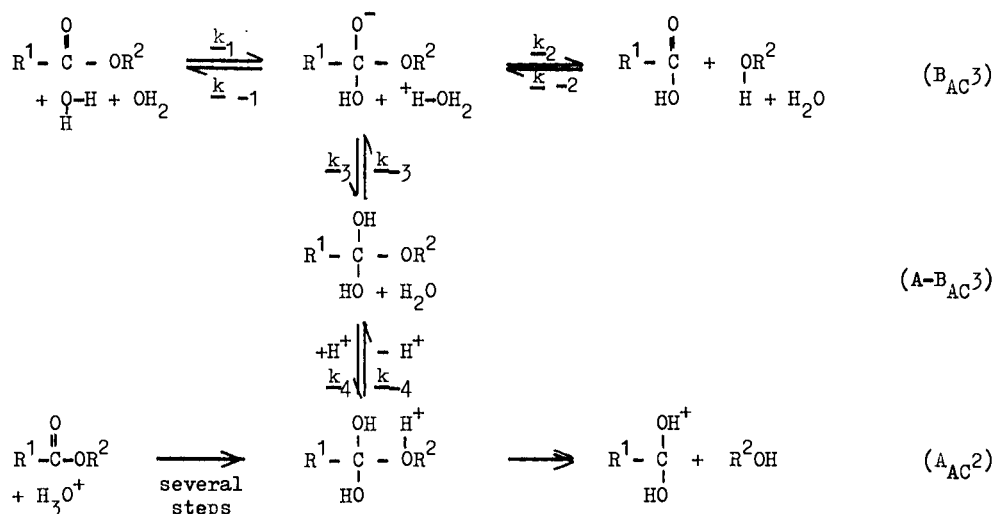
| Isomer | $\frac{k}{10^{-3} \text{ s}^{-1}}$ | $\frac{\Delta H^\ddagger}{\text{kJ mol}^{-1}}$ | $\frac{\Delta S^\ddagger}{\text{J mol}^{-1} \text{ K}^{-1}}$ | $\frac{\Delta C_p^\ddagger}{\text{J mol}^{-1} \text{ K}^{-1}}$ |
|--------|------------------------------------|--|--|--|
| Z | 1.526 ± 0.003 | 34.9 ± 0.1 | -182.0 ± 0.4 | -84 ± 8 |
| E | 1.073 ± 0.003 | 33.8 ± 0.1 | -188.3 ± 0.4 | -46 ± 8 |

An interesting case is presented by Rossi (32), who studied the hydrolysis of the isomeric 1,2-dichloro-1-propenyl 2-chloropropionates. The observed clear differences are shown in Table 4. Structurally the isomers differ in regard to whether the 2-chlorine or the 2-methyl of the propenyl component comes in the vicinity of the carbonyl group in the main conformer with the plain of the vinyl group about perpendicular against the carbonyl group. The water structure around these groups was proposed to be the most important factor.

ACID CATALYSIS DUE TO UNSYMMETRICALLY CATALYSED PARTITION OF THE TETRAHEDRAL INTERMEDIATE IN NEUTRAL ESTER HYDROLYSIS (A-B_{AC}^3)

Esters which have an appreciable neutral hydrolysis exhibit an acid-catalysed hydrolysis with several exceptional features (Ref. 2) as shown by Euranto and Cleve (36). (i) Polar factors are more important than in the case of common esters. Electronegative substituents increase the rate, which then is higher than estimated. (ii) They have a lower activation enthalpy and a more negative activation entropy than ordinary esters. (iii) There is often a rate maximum at ca. 2 M acid followed by a minimum at higher acidities. The maximum is partly due to a negative salt effect in the accompanying neutral hydrolysis, but also the rate calculated as the difference between rates at equal concentrations of an acid and a corresponding salt and the rate measured at constant ionic strength behave exceptionally. The plot of the rate against the acid concentration is first concave downwards and rises steeply at higher concentrations. The rise was shown (Ref. 37) to represent the normal A_{AC}^2 reaction. (iv) There is a strong negative salt effect as in neutral ester hydrolysis, but in contrast to the normal acid-catalysed hydrolysis. (v) Added organic solvent components decrease their rate much more than the rate of simple esters. (vi) The kinetic deuterium oxide solvent isotope effect is the opposite to that of other esters, but in accordance with neutral ester hydrolysis.

The above-mentioned several similarities of this exceptional acid catalysis with neutral ester hydrolysis suggested a special mechanism with a common intermediate which, in addition to the general acid-catalysed partition to reaction products and starting materials, could also decompose via another path requiring an additional proton. This path was supposed to lead to the same intermediates that lie on the reaction path of the A_{AC}^2 hydrolysis. No conclusive evidence for this mechanism, which we have also called a general A_{AC}^1 base-specific oxonium ion catalysis, could then be presented. A reaction scheme, represented on the next page, was suggested. Last year, Kurz and Farrar (38), in a very thorough and elegant experimental and theoretical study of the hydrolysis of ethyl trichloroacetate, presented very convincing evidence for essentially the same mechanism. The notation A-B_{AC}^3 is now proposed for it because of the experimental acid catalysis and of the common intermediate with the B_{AC}^3 reaction.



It may be expected that also vinyl esters exhibit the above-mentioned acid catalysis. Because the factors which determine the relative contributions of the different reaction paths are very poorly known, we have performed experiments with 2,2-dichlorovinyl chloroacetate. The results are shown in Fig. 7. Somewhat unexpectedly the added acid acts as an inhibitor of the reaction. However, sodium perchlorate lowers the rate more strongly. The difference

$$\frac{k_{\text{H}}}{k_{\text{H}}} = \frac{k}{k} (\text{HClO}_4) - \frac{k}{k} (\text{NaClO}_4) \quad (5)$$

is positive and can be considered to represent acid catalysis. As a function of acid concentration, the values of k_{H} give a slightly downward concave curve with initial slope of $3.3 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$. A similar value, $3.0 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$, was obtained from runs performed at a constant ionic strength of 1 M. The low accuracy achievable in these measurements prevents a detailed analysis of the results. The general form of the rate curves and the observed increase of the rate in the range of 4 to 11 M perchloric acid suggests that the acid-catalysed hydrolysis at low acidities follows the A-B_{AC}³ mechanism. The values of the rate coefficients are higher than those for the A_{AC}² hydrolysis of ethyl acetate, ethyl chloroacetate, and vinyl acetate with the $k_{\text{H}}/(10^{-4} \text{ M}^{-1} \text{ s}^{-1})$ values of 1.12, 0.81 (Ref. 2), and 1.45 (Ref. 5), respectively.

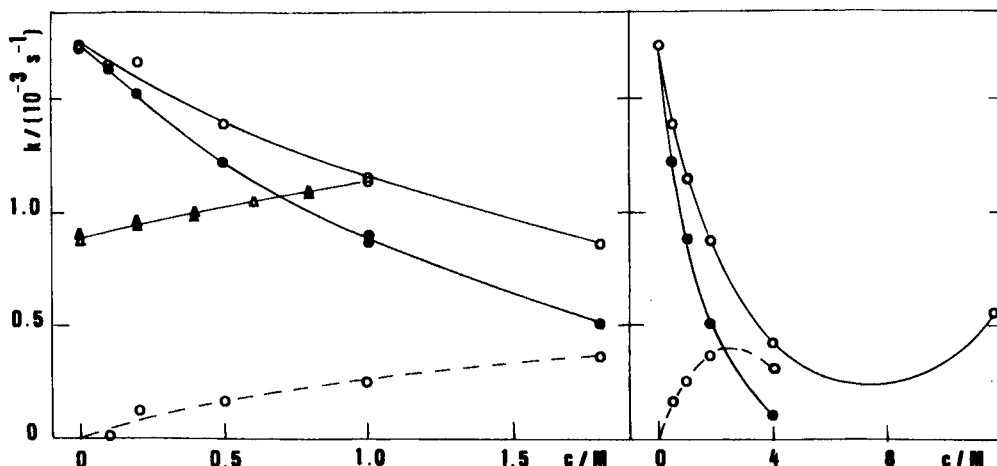


Fig. 7. The first-order rate coefficients for the hydrolysis of 2,2-dichlorovinyl chloroacetate in aqueous perchloric acid solutions with variable (o) or constant (Δ) ionic strength of 1 M and in sodium perchlorate (●) solutions at 25°C. The dotted curve is calculated from equation (5).

BIMOLECULAR ACID-CATALYSED HYDROLYSIS (A_{AC}²)

Skrabal and Zahorka (4) were the first to study the acid-catalysed hydrolysis of vinyl acetate. On the basis of the reaction rate Skrabal (39) concluded that the reaction takes place by the same mechanism as the hydrolysis of "ether-like" esters. Palomaa *et al.* (40)

TABLE 5. Kinetic data for the acid-catalysed hydrolysis of esters $R^1COOCR^2=CH_2$,

| R^1 | R^2 | Solvent (Note a) | t °C | $\frac{k_H}{10^{-4}M^{-1}s^{-1}}$ | $\frac{k_{rel}^{sat}}{\text{(Note b)}}$ | $\frac{k_H(H_2O)}{k_H(D_2O)}$ | $\frac{\Delta H^\ddagger}{kJ\ mol^{-1}}$ | $\frac{\Delta S^\ddagger}{J\ mol^{-1}K^{-1}}$ | Ref. | |
|---|-----------------|---------------------|-----------|-----------------------------------|---|-------------------------------|--|---|-------|----|
| CH ₃ | H | W | 25 | 1.45 | 1.36 | 0.75 | 61.7 | - 112 | 5 | |
| | | 50% DW | 65 | 20.0 | | | 64.3 | - 108 | 5, 43 | |
| | | 11M DW | 80 | | | | 72 | - 88 | 44 | |
| H | H | W | 25 | 46.7 | 1.52 | | | | 45 | |
| | | 50% AW | 25 | 17.8 | | 61.2 | - 92 | 45 | | |
| CH ₃ CH ₂ | H | 50% DW | 65 | 15.4 | | | 55.5 | - 136 | 43, 5 | |
| CH ₃ CH ₂ CH ₂ | H | 50% DW | 65 | 9.12 | | | 61.5 | - 123 | 43, 5 | |
| | | 11M DW | 80 | | | 0.70 | 68 | - 105 | 44 | |
| C(CH ₃) ₃ | H | 50% DW | 65 | 1.21 | | | 84 | - 72 | 43, 5 | |
| CH ₂ Cl | H | 11M DW | 60 | | | | 59 | - 133 | 41 | |
| C ₆ H ₅ CH ₂ | H | 11M DW | 60 | | | | 77 | - 73 | 41 | |
| CH ₃ | CH ₃ | W | 25 | 0.847 | 1.37 | | 74.4 | - 73 | 5 | |
| | | 50% DW | 25 | 0.495 | | | | | | 5 |
| | | 5.6M DW | 80 | | | | 0.78 | 86 | - 53 | 42 |

Note a. W = water, 50% AW = 50 wt.% acetone-water, 50% DW = 50 wt.% dioxane-water, 11M DW = dioxane-water with $c(H_2O)$ 11 M, 5.6M DW = dioxane-water with $c(H_2O)$ 5.6 M.

Note b. $\frac{k_{rel}^{sat}}{k_H} = \frac{k_H(R^1COOCR^2=CH_2)}{k_H(R^1COOCHR^2CH_3)}$

observed, however, the approximate equality of the temperature coefficients for vinyl and primary and secondary acetates. Kiprianova, Rekasheva, Kulish, and co-workers (Ref. 19, 41 & 42) performed oxygen-18 experiments with several vinyl and isopropenyl esters and found only little incorporation of oxygen-18 from water to the produced acids. They concluded therefore that the hydrolysis occurred by alkyl-oxygen fission with a mechanism similar to that of vinyl ethers (Ref. 1). On the basis of these oxygen-18 results and his own kinetic investigations, Landgrebe (43) proposed several mechanisms with alkyl-oxygen fission, which differed from the above mechanism. Yrjänä (5) showed that the values of activation entropy were erroneously calculated in Landgrebe's paper and ca. 26 cal/(mol K) too high. He performed a thorough kinetic investigation of several vinyl esters. The most essential kinetic information about the acid-catalysed hydrolysis of vinyl esters known in 1968 is shown in Table 5. All these kinetic data are in full agreement with the opinion that vinyl esters without strong electronegative or -positive substituents obey the $A_{AC}2$ mechanism in aqueous solutions with low acidity. Because the above-mentioned oxygen-18 experiments were inconsistent with the kinetic data we redetermined the site of bond fission (Ref. 46). Oxygen exchange between acetic acid and water was determined separately under the experimental conditions and taken into account when the expected oxygen-18 excesses were calculated. The experimental results were in accordance with those calculated for acyl-oxygen but not for alkyl-oxygen fission in the case of both vinyl and ethyl acetate. On the other hand, the results for tert-butyl acetate showed alkyl-oxygen fission.

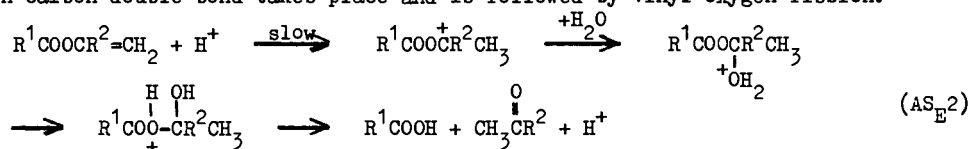
UNIMOLECULAR ACID-CATALYSED HYDROLYSIS ($A_{AC}1$)

The only case where a unimolecular acid-catalysed hydrolysis with acyl-oxygen fission probably takes place in the hydrolysis of vinyl esters is that of diketene studied by Briody and Satchell (24). They concluded from the linear dependence of $\log k$ against H_0 with a slope of 0.91 that this unimolecular mechanism prevails analogically with other β -lactones. The observed rate was 20-30 times higher than that of β -propiolactone.

ACID CATALYSIS INVOLVING RATE-LIMITING PROTON ATTACK ON CARBON (AS_E2 MECHANISM)

Vinyl esters differ from other esters in that the carbon-carbon double bond is a second potential functional group. Thus the AS_E2 mechanism, known to be involved in vinyl ether hydrolysis, is possible. Its occurrence in vinyl ester hydrolysis was first proposed by Kiprianova and Rekasheva (19). Even though their interpretation was considered to be wrong in the above-mentioned cases, their data include cases where this mechanism very probably is functioning. They found that the rates of vinyl benzoate and anisate (Ref. 44) and isopropenyl benzoate (Ref. 42) followed H_0 rather than c_H^+ in aqueous dioxane solutions where the water concentration was low (0.44 M). They also found that the rate was higher by a factor of 1.5-2 in ordinary water than in deuterium oxide under similar conditions. A change in

mechanism is also indicated by the about 60 times higher rate of isopropenyl than of vinyl benzoate (Ref. 42). Also the values of Hammett's reaction constant ρ , -1.3 for vinyl benzoates (Ref. 44) and -1.1 for isopropenyl benzoates (Ref. 42), are in accordance with this mechanism. Landgrebe (47) investigated by proton NMR spectroscopy the behaviour of isopropenyl acetate in strong sulfuric and deuteriosulfuric acids and showed that protonation of the carbon-carbon double bond takes place and is followed by vinyl-oxygen fission.



Noyce and co-workers thoroughly studied substituent effects, the dependence of rate on acid concentration, and solvent isotope effects in the hydrolysis of several vinyl esters and showed convincingly that the $\text{A}_{\text{AC}2}$ mechanism really is accompanied by the $\text{AS}_{\text{E}2}$ mechanism (Ref. 6, 48 & 49). The last-mentioned mechanism is favoured by high acidities and the stability of the carbenium ion formed. The plots of $\log k$ against Hammett's acidity function H_0 are for esters with electron-donating substituents, like *p*-methoxy- α -acetoxystyrene, almost linear with slopes between -1.0 and -1.1 . For other vinyl esters the plots are more or less complex and they could be quantitatively analysed in terms of the two mechanisms. By this method it could be estimated (Ref. 6) that at $\text{H}_0 = 0$ the $\text{AS}_{\text{E}2}$ mechanism accounts less than 0.5% of the rate for vinyl acetate but about 20% of the rate for isopropenyl acetate. When the $\text{A}_{\text{AC}2}$ mechanism prevails, an inverse isotope effect ($k(\text{H}_2\text{O}) / k(\text{D}_2\text{O}) \approx 0.75$) was obtained, whereas normal isotope effects in the range of 2.5-3.2 were found when the mechanism was $\text{AS}_{\text{E}2}$.

METAL ION CATALYSIS

Kiprianova, Rekasheva, and Samchenko investigated the site of bond fission (Ref. 19) and the kinetics of the hydrolysis of vinyl esters catalysed by mercury(II) acetate or perchlorate in acid solutions (Ref. 50 & 51). Halpern *et al.* (Ref. 52 & 53) studied by NMR and IR spectroscopy the kinetics of the mercury(II) and thallium(III) ion-catalysed hydrolysis of isopropenyl acetate. Both groups proposed essentially similar mechanisms with somewhat different views of the structures of the intermediates and of the rate-limiting stage. The mechanism presented by Abley, Byrd, and Halpern (53) seems to be based on a more detailed experimental study. It is essential that the catalyst adds to the double bond and thus helps the addition of water. The rate-limiting step is the alkyl-oxygen fission of the addition compound. It differs in this respect from the otherwise similar $\text{AS}_{\text{E}2}$ mechanism. Actual catalysts are organomercury(II) and bis(organo)thallium(III) ions, which also can be formed from the ester and inorganic ions.

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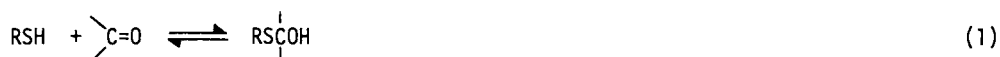
GENERAL ACID-BASE CATALYSIS OF CARBONYL AND ACYL GROUP REACTIONS*

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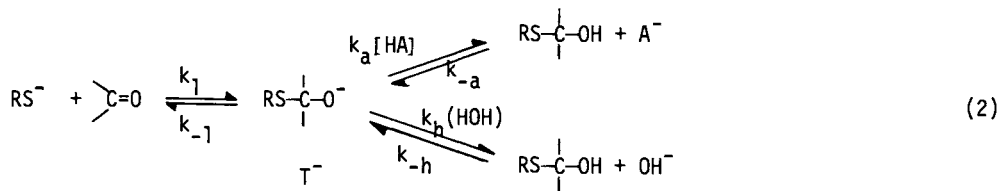
Abstract - The addition of thiols to the carbonyl group illustrates most of the range of mechanisms of general acid-base catalysis that are available for reactions of carbonyl and acyl groups. Strongly basic thiol anions add without significant acid catalysis to form an anionic intermediate T^- , which abstracts a proton from water to give the hemithioacetal in a subsequent fast step. Methyl mercaptoacetate anion generates a less stable intermediate, T^- , and exhibits catalysis through trapping by rate-determining stepwise protonation of this intermediate. Less basic thiol anions exhibit general acid catalysis by hydrogen bonding of HA to the carbonyl oxygen atom in the transition state, which becomes significant largely because of the short lifetime of the intermediate. General acid catalysis of the addition of RSH may represent concerted catalysis that is enforced by the nonexistence of the "intermediate" T^\pm .

Several aspects of our present understanding of the mechanism of catalysis of carbonyl and acyl group reactions may be illustrated by a consideration of the reversible addition of thiols to aldehydes and ketones (eq. 1). Reactions involving the thiol anion as the



attacking (or leaving) nucleophile are relatively simple because only a single proton transfer is required to form the stable product and the site of catalysis is unambiguous, i.e. proton transfer to and from the carbonyl oxygen atom. Similar mechanisms of catalysis are presumably involved in more complex reactions of other carbonyl and acyl compounds that commonly involve two bond forming or breaking steps of heavy atoms and two or more proton transfers.

The situation until recently was the following. (a) Basic thiol anions were known to attack the carbonyl group without detectable acid catalysis and with a very small dependence of the rate on the basicity of the thiol (1). The absence of detectable acid catalysis is typical for the attack of basic, strong nucleophiles and indicates that stabilization of the transition state by acids through hydrogen bonding or other mechanisms is of little or no significance in these reactions. (b) However, the addition of less basic anions of thiophenols and thioacetic acid had been shown to exhibit general acid catalysis with a Brønsted slope α of approximately 0.2; this is equivalent, in the reverse direction, to general base catalysis of hemithioacetal breakdown with a Brønsted β value of 0.8 (2). It was suggested that the mechanism of this catalysis was, in some sense, "concerted" with significant perturbation of the proton in the transition state, as opposed to a stepwise mechanism involving rate-determining protonation of an initially formed anionic addition compound, T^- (k_a , eq. 2). (c) The rate of the reverse, breakdown reaction catalyzed by hydroxide ion



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was known to approach the diffusion controlled limit (2).

Although the rate constants for catalysis of the breakdown reaction by general bases do not follow the "Eigen curve" that would be expected if proton transfer were rate determining with these catalysts (3), the absolute values of the rate constants are close to those that would be expected for the proton transfer step, k_{-a} . The rate constants k_a and k_{-a} may be calculated from the estimated pK_a of the hemithioacetal (see Note a) and a value of $k_a = 10^9 \text{ M}^{-1}\text{s}^{-1}$ for the protonation of T^- by a relatively strong acid (3). The rate constant k_h for protonation of T^- by water may be estimated from the pK_a in a similar manner, assuming that the reverse reaction of the hemithioacetal with hydroxide ion is diffusion controlled with $k_{-h} = 10^{10} \text{ M}^{-1}\text{s}^{-1}$ (2). Such calculations showed that the rate of protonation of T^- by water was not fast enough to keep up with the known rate of formation of T^- by the attack of methyl mercaptoacetate anion on acetaldehyde in the absence of added catalysts. In other words, some of the molecules of T^- that are formed from the attack of RS^- on acetaldehyde return to reactants (k_{-1}) before they are protonated by water (k_h). The estimated values of k_{-1} and k_h for the methyl mercaptoacetate reaction were similar, $2 \times 10^8 \text{ s}^{-1}$ and $2.5 \times 10^8 \text{ s}^{-1}$, respectively. In this situation the rate of product formation must be increased by the addition of buffer acids to the solution, because protonation of T^- by these acids provides an additional pathway for the proton transfer step and prevents the reversion of T^- to starting materials. It was predicted that the rate would increase with increasing concentration of added acid catalyst until all of the molecules of T^- that are formed are trapped by protonation ($k_a[\text{HA}]$) and would then level off at the rate of the addition reaction, k_1 .

This behavior was observed upon the addition of a number of different buffer acids to the reaction mixture and provides unequivocal evidence for a change in rate-determining step with increasing buffer concentration and, hence, a reaction mechanism for methyl mercaptoacetate that involves at least two steps and an intermediate. For a simple reaction of this kind, these steps must almost certainly be the attack of the thiol anion (k_1) and protonation of the intermediate ($k_a[\text{HA}]$ and k_h). The values of k_{-1} and k_h may be calculated from the observed rate constants, assuming a value of $k_a = 10^9 \text{ M}^{-1}\text{s}^{-1}$, and the resulting values of $k_{-1} = 1.3 \times 10^8 \text{ s}^{-1}$ and $k_h = 5 \times 10^8 \text{ s}^{-1}$ are close to the predicted values. The values of k_{HA} for acid catalysis cannot be determined accurately because of the small and nonlinear increase in rate caused by the change in rate-determining step, but the results do show that (a) the catalytic effectiveness of acids with pK_a values in the range 2 to 9 is the same within experimental error, (b) the proton is more effective than other catalysts, and (c) weaker acids, of pK 10 to 12, are less effective than other acids. This is the behavior expected for a simple stepwise proton transfer reaction and the approximate catalytic constants follow the nonlinear "Eigen curve" that is expected for such a proton transfer, with a break point at $\Delta pK = 0$, close to the estimated pK_a of the hemithioacetal product (Fig. 1, curve A).

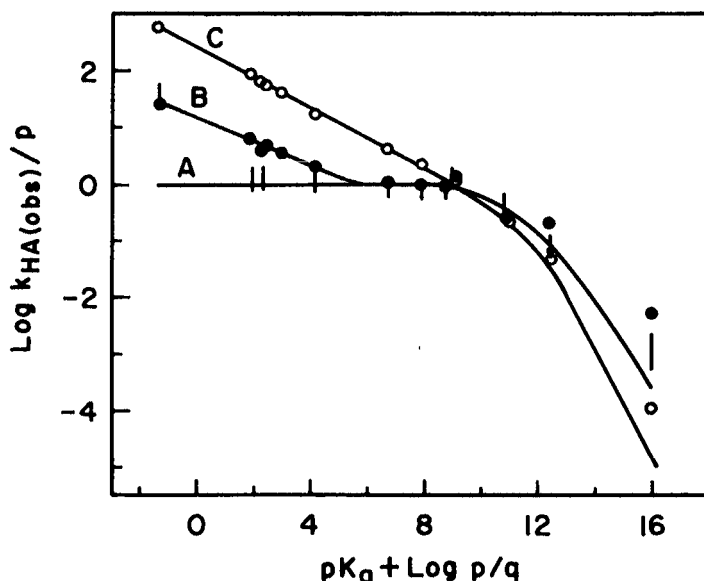


Fig. 1. Brønsted plots for catalysis by oxygen acids of the addition of thiol anions to acetaldehyde normalized to the same rate constant for catalysis by T^- . "Eigen curves" for simple proton transfer to T^- are drawn with $\Delta pK = 0$ at 12.4 for A and B and 11.1 for C. Deviation of points above 0 represents hydrogen bond catalysis. (A) (○) $\text{MeOOCCH}_2\text{SH}$. (B) (●) $p\text{MeOArSH}$. (C) (○) F_5ArSH .

Note a. A pK value of 12.4 for $\text{HOEtSCH}_2\text{OH}$ has been determined by R. G. Kallen (personal communication) and pK values of related compounds may be estimated from $\rho_1\sigma_1$ correlations.

The reaction mechanism for methyl mercaptoacetate is illustrated by the reaction coordinate diagram of Fig. 2b. The barriers for reaction of the intermediate T^- to give reactants

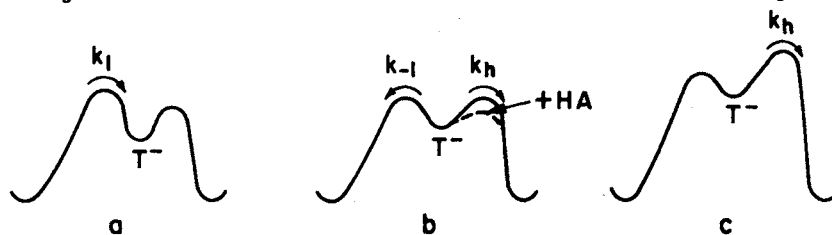
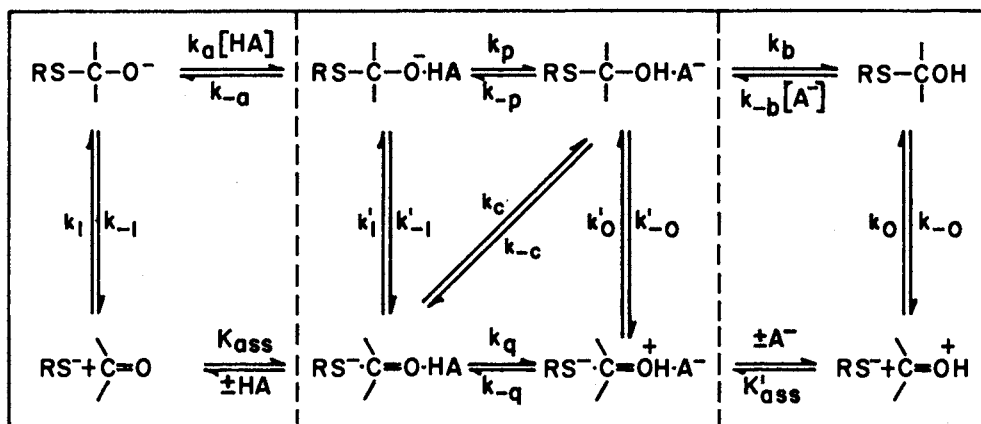


Fig. 2. Reaction coordinate diagrams for (a) rate-determining nucleophilic attack with basic thiol anions, (b) nucleophilic attack and proton transfer both partially rate determining in water and a change to rate-determining nucleophilic attack in the presence of added acid, and (c) rate-determining protonation of T^- that gives rise to general acid catalysis by trapping.

(k_{-1}) and products (k_h) are similar so that both the k_1 and k_h steps are partially rate determining. The addition of acid provides an additional, lower energy pathway for the proton transfer step (k_a) so that the rate increases until the effective barrier for the proton transfer is decreased and k_1 becomes fully rate determining. A more basic thiol anion, such as EtS^- , is a poorer leaving group (k_{-1} is smaller) so that k_1 is always rate determining and no catalysis by trapping is observed (Fig. 2a). A less basic thiol anion, such as $p\text{-CH}_3\text{OPhS}^-$, is a better leaving group (k_{-1} is larger) so that the proton transfer step, k_h , is always rate determining (Fig. 2c) and the observed rate increases linearly with increasing concentration of acid catalyst.

For moderately strong acids, such as acetic acid, the rate-determining step of the proton transfer is the diffusion-controlled encounter of the acid and T^- , with the rate constant k_a (eq. 2 and Scheme 1). However, there is another pathway to the species $T^- \cdot HA$ that

SCHEME I



bypasses the diffusion-controlled step. This pathway involves a preliminary association of thiol anion, acetaldehyde and catalyst in an encounter complex (K_{ass}) followed by nucleophilic attack (k_1') to give T^- with the catalyst already in position to trap the intermediate through a fast proton transfer (k_p). If the transition state for the rate-determining k_1' step is sufficiently basic that it forms a stronger hydrogen bond to HA than to water, this pathway will be stabilized by such hydrogen bonding. If this hydrogen bonding is strong enough, buffer acids will stabilize k_1' relative to k_1 and catalysis by hydrogen bonding will always be important. We know that this is not the case for the addition of basic thiol anions and other strong nucleophiles because little or no acid catalysis is observed when nucleophilic attack is rate determining. On the other hand, acid catalysis is significant for the attack of weakly basic thiol anions and exhibits a Brønsted α value of 0.2. This Brønsted slope is inconsistent with the value of $\alpha = 0$ that is expected for diffusion-controlled trapping by moderately strong acids, but is in the expected range for stabilization by hydrogen bonding.

Advantages of the hydrogen-bonding mechanism. In order to understand why catalysis by hydrogen bonding is more important with weakly basic than with strongly basic thiol anions, we must examine the effect of the stability of the addition intermediate on the relative importance of different reaction pathways. As the intermediate becomes progressively more unstable, catalysis by hydrogen bonding becomes progressively more important. We will

consider (a) the ratio of the observed rate constant, k_{HA}' , for catalysis through the k_1' pathway to the rate constant for the uncatalyzed or "water" reaction, (b) the ratio $k_{\text{HA}}'/k_{\text{HA}}$ for catalysis by hydrogen bonding and by trapping, and (c) changes in the Brønsted coefficient α .

(a) In order for catalysis by hydrogen bonding to be significant with strongly basic nucleophiles, for which k_1 is rate determining, the transition state for the hydrogen bonding pathway (k_1') must be of comparable or lower energy than that for k_1 . This is evidently not the case for basic thiol anions. However, with less basic thiols the rate-determining step is trapping through k_h (eq. 2, $k_{\text{HOH}} = k_1 k_h / k_{-1}$), so that the hydrogen bonding pathway only has to be of lower energy than the transition state for the k_h step in order to be significant. Since the hydrogen bonding mechanism is expected to maintain approximately the same energy relative to k_1 , but the observed rate constant k_{HOH} is now smaller than k_1 by the factor k_h/k_{-1} , the hydrogen-bonding mechanism will become relatively more important. This additional advantage, by the factor k_{-1}/k_h , is the principal reason why catalysis by hydrogen bonding is more likely to be observed with weak nucleophiles that are easily expelled from the addition intermediate (large k_{-1}).

(b) The factors that determine the relative importance of the pathways for acid catalysis by trapping (k_{HA}) and by hydrogen bonding through the k_1' pathway (k_{HA}') may be illustrated by the reaction coordinate diagram of Fig. 3. (i) Consider first a reaction in which there

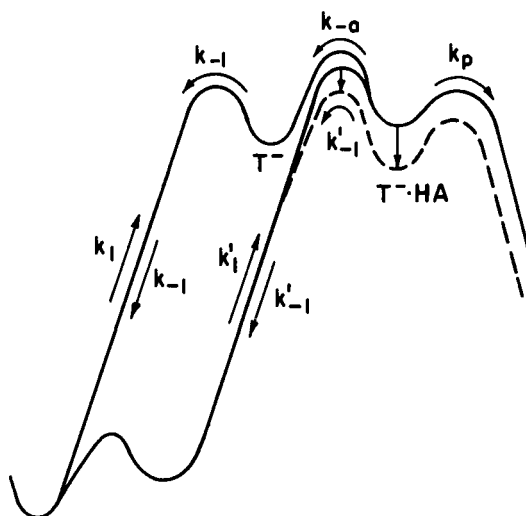


Fig. 3. Reaction coordinate diagram for general acid catalysis with rate-determining trapping (upper line) and rate-determining nucleophilic attack by a pre-association mechanism (lower lines). The dashed line and the vertical arrows indicate the additional stabilization brought about by hydrogen bonding to an acid HA.

is no stabilization of the transition state of the $k_1' - k_{-1}'$ step by hydrogen bonding to HA ($\alpha = 0$). This pathway (lower solid line, Fig. 3) will still be preferred to the trapping mechanism (upper line) when the intermediate $T^- \cdot \text{HA}$ breaks down faster (k_{-1}') than HA can diffuse away from it (k_{-a}). This pre-association or "spectator" mechanism (4-6) is useful because it generates the intermediate $T^- \cdot \text{HA}$, which is immediately trapped by an ultrafast proton transfer, by a pathway that avoids the diffusion-controlled step $k_a - k_{-a}$. The relative importance of the diffusion-controlled and pre-association pathways is given by the ratio k_{-1}/k_{-a} (in the absence of stabilization by hydrogen bonding, $k_{-1}' = k_{-1}$).

(ii) If there is stabilization of the transition state of the $k_1' - k_{-1}'$ step by hydrogen bonding (dashed line, Fig. 3) this stabilization is expected to increase with increasing acidity of HA, following a Brønsted coefficient α . This additional advantage is given by $\text{antilog } \alpha$ ($15.74 - \text{p}K_{\text{HA}}$) and represents the increase in the ratio k_{-1}'/k_{-a} when the acid that is hydrogen bonded to the transition state is changed from water to HA. Since k_{-a} and k_{-1}' are both first order constants for reactions of $T^- \cdot \text{HA}$, this ratio is dimensionless and there is no ambiguity regarding standard states. For an α value of 0.2 and an acid of $\text{p}K$ 4.7, the advantage from hydrogen bonding is by the factor $\text{antilog } 2.2 = 160$. The value of α , and hence the advantage from hydrogen bonding, is expected to increase with increasing basicity of the transition state and will follow some relationship such as that proposed by Hine (7).

Thus, the relative importance of the stepwise trapping mechanism, k_{HA} , and the hydrogen bonding mechanism, k_{HA}' , is determined by (i) the hydrogen bond-independent factor k_{-1}/k_{-a} and (ii) the additional stabilization from hydrogen bonding (eq. 3). The relative energies of

$$k_{HA}'/k_{HA} = (k_{-1}/k_{-a}) \text{antilog } \alpha(15.74 - pK_{HA}) \quad (3)$$

the two pathways are shown by the upper solid line and the dashed line in Fig. 3.

A numerical example may clarify these points. Suppose that the basicity of a transition state for nucleophilic attack is such that $\alpha = 0.1$ for stabilization by hydrogen bonding and k_h for trapping of the intermediate by water is $2 \times 10^8 \text{ s}^{-1}$. Then, if $k_{-1} = 10^7 \text{ s}^{-1}$ or less, attack of the nucleophile (k_1) is rate determining and the observed ratio of k_{HA}'/k_1 for an acid of pK 4.7 is $\text{antilog}[0.1(15.7 - 4.7) - 1.74] = 0.23$. Since this ratio gives only a 23% rate increase at 1 M acid, general acid catalysis would be of borderline significance, at best. The term 1.74 = $\log 55$ in this calculation arises from the molarity of liquid water, which competes with the acid HA for hydrogen bonding to the transition state. However, if k_{-1} is 10^9 s^{-1} and the rate constant k_a for diffusion-controlled trapping of T^- by HA is $10^9 \text{ M}^{-1}\text{s}^{-1}$, then the ratio $k_{HA}/k_{HOH} = k_a/k_h = 10^9/2 \times 10^8$ for catalysis by trapping is 5. The relative importance of catalysis by hydrogen bonding and by trapping (eq. 3) is $k_{HA}'/k_{HA} = (0.1)\text{antilog } 0.1(15.7 - 4.7) = 1.26$, assuming that $k_{-a} = 10^{10} \text{ s}^{-1}$. The ratio $(k_{HA} + k_{HA}')/k_{HOH}$ is then $5 + 1.26 \times 5 = 11$ and the observed rate will be doubled by less than 0.1 M added acid catalyst. If k_{-1} is 10^{10} s^{-1} the ratio $(k_{HA} + k_{HA}')/k_{HOH} = 68$ and the observed rate will be doubled by 0.02 M acid. Thus, the importance of catalysis by hydrogen bonding increases sharply as the intermediate becomes less stable and k_{-1} increases. The effect of the lifetime of the intermediate (k_{-1}) on the importance of the rate constants for general acid catalysis by trapping and by hydrogen bonding is summarized in Table 1.

TABLE 1. The relative importance of catalysis by trapping and by hydrogen bonding as the lifetime of T^- decreases (k_{-1} increases)^a

| k_{-1} s^{-1} | $\frac{k_{HA}}{k_{HOH}}$ M^{-1} | $\frac{k_{HA}'}{k_{HOH}}$ M^{-1} | $\frac{k_{HA} + k_{HA}'}{k_{HOH}}$ M^{-1} | [HOAc] to double rate M | Percent of catalysis due to Trapping | H-bonding |
|-----------------------------|---|--|---|----------------------------------|---|-----------|
| 10^8 | ^b | 0.6 | 0.6 | 1.6 | ^b | 100 |
| 10^9 | 5 | 6 | 11 | 0.1 | 45 | 55 |
| 10^{10} | 5 | 63 | 68 | 0.015 | 7 | 93 |
| 10^{11} | 5 | 630 | 635 | 0.0016 | 1 | 99 |

^aBased on $\alpha = 0.1$, $k_a = 10^9 \text{ M}^{-1}\text{s}^{-1}$, $k_{-a} = 10^{10} \text{ s}^{-1}$ and $k_h = 2 \times 10^8 \text{ s}^{-1}$.

^bCatalysis by trapping can result in only a 50% rate increase over k_{HOH} before attack (k_1) becomes rate determining; any additional catalysis must represent hydrogen bonding.

(c) Still another factor that may increase the importance of hydrogen-bond catalysis with weak nucleophiles is a "Hammond Postulate" type effect that leads to an increase in the Brønsted slope α . With weak nucleophiles the transition state for nucleophilic attack may be reached later along the reaction coordinate and develop a larger negative charge and basicity on the carbonyl oxygen atom. This will lead to an increase in the Brønsted α coefficient with a resulting increase in catalysis by moderately strong acids relative to water.

The shapes of some Brønsted curves for general acid catalysis that would be expected from these considerations are shown in Fig. 4. An "Eigen curve" for rate-determining trapping by proton transfer is shown in Fig. 4A, with the arrow indicating the break point at $\Delta pK = 0$. A pre-association mechanism with no stabilization by hydrogen bonding (Fig. 4B) shows a break point at a lower pK value (6). A reaction in which catalysis by hydrogen bonding is facilitated by the short lifetime of the addition intermediate (Fig. 4D) exhibits a Brønsted slope >0 , but breaks to a steeper slope with weak acids as the proton transfer itself becomes rate determining. It is this break and the relatively small rate constant for water ($k_{HOH} = k_h k_1 / k_{-1}$) that makes catalysis so significant experimentally. With a longer lifetime of the intermediate there is less facilitation of hydrogen-bond catalysis and this mechanism becomes important only for the stronger acids, so that there is an additional break in the Brønsted curve (Fig. 4C).

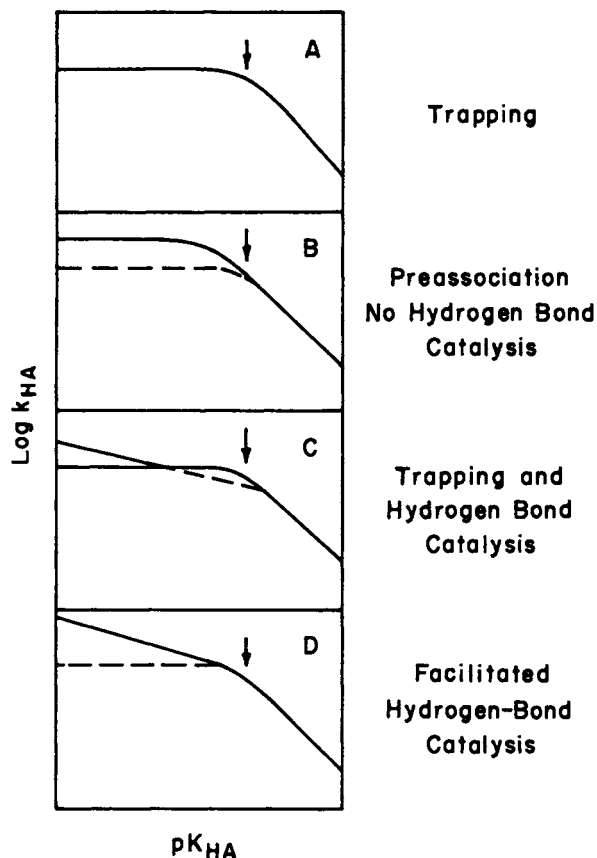


Fig. 4. Schematic Brønsted curves for general acid catalysis.

Although it is difficult to determine k_{-1} for the expulsion of thiol anions from T^- directly, this rate constant can be estimated from the pK and the observed rate constants for the breakdown of hemithioacetals of basic thiols. For expulsion of the anions of ethanethiol, methoxyethanethiol and methyl mercaptoacetate from T^- the values of k_{-1} are $1.6 \times 10^7 \text{ s}^{-1}$, $4.7 \times 10^7 \text{ s}^{-1}$, and $1.3 \times 10^8 \text{ s}^{-1}$, respectively. The rate constants increase with decreasing basicity of the leaving group and extrapolation to the pK values of 6.5 and 2.7 for *p*-methoxythiophenol and pentafluorothiophenol gives values of $k_{-1} = \sim 10^9 \text{ s}^{-1}$ and $10^{10} - 10^{11} \text{ s}^{-1}$, respectively, well into the range in which catalysis by hydrogen bonding should be facilitated. The Brønsted plot for general acid catalysis of the pentafluorothiophenol reaction (curve C, Fig. 1) exhibits a slope of $\alpha = 0.26$ and suggests that facilitated hydrogen bonding is the predominant mechanism of catalysis for this compound, in accord with the large value of k_{-1} . The Brønsted plot for the *p*-methoxythiophenol reaction (curve B, Fig. 1) is clearly different from that for pentafluorothiophenol and is similar to that in Fig. 4C, suggesting that catalysis involves rate-determining trapping with weak acids and hydrogen bonding with a Brønsted slope $\alpha > 0$ for stronger acids.

These results support the conclusion that catalysis by facilitated hydrogen bonding increases in importance as the intermediate becomes less stable and k_{-1} increases. The concentrations of acetic acid needed to give a twofold increase in the observed rate are 2.6 M, 0.4 M and 0.001 M for the reactions with methyl mercaptoacetate, *p*-methoxythiophenol and pentafluorothiophenol anions. Since no hydrogen-bonding catalysis can be observed with basic thiol anions ($\alpha < 0.1$) and the observed Brønsted slope is 0.26 for pentafluorothiophenol anion, it is also probable that there is a later, more basic transition state and larger Brønsted α with less basic thiols.

We do not know at this time what pathway is followed after the transition state of the rate-determining step for hydrogen bonding catalysis. Of the three pathways shown in the reaction coordinate diagram of Fig. 5 the simplest is (a), in which the immediate product is $T^- \cdot HA$ and proton transfer occurs in a subsequent, separate step. We know that the intermediate T^- has a finite existence with respect to expulsion of RS^- for at least some thiols, but we do not know how fast a proton is transferred (possibly through a water molecule) from HA to T^- so that it is not certain that T^- can exist as a discrete intermediate. The other possible

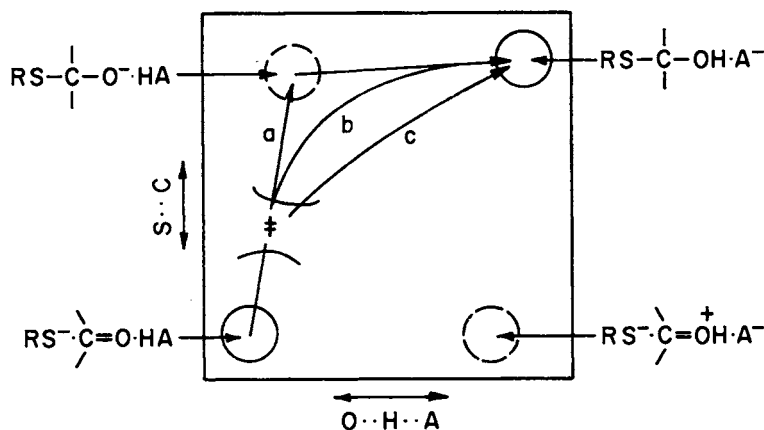
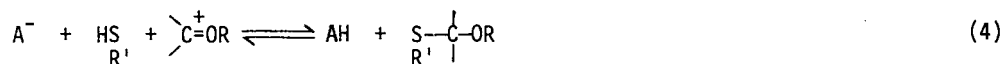


Fig. 5. Reaction coordinate diagram showing different pathways to products after a transition state with hydrogen bonding.

pathways are (b), which is similar to (a) except that it does not involve T^- as an intermediate, and (c), which is a fully concerted reaction mechanism with an early transition state.

Finally, we can ask what will be the mechanism of catalysis when the nucleophile is still weaker than pentafluorothiophenolate anion. Assuming that k_{-1} continues to increase as the nucleophile becomes less basic, a point will be reached at which the addition compound T^- ceases to exist as an intermediate with a significant lifetime when k_{-1} approaches 10^{14} s^{-1} , in the range of a vibration frequency. There are experimental obstacles to the study of such weakly basic anions, but the free thiols, RSH, are extremely weak bases and exhibit general acid catalysis of their addition to acetaldehyde (1). Although this reaction has not been studied in detail, the available data indicate that α is large. It is unlikely that the reaction involves equilibrium protonation of the carbonyl group and catalysis of proton removal from the attacking thiol (eq. 4, R = H) because no buffer catalysis is observed in the analogous reaction of thiol expulsion from a mixed acetal (eq 4, R = Me)(8). It is



tempting to speculate that general acid catalysis of the addition of a free thiol represents concerted catalysis (path c, Fig. 5) which is enforced by the short lifetime, indeed the nonexistence of the initial addition "intermediate" $^+RSHCHR'O^-$. Other addition reactions of weak bases, such as the addition of the nitrogen atom of urea (9,10) exhibit Brønsted α coefficients near 0.5 and are also candidates for a concerted mechanism of catalysis that is enforced by the nonexistence of the addition compound that would be formed in the absence of proton transfer.

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STRAIN ENERGY MODELING OF SIMPLE AND CROWDED ALIPHATIC KETONES :
SPECTROSCOPIC PROPERTIES

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Abstract - Spectroscopic properties of ketones have been correlated with a structure-frequency micro-correlation made possible by dividing the ketone population into sub-populations, $\mathcal{P}_{i,i}$. The structure and comportment of those ketones of the population that remain outside the correlations are treated in the discussion. The DARC/PELCO topological treatment is explained and demonstrated : it is based on the notion of ordered populations considered as hyperstructures or formal graphs. The correlations thus obtained, in IR, UV and ^{13}C NMR spectroscopy, are more exhaustive than those obtained with the above-mentioned micro-correlations, and their prediction potential, or "proférence", is very high. Variations in the geometry of compound structures resulting from an abundance of substitutions, as well as their relationship to conformational problems, are shown. A gem-persubstituted β effect associated with a major strain release, leads to major deformations of angles and of interatomic distances.

INTRODUCTION

The structural environment of the carbonyl group influences the spectral characteristics of ketones. Although this fact has long been known, its interpretation is still subject to speculation. Relationships between structure and spectral properties can be approached through isolated cases or via an ordered family of ketones.

The purpose of studying highly substituted ketones, such as tetratertiobutylacetone or triisopropylmethyl-neopentylketone, synthesized in our laboratory, was to verify the hypothesis of an internal strain due largely to repulsions between non-bonded atoms. In fact, we discovered that the situation is somewhat different and that the structures undergo certain important deformations in order to dissipate or redistribute the imposed strain. The real geometry could be considered as resulting from structural deformations of the standard structure because of potential strain. The virtual passage from a standard structure to a real structure would be accompanied by strain release. Such a real structure is said to be "decongested" and its true description is of a topographical nature.

Are the angle and bond modifications observed in highly substituted environments following strain release apt to modify the balance between rotamers? This is the question we asked ourselves during our ketone studies, in which we made use of appropriate spectroscopic treatments as well as extrathermodynamic "structure-property" correlations for our interpretations.

The structures used make it possible to study intragroup interactions developed in alkyl groups, as well as intergroup interactions between the radicals of the sp^2 carbon valence angle.

We approached this difficult area of aliphatic ketones, where the conformational aspect is essential, by supposing the existence of conformational filiations between privileged rotamers of different ketones. The problem with these filiations lies in the assigning of reference conformations, and we shall show how we have sought to assure the validity of our propositions by constantly improving the convergence of deductions based not only on diverse experimental data, but also on various calculations on the existence probability of the rotamers.

In this presentation, our aim is to report on the current state of research, linking present results to the attribution of the real geometries of aliphatic ketones. This analysis will be based on the continual use of the notion of conformational filiation, as well as on the evaluation of changes in molecular dimensions for certain borderline cases of highly substituted structures. We shall show that the evaluation of interactions in terms of energy is not yet entirely satisfactory, although analyses of tendencies yield interesting

results for structure assignment. The latter are neither complete nor final though reported progress on the coherence of deductions seems satisfactory and most promising.

OUTSTANDING FEATURES IN UV AND IR SPECTROSCOPY OF KETONES

In UV as well as in IR spectroscopy, the influence of structure and solvent on the absorption maximum shift has led to a great number of studies: here, we have considered only the most outstanding of these studies.

$n \rightarrow \pi^*$ absorption band of saturated ketones

The effect of substituents on the absorption band of aliphatic ketones was studied experimentally and rationalized by us in 1954 (1). The absorption band undergoes a strong bathochromic shift (from $35\,990\text{ cm}^{-1}$ to $33\,650\text{ cm}^{-1}$ in hexane) by increasing substitution from acetone to hexamethylacetone. Each substituent of the molecule contributes to this bathochromic shift by a characteristic increment.

When seeking to extend and develop the relationships between the molecular structure and the energy of the $n \rightarrow \pi^*$ transition, we encountered the difficulty of determining the position of the band with precision, due to the presence of important vibration fine structure for certain aliphatic ketones (2a).

In 1970, our study bearing on a population of 50 aliphatic ketones which was very rich in highly substituted compounds showed the existence of somewhat intense fine structure which, for certain compounds, is analogous to that observed for acetaldehyde or cyclobutanone.

In order to render the analysis of this spectral modulation less subjective, we deemed it necessary to define a fine structure (FS) index, i.e. an index quantitatively describing the intensity of the modulation (Fig. 1). The index scale thus obtained permits situating the importance of the fine structure within the absorption phenomenon and comparing the fine structure of two carbonyl derivatives.

Thus, ditriptylketone $t\text{Bu}(\text{Me})_2\text{CCOC}(\text{Me})_2t\text{Bu}$: ($\text{FS} = 10.2 \times 10^{-2}$) and tetratertiobutylacetone $t\text{Bu}_2\text{CHCOCH}t\text{Bu}_2$: ($\text{FS} = 9.4 \times 10^{-2}$) have a vibrational structure whose intensity is near that of cyclobutanone ($\text{FS} = 11 \times 10^{-2}$) and corresponds to a third of that of cyclopentanone ($\text{FS} = 27.7 \times 10^{-2}$).

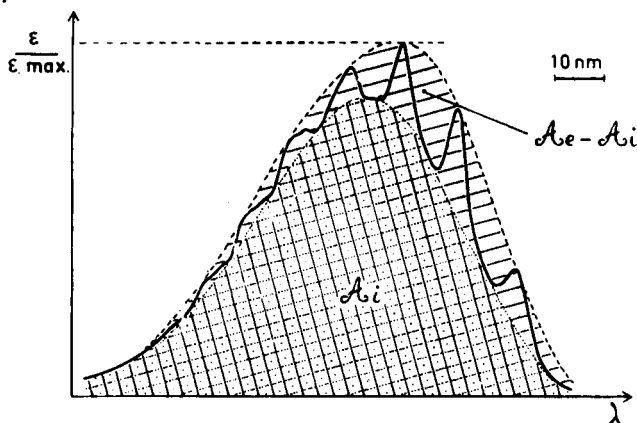


Fig. 1. Definition of the fine structure index $\text{FS} = (\mathcal{A}_e - \mathcal{A}_i) / \mathcal{A}_i$.

The rules governing the existence of this fine structure are not clearly established. It is observed that the practically inexistent fine structure for acetone tends to become more marked with substitution on the carbons α and β to the carbonyl group. In general, the modulation increases as the hindrance around the carbonyl group also increases; however, there are a certain number of exceptions. The solvent also plays a determining role: the fine structure index is a non-increasing function of the solvating power. However, depending on the nature of the ketones studied, there are several types of comportment with respect to changes in the medium (2b). We especially wish to point out, what, to our knowledge, is the first observation of an intense modulation which resists the increase of the solvating power: $(t\text{Bu})(\text{Me})_2\text{CCOC}(\text{Me})_2(t\text{Bu})$.

The varied character of the modulation with the solvent or structure poses the problem of defining an absorption wave number permitting the comparison of highly modulated spectra

with those bands lacking a fine structure. Locating the maximum of the internal envelope yielded some satisfactory results for our study of the bathochromic shift of the substituents, as well as for our study of the hypsochromic shift of the solvents.

Solvent shift and privileged conformations. We have shown the diversity of the relationships between the hypsochromic shifts of solvents on the $n \rightarrow \pi^*$ transition and the wave number found for a reference solvent (hexane): three different types of comportment are obtained, depending on the hindrance of the two radicals, R and R' (2c) (Fig. 2).

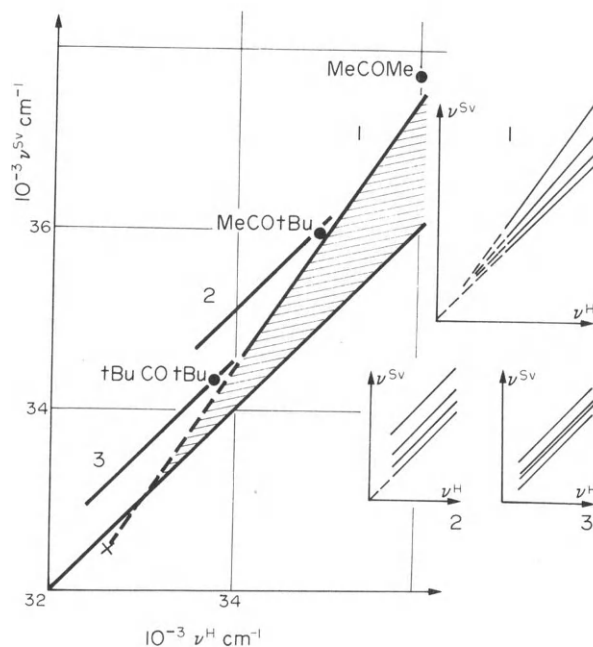
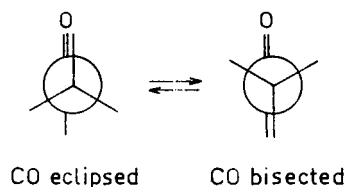


Fig. 2. The two parallel networks and the convergent network of saturated aliphatic ketones RCOR'.

For each of these comportments, straight lines $\nu^{Sv} = f(\nu^H)$, characterizing the solvents Sv, are organized into networks:

- a convergent network, 1, if both radicals R and R' are only slightly hindered;
- a parallel network, 2, for ketones MeCOR with hindered radical R;
- a parallel network, 3, different from the preceding network (the amplitude of the solvent effect is weaker) if both radicals, R and R', are hindered.

Comparison of these results with those of the hypsochromic shift of cyclanones having locked environments justified the following conformational interpretation: the carbonyl group of the slightly substituted RCOR' compounds is eclipsed by a C-C or C-H bond of the slightly hindered radical R. In hindered compounds, the carbonyl group would be bisected by the hindered bonds of the radical R (or R'). Thus, the growing interaction between the carbon atoms of the radical R at β or γ with respect to the carbonyl group and the carbonyl group itself would favor a bisected carbonyl group conformation, or at least one that is sufficiently staggered with respect to the eclipsed carbonyl group (2c).



Structural effect of the $n \rightarrow \pi^*$ transition and linear free energy relationships. A study in 1963 on a restricted population of slightly hindered ketones (11 ketones RCOR' where R and R' = Me, Et, Pr, iBu) showed us that it is possible to express the influence of environment with a linear free energy relationship when using two structural parameters: $\Delta\nu = -16\ 320\sigma^* + 1\ 490(n - 6) + 42\text{ cm}^{-1}$. "n" is the number of hydrogens α to the carbonyl group.

However, the slight deviation of "the most highly substituted" ketone, di-isobutylketone, already showed that it would be necessary to use other structural parameters in order to attain a satisfactory correlation (3).

Carbonyl stretching vibrations of ketones

Our recent studies bearing on a vast population of ketones have shown us the interest of the shape of the $\nu_{C=O}$ band in the analysis of the structural effect, as well as in that of solvent effects.

A systematic study has led us to a true typology of $\nu_{C=O}$ bands. It should be pointed that we have split those bands having marked shoulders into two bands of the Lorentzian type (4), using a Dupont de Nemours 310 curve analyzer (5) (Fig. 3).

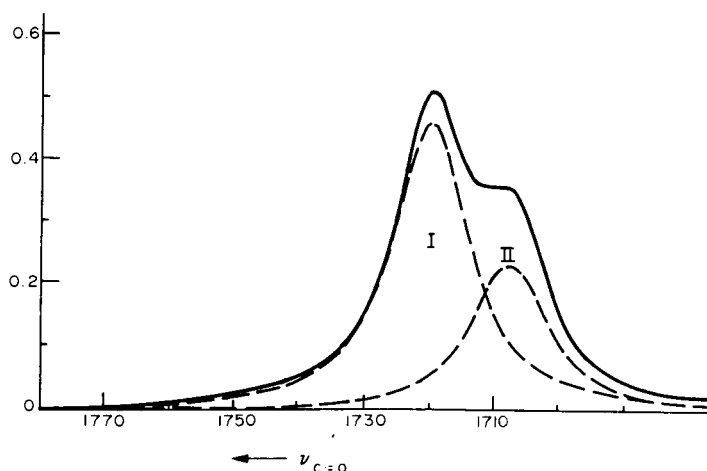


Fig. 3. Shape of the $\nu_{C=O}$ band for neoP-CO-Me in CCl_4

The results show that higher frequency band I corresponds to the only band existing in the gas phase. The relative importance of bands I and II depends on the solvent and varies roughly with Allerhand and Schleyer's solvent parameter, G (6). For example, the area of band II for methylneopentylketone varies from 0% in the gas phase to 55% in $CHBr_3$. In a solvent such as CCl_4 , band I is generally preponderant and its frequency corresponds markedly to that of the maximum of the envelope (7); it is this parameter that we have used to analyze the influence of the structural environment.

Ever since 1969, our first studies have allowed us to advance a certain number of results which are summarized in a "topology/ $\nu_{C=O}$ " relationship and in "reactivity parameter/ $\nu_{C=O}$ " relationships (8).

"Topology/ $\nu_{C=O}$ relationship. The sensitivity to structural effects of the stretching vibration of the carbonyl group of ketones in gas phase is interpreted by a topological analysis of the structural environment, using the DARC/PELCO method which we shall describe in the course of this presentation.

The correlation equation obtained shows that the contributions from the various substituents in positions α and β to the carbonyl group are constant and additive, but that, nevertheless, there are interaction terms between certain positions. These interaction terms express the difference from the strict additivity of contributions, not only within one of the alkyl groups ($tBu(Me)_2C-$), but also between both alkyl groups, on opposite sides of the carbonyl group for bitertiary ketones.

Furthermore, the various contributions from the α substitutions show that the decrease in frequency cannot be attributed only to the inductive effect whose values, which are defined by Taft's polar parameters, σ^* , are proportional to the number of α methyl groups. However, in the gas phase, as well as in the liquid phase, the $\nu_{C=O}$ frequency can be related to the σ^* parameters.

$\nu_{C=O}$ frequency and linear free energy relationship. The $\nu_{C=O}$ frequencies of 41 ketones measured in the liquid state have been correlated with the reactivity parameters (measuring the inductive, steric and hyperconjugation effects) (8a). Several expressions were obtained, which, although contradictory, are, quantitatively equally acceptable.

$$\nu_{C=O}^{liq} = 1720.3 + 124\Sigma\sigma^* - 9.4(n - 6) - 16.3(A_3)_1(A_3)_2 \quad (1)$$

$$\nu_{C=O}^{liq} = 1718 + 5.2\Sigma\sigma^* + 2.6\Sigma E_S^C - 15.6(A_3)_1(A_3)_2 \quad (2)$$

$$\nu_{C=O}^{liq} = 1717.3 + 2.9\Sigma E_S^C - 16(A_3)_1(A_3)_2 \quad (3)$$

The polar contribution in relationship 2 is considerably reduced and has been eliminated from relationship 3. These three correlations have similar characteristics (in relationship 2, $r = 0.992$ and $\Delta = 1.2 \text{ cm}^{-1}$)

Influence of molecular dimensions on the $\nu_{C=O}$ frequency. Bartlett and Stiles (9) have explained the low value of the $\nu_{C=O}$ frequency of two α' ditertiary ketones ($t\text{Bu}_2\text{CO}$ and TrCOtBu) by the existence of repulsions between the alkyl groups, thus provoking an opening in the $\widehat{\text{C-CO-C}}$ angle which would produce a variation in force constant $k_{C=O}$, by the hybridization change of the carbonyl carbon.

Afterwards, Zbiden (10) and Schleyer (11) even supposed that the force constant did not vary at all; this boils down to attributing the entire effect to coupling modifications provoked by the angular variation.

Moreover, calculations by Davis et al. (12) show that, without causing the angle to vary, geometrical changes, provoked by rotation of the alkyl groups around the carbonyl, indeed modify the frequency (12 cm^{-1} variation in diethylketone).

PRINCIPLES, CONCEPTS AND METHODS USED FOR THE ANALYSIS OF SPECTROSCOPIC DATA

Our analysis of spectroscopic data is based on the notion of a discrete environment, a fundamental concept of the DARC system, which allows formulating the notion of formal filiation and is the basis of topological correlations. Extrathermodynamic relationships for which we use the polar and steric factors of alkyl radicals, and several procedures for calculating steric energy, have also entered our analysis.

Representation of chemical compounds and compound families within the framework of the DARC system

The DARC (Description, Acquisition, Retrieval, Conception) System, developed since 1963, (13) constitutes a true management information system covering a range extending from the representation of data all the way to computer-aided design. It can be used to process any form or modelled structure by a chromatic graph (G_χ), i.e. a graph whose nodes and edges are symbolically differentiated by a color.

The DARC system is based on the concept of an Environment \mathcal{E} which is generated in an ordered and concentric manner. This concept permits the description of chemical formulas as ordered graphs and is essential for locating a formula (or structure) within a series, called a hyperstructure, which is itself represented by a graph whose edges are formal and whose nodes are real. The synchronous generation of a structure and its hyperstructure is a principle which simultaneously creates two graphs: a real one (S) and a formal one (HS).

Generation and description of an environment. A chemical formula is formally assimilated to a chromatic graph whose nodes represent the atoms other than hydrogen, and whose edges represent the bonds between these atoms. The chromaticity of the nodes corresponds to the nature of the atoms, and the chromaticity of the edges to the nature of the bonds. In this graph, we have distinguished two parts: the focus (FO), made up of an atom, a bond, or a group of atoms characterizing a series of compounds; the environment (\mathcal{E}), which comprises the remainder of the molecule, and which we have organized concentrically around the focus.

In order to generate an environment (\mathcal{E}), it is taken as a target and is constructed in an ordered fashion. This complex ordering is obtained by the propagation over the entire environment of an ordering module, or ELCO (Environment which is Limited Concentric and Ordered), whose amplitude is limited to two rows of atoms.

Once the entire environment is ordered, each site is located by a topological coordinate or total order label which is expressed by A_i or B_{ij} (Fig. 4).

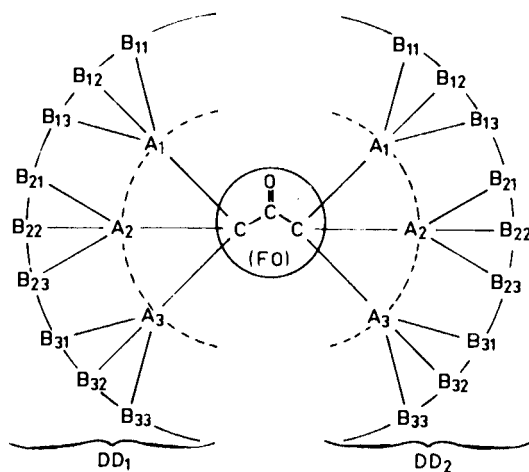


Fig. 4. An ordered and concentric graph of saturated aliphatic ketones. Since our study bears on ketones, the sub-structure common to all the individual members of the population has been chosen as the focus (FO): $\cong C - CO - C \leq$. The group having FO as a root, extends itself in two different directions of development: DD_1 and DD_2 .

For the description, we consider the graph of existence as the reference graph where each chromatic item of information concerning the multiplicity of the bonds and the nature of the atoms is associated to the index of the site to which it is related. The Descriptor of an Environment which is Limited (DEL) is constituted by the concatenation of the descriptors of each ELCO, each descriptor carries the topological description of the graph of existence (Fig. 5) and the chromatic data.

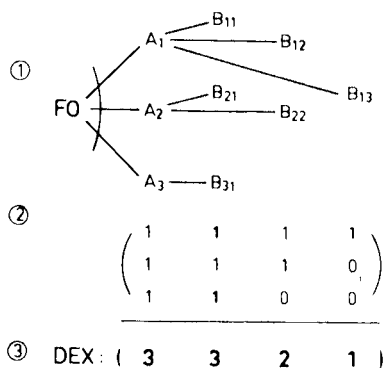


Fig. 5. Total ordering and topological descriptor. The Descriptor of EXistence (DEX) reflects the existence of total ordering labels of the ELCO. It is expressed by the following general formula: $DEX = (\sum_i A_i \sum_{i1} B_{i1} \sum_{i2} B_{i2} \sum_{i3} B_{i3})$.

Synchronism principle and hyperstructure (HS). When a target compound (X) is generated, a particular series of compounds, called a series of anteriologues associated to compound X, is engendered. All the anteriologues of X constitute a family whose members are located with respect to one another by a strict relationship. They constitute a hyperstructure (HS) whose generation is synchronous to the generation of target compound (X) (14).

A hyperstructure can be modelled by a graph whose nodes correspond to the compounds and whose edges correspond to the relationships between these compounds. Figure 6 shows the graph representing the anteriority hyperstructure of hexamethylacetone. We are presently in the process of generating and visually displaying the anteriority hyperstructure of a given target (15). Figure 7 shows the anteriority tree associated to hexatertibutylacetone ($tBu_3CCOEtBu_3$).

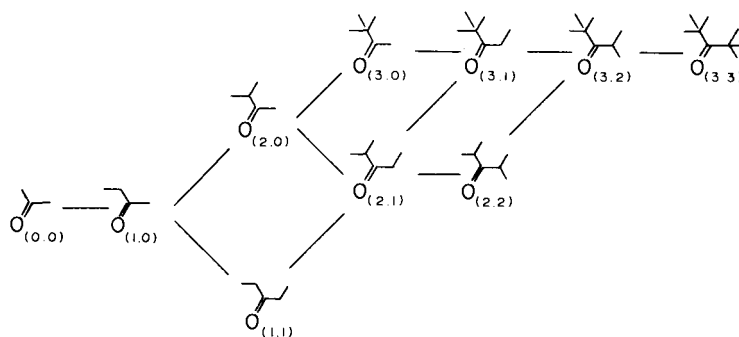


Fig. 6. The anteriority hyperstructure of hexamethylacetone

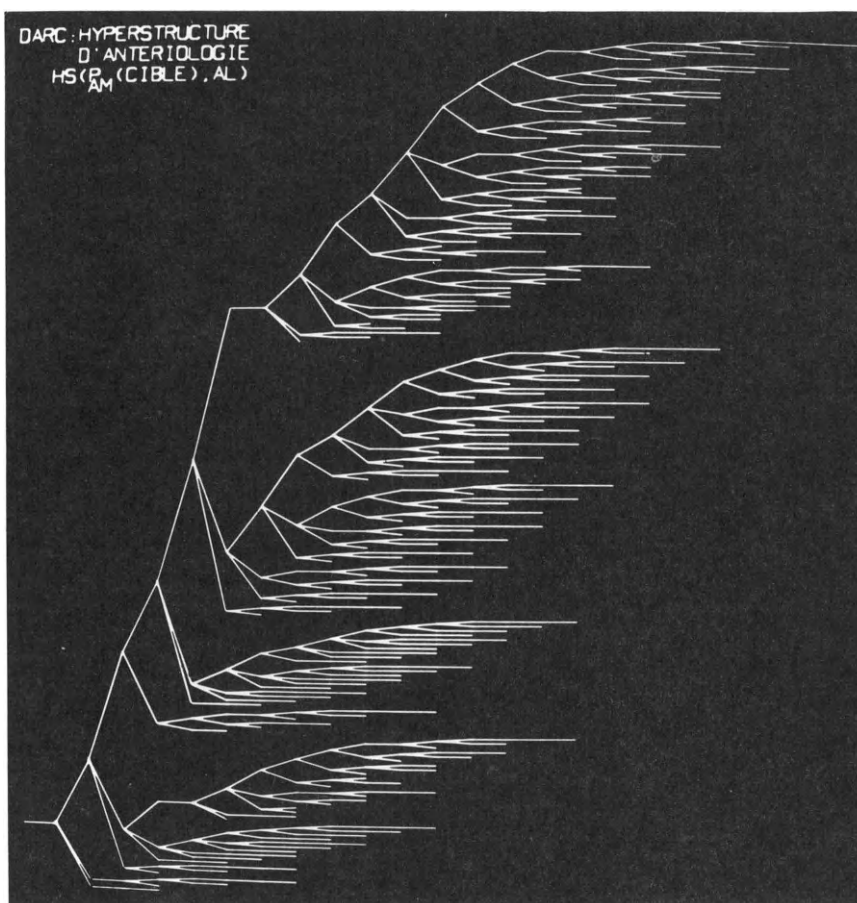


Fig. 7. Generation hyperstructure. The formal generation of 630 ketones whose environment associated to the focus $\cong\text{C}-\text{CO}-\text{C}\cong$ is made up of two rows of atoms at the very most; each node of the graph corresponds to a ketone, from its origin (acetone in the lower-lefthand corner) to the target (hexatertiobutylacetone in the upper-righthand corner); the isomers lie on the same vertical line.

"Structure-Properties" correlation. DARC/PELCO method

In order to approach the problem of structure-compartment correlations, one must have at one's disposal a quantitative variable expressing, in the best possible way, the chemical structure concept. The usual theories use groups or fragments and often imply that "the whole is equal to the sum of the parts". If the properties studied are not as additive as one would wish them to be, we then introduce "constitutive properties corrections" or

interaction increments.

In the DARC system, the correlation problem is approached in a more systematic manner, by considering the contribution of each ordered site to the environment of an active focus (16).

The principle of information generation. A true structural variable, the topological vector $T(\xi)$, characterizes the presence or the absence of each ordered site. It permits one to express, in an analytical manner, the principle of an ordered generation of information at the same time as that of the generation of the structure, through the use of the following Topology-Information correlation: $I(\xi) = \langle T(\xi) | I(m) \rangle$; where $I(m)$ is the characteristic vector of information, resulting from the study of m structures and $I(\xi)$ the contribution of the environment. Information $I(X)$, relative to the comportment of structure X , is calculated from information $I(X_0)$ corresponding to the reference structure whose environment reduces to hydrogen atoms: thus, $I(X) = I(X_0) + I(\xi)$.

Within the framework of the Topology-Information theory, calculation of I is carried out by various methods, one of which is the PELCO (Perturbation of Environments which are Limited, Concentric and Ordered) method. The information vector $I(m)$ is estimated by the method of least squares from data concerning the m compounds of the relevant population. In effect, a given site in a population may be reached by different generation pathways, which implies that the environments anterior to this site will be different according to the pathway followed. This "anterior environment" concept allows the definition of the relevant population.

Correlation search method. The method is made up of three main stages.

Selection of a relevant population. The problem of selection is very important since it conditions the value of the perturbation terms and, thereby, the predictive value of the correlations.

Selection comes into play at two levels; first of all on an overall level, by the following definitions:

Origin: the compound from which it is possible to generate all the individual members of the population

Trace: the graph obtained by uniting the various ordered environments.

Selection then operates on a local level at each site of the trace. In the generation sense, each site is characterized by its minimal and maximal anterior environments; this allows defining a key-population.

Estimation: Topology-Information correlation. The perturbation due to each site is evaluated. The deviations in the strict additivity of the perturbation terms are represented by interactions. The totality of these results can be represented globally and synthetically by a valuated graph (Fig. 8). In the section devoted to "Structure-Spectroscopy" topological correlations, we shall see examples of calculations of properties on the basis of a valuated graph with and without interaction.

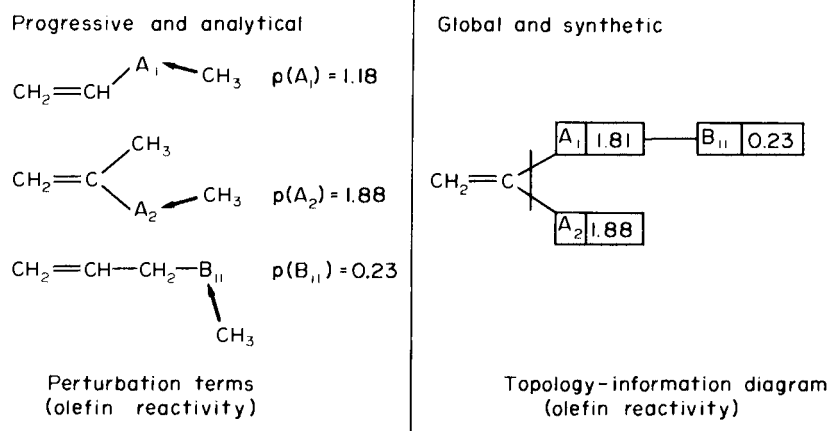


Fig. 8. PELCO method: Presentation of correlation results.

Prediction aptitude. Once the perturbation due to each site of the trace has been determined, it is possible to estimate, by topological interpolation, the comportment of all the compounds included in this trace.

The prediction aptitude, or "proférence", is thus equal to the difference between the number of compounds generated in the trace and the number of compounds in the key-population. The reliability of the proférence depends on the existence or on the possibility of interactions.

Correlation search strategies. There are several possible strategies. We shall briefly review two of them used in our work.

- Strategy with symmetrization of the directions of development: used in a first approximation when one wishes to determine the main tendencies. It is considered a priori that both radicals of the carbonyl group have the same influence: A_1 of DD_1 and DD_2 are thus equally valuated.
- Strategy without symmetrization of the directions of development: used for a fine prediction of properties. Two sites are declared to be equivalent only when the correlation shows their perturbation terms to be extremely near each other, with the difference between them being well below the experimental error.

Polar and steric parameters of alkyl radicals

We did not have the σ^* and E_S parameters of certain alkyl radicals needed to extend the correlations of the $\rho\delta + \delta E_S$ type proposed for spectroscopic data concerning restricted (UV) or average (IR) populations. We thus calculated the missing σ^* values by using a σ/σ^* topological correlation (17). New experimental determinations were required for the E_S parameters, before approaching the correlation. The esterification reaction of hindered acids in methanol provided us with a homogeneous scale with a real boundary, $E_S = -7.5$ (18).

Calculation of the steric energy

Here we present mainly the results pertaining to the determination of the most privileged conformation, obtained by using Allinger's version of the empirical potential method (19), that we are presenting. This represents only a part of the in-depth study we are presently carrying out on carbonyl compound conformations (20).

In a refined analysis, the study of the conformational properties of an isolated molecule cannot be limited to determining the most energetically favored conformation. It thus appears to be necessary to determine a surface of conformational energy having as many dimensions as there are parameters that may be easily modified. It is in this manner that we determine preferential zones of stability and forbidden conformational zones.

All of this requires calculating a sufficiently large number of points on the conformational surface, a fact which in itself leads to the choice of a fast calculation method given the size and complexity of the molecules we are interested in.

We thus have recourse to two types of methods:

- Empirical methods, taken from classical mechanics and from statistical thermodynamics. In these methods the total energy is the sum of various additive energetic contributions (torsion energy, interaction energy between non-bonded atoms, participation of hydrogen bonds, contributions from bond lengths and from valence angles,...). These terms are expressed as a function of the adjustable parameters on the basis of experimental information. We have used two versions of this empirical potential method: the Liquori version (21) and the Allinger version (BIGSTRN Program) (19); the second differs from the first, in that a term which stabilizes conformations with the methyl group eclipsing the carbonyl group has been introduced.
- Quantum mechanical methods. We have used the PCILO method (22) (minimization by perturbation (23)) as well as CNDO/2 (24) and INDO (25) methods (minimization by the variation principle) (26).

Nevertheless, the conformational results obtained by any one of these methods always depend on the basic parameters; it is a well-known fact that they are often conflicting on certain important points, as well as with experiment. Thus, for $iPr-CH_2-CO-Me$, the most stable conformations are: a bisected carbonyl conformation for the PCILO method, a conformation with a C-H bond eclipsing the carbonyl group for the Liquori version, and a conformation where the isopropyl group eclipses the carbonyl group for the Allinger version.

Our efforts were thus directed more towards the analysis of conformational tendencies within a series of compounds, rather than towards the particular results obtained with any one of the methods.

ANALYSIS OF SPECTROSCOPIC DATA

Ultraviolet spectroscopy

σ^* , E'_S/ν_i^H structure-spectroscopy correlation. We have sought to extend the correlation established in 1963, for biprimary ketones, between the σ^* parameters of alkyl radicals R and R' and the position of the maximum of the $n \rightarrow \pi^*$ absorption band. The study reported herein concerns 81 ketones. Figure 9 shows that it is impossible for the entire population to establish a simple link between the σ^* parameters and the maximum of the internal envelope of the absorption band in hexane, ν_i^H (27).

By contrast, we have noticed a tendency towards partitioning depending on the number of substitutions at α and at α' to a carbonyl. The ketones beginning each series are included in $(CH_3)_3CCOC(CH_3)_3$ or $FO(3000)(3000)$. They correspond to the hyperstructure in Fig. 6. Each sub-population is designated by $\mathcal{P}_{i,i'}$, where i and i' are the number of alkyl groups on α and α' which correspond to the number of A and A' sites.

For five of these sub-populations containing about ten points, the correlations carried out by the least-squares method give satisfactory results. The slopes of the straight lines $\nu_i^H = f(\sigma^*)$ are parallel in a first approximation (Fig. 9). However, these sub-populations cannot be brought together in the same correlation by introducing a hyperconjugation term because the deviation for acetone, which is the reference ketone, is not related in a simple way to the number of α and α' substituents.

Taking into account the steric influence within the correlation improves the correlation only to a very slight degree. The δ coefficient of the steric factor E'_S diminishes as the ramification of the ketones increases. This somewhat surprising result leads to attributing a percentage of steric influence on ν_i^H which becomes all the more weaker as the alkyl radicals become more hindered!

| | | |
|--|----------------------|-----------------|
| iBu-CO-iBu | % σ^* : 83% | % E'_S : 17% |
| (iPr)(Me) ₂ C-CO-C(Me) ₂ iPr | % σ^* : 98.5% | % E'_S : 1.5% |

The ketones which deviate from the correlation when only the σ^* polar factor is considered remain outside of the correlation when the E'_S steric factor is introduced. The ketones present a definite structural analogy; they bear at least one $-CH(iPr)_2$ radical or a radical derived from it by substitution $-CH(iPr)(tBu)$, $-CH(tBu)_2$.

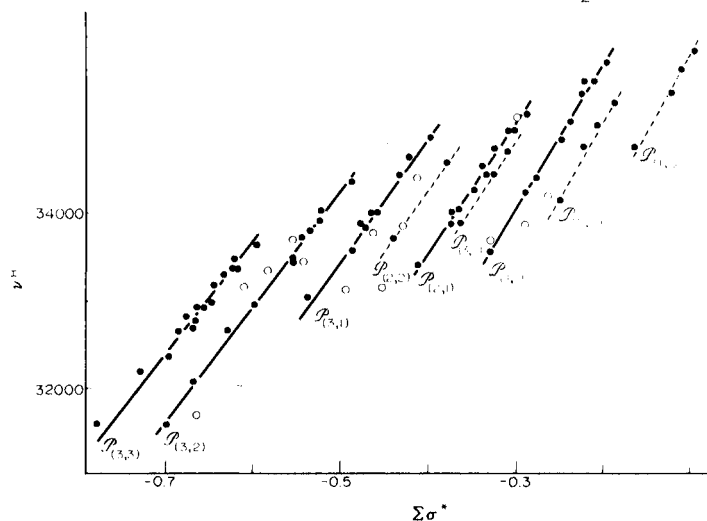


Fig. 9. Parametric correlation σ^*/ν_i^H UV spectra of ketones. Absence of a simple relationship between the σ^* polar parameter and ν_i^H . The ketones have a tendency to fall into a network of parallel straight lines characteristic of the $\mathcal{P}_{i,i'}$ sub-populations (i and i' being the number of alkyl substituents at α and α' of CO).

Topological correlation: ϵ/ν_i^H . The key-population on which the correlation has been established has 48 ketones. A study of the valuated graph summarizing the totality of the information shows the relative influence of the sites and the presence of interactions. The perturbations arising from each site diminish the wave number of the absorption maximum, whereas the interactions increase it (Fig. 10) (27).

The site whose perturbation term has the highest value is A_3 , which corresponds to the 6th substitution at A, i.e. to the bitertiary structures. Sites A_2 , A_2' (corresponding to the secondary radicals 2jkl), B_{13} and B_{13}' (radical neop: (1111)) also have a very high perturbation value. Thus, in our study of conformational filiations, special attention has been paid to the radicals in which these sites intervene.

The weaker perturbation values of sites B_{31} , B_{32} and B_{31}' indicate an attenuation of the effects; however, the partial overlapping of these sites in the correlation might not permit identifying the presence of possible interactions.

A correlation with three interactions permits accounting for the experimental wave numbers for 25 ketones not included in the key-population, with the experimental wave numbers of 8 ketones being uncorrelatable. This correlation reliably covers 291 compounds, 48 of which have been used to establish the correlation. The preference is thus $291 - 48 = 243$ compounds.

If we introduce two new interactions, $I(B_{22}-B_{13}')$ and $I(B_{23}-B_{13}')$, we account for the experimental wave numbers of five new compounds; the correlation is good ($r = 0.998$, $\Psi = 0.07$, $\Delta = 65$) and the perturbation term values are very slightly modified. The range of this new 5-interaction correlation covers 332 compounds.^{††}

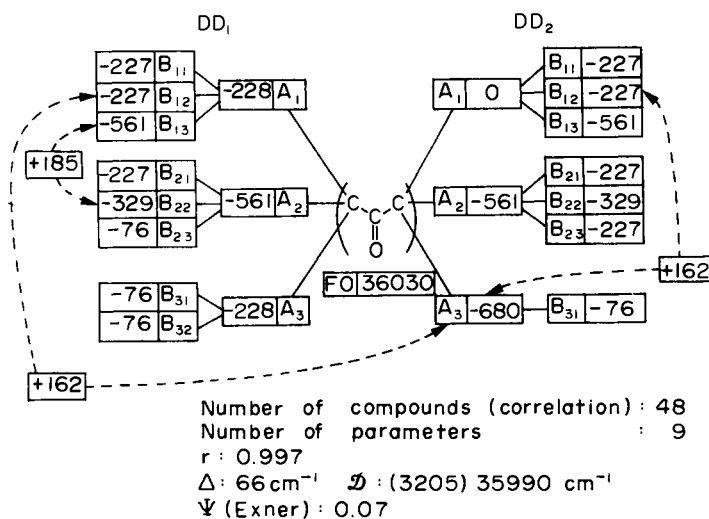


Fig. 10. DARC/PELCO correlation ϵ/ν_i^H UV spectra of ketones

Infrared spectroscopy

Seeking linear free energy relationships applied to $\nu_{C=O}^{CCl_4}$. As in UV spectroscopy it is impossible to establish a simple linear relationship between the frequency of the maximum of absorption and the σ^* parameters (Fig. 11) (27).

[†] In order to simplify the writing, sites DD_1 are designated by A_i and B_{ij} ; sites DD_2 are designated by A_i' and B_{ij}' .

^{††} Those ketones bearing a $-\text{CH}(\text{iPr})_2$ radical or (2220) for DD_2 whose particular compartment would be expressed by other interactions have not been introduced into this correlation.

The same redistribution is found in sub-population $\mathcal{P}_{i,i'}$, but in contrast to what occurs in UV spectroscopy, the parallelism of the straight lines of the correlations is no longer observed. Furthermore, a large number of the ketones deviate from these correlations; aside from some of the bitertiary ketones, those ketones with a particular compartment bear strong structural analogies: they either possess a $-\text{CH}(\text{iPr})_2$ radical or one of its derivatives as in UV spectroscopy, or a neopentyl radical $-\text{CH}_2\text{tBu}$ or its triptyl derivative $-\text{CMe}_2\text{tBu}$. Introducing a steric term does not render these correlations more significant.

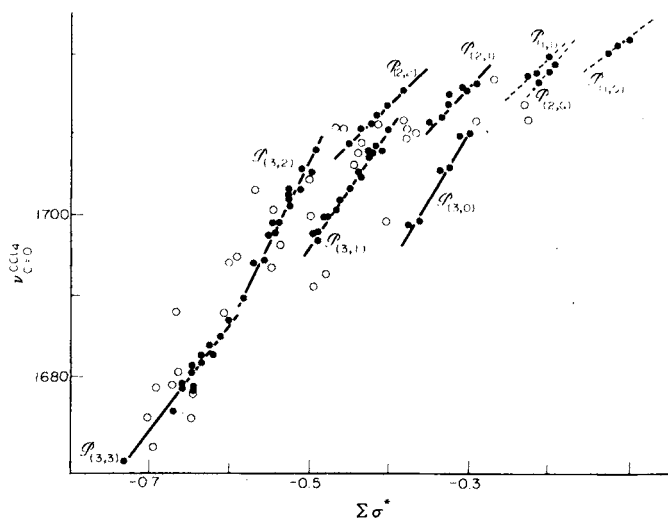


Fig. 11. Parametric correlation $\sigma^*/\nu_{\text{C=O}}^{\text{CCl}_4}$ IR spectra of ketones

Topological correlation $\mathcal{E}/\nu_{\text{C=O}}^{\text{CCl}_4}$. The key-population on which the correlation is established consists of 47 ketones. The valuated graph (Fig. 12) shows that the perturbations arising from sites A_i and B_{ij} ; and from the interaction A_3-B_{13} lessen the $\nu_{\text{C=O}}^{\text{CCl}_4}$ frequency; the three perturbations corresponding to sites A_1 , and to B'_{13} and B'_{31} are an exception to this (27). As in UV spectroscopy, the perturbation arising from site A'_1 is nil; sites A_2 and A'_2 are equivalent as are a certain number of B_{ij} positions. However, in contrast to the results obtained in UV spectroscopy, the perturbations of the A sites increase in the A_1, A_2, A_3 order; the exceptionally important value of A'_3 shows the effect of the 6th substitution at α .[†] The B_{ij} perturbations which deviate notably from the others, i.e. $B_{23}, B_{32}, B'_{13}, B'_{22}$ and B'_{31} , express respectively the particular compartments of $-\text{CH}(\text{tBu})_2$, $-\text{C}(\text{iPr})_3$ in DD_1 , $-\text{CH}_2\text{tBu}$, $-\text{CH}(\text{iPr})_2$, $-\text{C}(\text{Et})_3$ in DD_2 and of their derivatives.

With this correlation we account for frequencies of 42 ketones not included in the key-population, 17 ketones lying outside of the correlation. The excluded ketones are bitertiary, one of whose radicals is triptyl (3111), or tertiary-secondary ketones, whose secondary radical is either derived from neopentyl by substitution ($-\text{CH}(\text{Me})(\text{tBu})$ or 2111) ($-\text{CH}(\text{Et})\text{tBu}$ or 2211), or the radical $-\text{CH}(\text{iPr})_2$ or one of its derivatives. The necessary interactions for integrating these compounds to the correlation bring into play sites B_{13} and B'_{13} . The reliable proférence of the correlation is $176 - 47 = 129$ compounds.

[†] The results of this correlation which concerns solution measurements are complementary to those which we had established in the vapor phase (8c); the deviations between the contributions, in both cases, can be attributed either to the solvent effect, or to the treatment used (e.g., introducing an $A_3-A'_3$ interaction in order to express the effect of the 6th substitution in symmetrized correlation with $\nu_{\text{C=O}}^{\text{gas}}$).

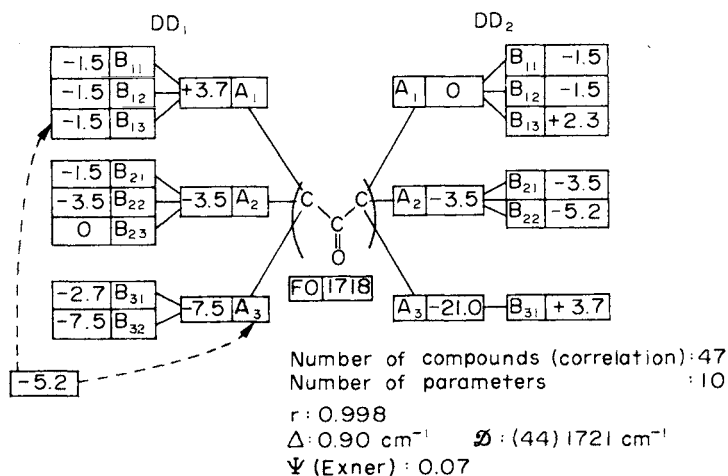


Fig. 12. DARC/PELCO correlation $\mathcal{E}/\nu_{\text{C=O}}^{\text{CCl}_4}$ IR spectra of ketones

^{13}C Nuclear magnetic resonance and gem-persubstituted β effect

UV and IR spectral observations have shown a particular comportment for structures that are hexasubstituted on the α carbons of the carbonyl group. Confirmation of this comportment was sought by ^{13}C study. In contrast to the previously cited techniques which yield focalized information only on the carbonyl group, ^{13}C resonance permits detecting, at the level of the various sites, the perturbations induced by alkyl substitution. In particular we examined the chemical shifts of the carbon atom of the carbonyl group (28a-b), and those of the sp^3 carbons in the neighborhood of this group (28c).

A \mathcal{E} /chemical shift (δ) correlation, corresponding to chemical shifts obtained on pure liquids, was proposed and tested for a population of 53 ketones with a chemical shift variation of 12.8 ppm: for MeCOMe, $\delta = 12.0$ ppm; for iPrCOTr, $\delta = 24.8$ ppm (downfield from external CS_2). The outstanding facts are the attenuation of the A_1 perturbations on the heavily ramified C's, the low contribution of the B_{ij} positions, the existence of internal interactions in very ramified groups, such as $\text{C}(\text{Me})_2\text{tBu}$, and the particular values of A_3^1 . Thus, the 6th substitution corresponds to an upfield shift of the carbonyl signal: iPrCOCMe₂tBu, $\delta = 24.8$ ppm; tBuCOCMe₂tBu, $\delta = 24.2$ ppm.

This study is currently underway for the purpose of determining the role played by the internal and external environments in the behavior observed.

The particular role of the 6th α substitution is also detected on the chemical shift of the sp^3 carbons on α of the carbonyl group. Thus, in passing from penta- to hexa- substituted ketones, an important increase (ca. 11 ppm) of the α effect,[†] and γ downfield effects (1 to 2 ppm) for these carbons, are noted - as opposed to the usual effects detected for less ramified structures. For example, between iPrCOiPr and iPrCOTBu, α effect = 5.9 ppm and shielding γ effect = - 4.9 ppm; between iPrCOTBu and tBuCOTBu, α effect = 11.8 ppm and deshielding γ effect = 1.

All the observations relative to the $\delta^{13}\text{C}$ of the carbonyl and of the adjacent sp^3 carbons confirm the IR and UV results, and converge on the remark of a particular comportment of the structures having a hexasubstituted $\text{>C-C}_{\text{sp}^2}\text{-C}\leq$ link (gem-persubstituted β effect); this is in contrast to the monotonic evolution of substitution effects in less ramified molecules (suggesting a breakdown in the conformational filiations).

Spectroscopic results are still too fragmentary to permit a complete characterization of the specific properties of the $\text{>C-C-C}\leq$ module on numerous other systems. However, a first verification has been obtained on an analogous population of compounds having the same

[†] In the $\text{>C}_1\text{-CO-C}_2\leq \rightarrow \text{>C}_1\text{-CO-C}_2\leq$ substitution, C_1 undergoes a γ effect; and C_2 undergoes an α effect.

$\equiv C - C_{sp^2} - C \equiv$ module: $H_2C=CRR'$ geminated alkenes, for which a complete compartment analogy with homologous ketones is observed in IR as well as in ^{13}C NMR spectroscopy. For example:

- the 6th A_i substitution leads, for $\delta^{13}C$, to a variation in a sense opposed to that of the effects of the first five A_i substitutions; this is true for both of the ethylenic carbons (29);

a compartment/compartment correlation in IR spectroscopy, concerning the group frequency variation of $\nu_{C=O}/\nu_{C=C}$, shows the important lowering of frequency brought about by the 6th A_i substitution for olefins as well as for ketones (30).

CONFORMATION, GEOMETRY AND STERIC ENERGY[†]

In order to account for the compartment of certain ketones, we have used calculation methods to test the hypotheses of conformational filiation and their discontinuity, and of changes in molecular dimensions.

Conformational filiations

The DARC/PELCO topological correlations are based on the notion of topological filiations. These correlations lead to a compression of information; in particular, information bearing on the positions of the sites in space is not taken into account.

In order to reach the conformational filiations, topographical correlations must be established, i.e. values must be assigned to perturbations occurring at different positions in 3-D space. To do this, a set of spatial references must be fixed; this set can be chosen using a calculation method, or by analogy with a similar model.

Thus, beginning in 1971, an attempt has been made, in UV spectroscopy, to associate bathochromic contributions to carbon atoms, as a function of their position in space. This has been done by joint use of locked conformations in the alicyclic series and of a physical model (31).

We have used results from energy calculations, in a similar manner, to establish topographical correlations of $\nu_{C=O}^{gas}$ frequencies in IR spectroscopy.

As already indicated (cf. "calculation of the steric energy"), the various methods of calculation (quantum mechanical methods and empirical potential methods) provide divergent results on particular points. However, they all point to the following tendential law (20): the bisection of the carbonyl group is more probable as the compound is more hindered. There is thus a discontinuity in the conformational filiation: the slightly substituted carbonyl group would be eclipsed, whereas the very hindered carbonyl group would be bisected.

This is a tendency; however, it is very difficult to determine precisely the radical for which the inversion occurs, since the energy deviations are weak. With the BIGSTRN program (19), we ascertain (32) that in both of the series tested ($tBuCOME$ to $tBu(Me)_2CCOME$ and $tBuCOtBu$ to $tBu(Me)_2CCOtBu$) the staggered conformation becomes favored for the triptyl radical $-C(Me)_2tBu$; this would be in good correspondence with the spectroscopic observations.

We have used these results to establish a topographical correlation of the $\nu_{C=O}^{gas}$ frequencies in infrared spectroscopy. For $CH_3COCH_2CH_3$ we have postulated an eclipsed conformation; for CH_3COCH_2tBu we have postulated two conformations, an eclipsed one and a staggered one, in order to account for the two bands^{††} obtained for this ketone. We thus attribute a site value to a position in space (Fig. 13) (33).

[†] According to Allinger's notation (19), the steric energy corresponds to the sum of the energy terms associated with the deformations of the bond lengths, the valence and torsional angles, and with the interactions between non-bonded atoms.

^{††} These splittings only appear in solution; however, it is possible to obtain an extrapolated value for the band not existing in the vapor phase by applying Allerhand and Schleyer's relationship: $\nu^{Sv} = \nu^g - a\nu^g G$.

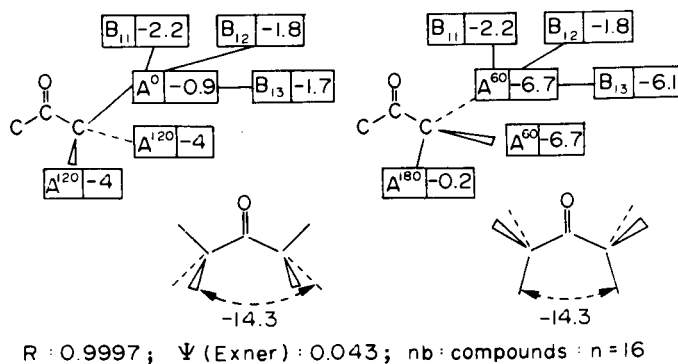
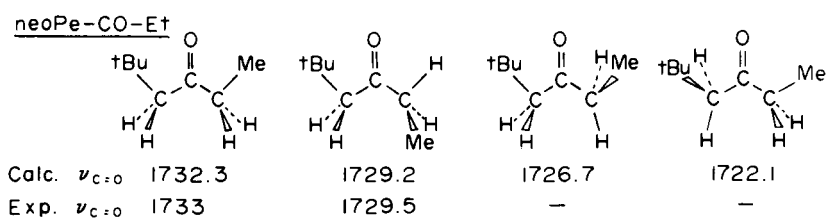


Fig. 13. DARC/PELCO topographical correlation of $\nu_{C=O}^{gas}$ gas phase frequencies

This study constitutes an initial approach which will have to be refined. For example, in this symmetrized treatment, the B positions carried by an A position that is eclipsed (position A^0) and by a position that is staggered (position A^{60}) should certainly be distinguished from one another. However, the initial results are encouraging ($r = 0.9997$; $\Psi = 0.043$) and, for the ketones where a band-splitting has been performed, we have been able to attribute a conformation to each band.



Changing molecular dimensions

The gem-persubstituted β effect can be interpreted by an important change in molecular geometry. The theoretical calculations indicate a major difference at the sp^2 hybridization ($\overline{C-CO-C}$ angle) when passing from five α substituents ($tBuCOiPr$) to six α substituents ($tBuCOtBu$) (Fig. 14). A noteworthy opening of the $\overline{C-CH-C}$ angle (deviation from sp^3 hybridization) is also calculated for the passage of $MeCOCH(tBu)(iPr)$ to $MeCOCH(tBu)_2$.

| number of neighbors | R | R' | | |
|---------------------|---|----|-------|-------|
| 6 | | | 126° | 125° |
| 5 | | | 120° | 121° |
| 4 | | | 119°5 | 119°9 |

Fig. 14. Gem-persubstituted β effect and changing of molecular dimensions. The 6th substitution provokes a notable change of angle. The calculations are carried out with the help of Allinger's version of the empirical potential method. The PCILO method provides an angle of 132° for $tBuCOtBu$ and an angle of 125° for $MeCOCH(tBu)_2$.

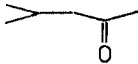
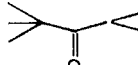
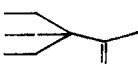
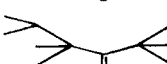
These changes in molecular dimensions correspond to a geometry that is more decongested than the standard geometry, thus leading to a considerable minimization of interactions between non-bonded atoms, at the price of a much more moderate increase in energy contributions resulting from bond lengthenings, and from deviations of angles involving sp^2 and sp^3 hybridized atoms from their classical values.

With the PCILO method, an appreciation of this strain release of the tBuCtBu module is provided by an evaluation of the rotation barriers of a tBu group with respect to the other tBu group in a standard geometry (≈ 30 KC for $(tBu)_2CO$; ≈ 200 KC for $(tBu)_2CH$) and in unstrained geometry (< 10 KC). In hexamethylacetone, the rotation of the tBu groups seems to be practically free (1 KC barrier) in the unstrained geometry (20).

The hypothesis of such a strain release is confirmed by the kinetic results used in the determination of the steric parameters of the highly hindered radicals (18). A residual activity, which would be due to a change of the molecular dimensions, is observed; this is confirmed by the first crystallographic results on hindered acids.[†]

As with the observations on the conformational filiations, the results from the molecular geometry calculations on the changes in molecular dimensions indicate tendencies, not absolute values. Indeed, energy minimization programs parametrized for simple ketones must be employed with caution in the study of more hindered ketones.

In order to evaluate the reliability which can be granted to the preceding calculations, we confronted the heats of formation of ketones calculated by energy minimization with those calculated by a polyfocalized DARC/PELCO correlation (34). The results are comparable and near the experimental values whenever these latter are known. The difference becomes more marked (about 1 to 2 Kcal) when the ketone is clearly hindered.

| | ΔH°_f exp (Kcal/mol) | ΔH°_f PELCO | ΔH°_f energy minimization |
|---|---|-----------------------------|--|
|  | - 76.60 | - 76.46 | - 76.81 - 76.36 |
|  | - 80.86 | - 80.59 | - 80.96 - 80.19 |
|  | ----- | - 79.62 | - 79.18 - 79.14 |
|  | ----- | - 91.78 | - 93.38 - 93.24 |

Special molecular dimensions of the gem-di-tBu pattern and its comportment

We have also sought confirmation of molecular mechanics results by comparing molecular dimension data with real data which were measured by crystallography for two hindered molecules bearing the $C(tBu)_2$ pattern: tetra-tertio-butylacetone and ortho-tolyldi-tertio-butylcarbinol.

Tetra-tertio-butylacetone: The conformation which is most energetically favored according to calculations (BIGSTRN program) is fairly close to the conformation obtained from the crystallographic data (35). This favored conformation where, for each radical, a tBu group is situated perpendicularly to the carbonyl, is confirmed by both static and thermodynamic 1H and ^{13}C NMR observations (Fig. 15) (36). Comparing the real with the calculated data shows that the calculation opens the $\widehat{C-C-C}$ angles too much and shortens the C-C bonds. A similar observation is obtained by the PCILO method for the $CH(tBu)_2$ module of the $HCOCH(tBu)_2$ molecule. A shortening of the C-C bond lengths and an increase of the $\widehat{C-C-C}$ bond angles is also observed with respect to the experimental values.

[†] This work was carried out in collaboration with J. Hospital (Maître de Recherche, CNRS) from the University of Bordeaux I.

These divergencies, together with the slight difference in energy of the tested conformations, did not permit us to determine whether or not the interconversion of the two equivalent conformations which show up in ^{13}C NMR occurs by a synchronous movement of the "windshield wiper" type.

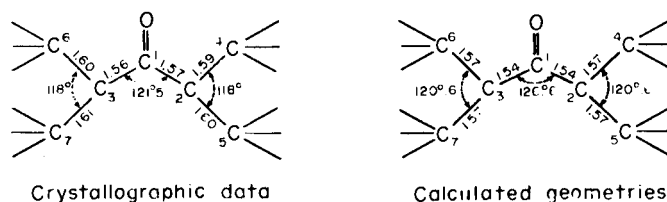
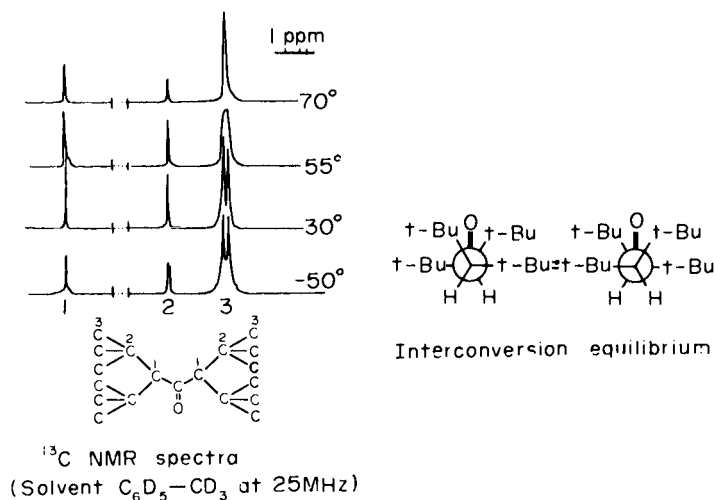
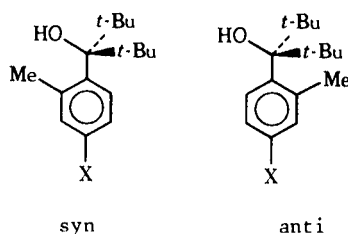


Fig. 15. Example of a strained ketone: tetra-tert-butylacetone; dynamic ^{13}C NMR and conformation. The ^{13}C resonance shows two equivalent privileged conformations whose interconversion is characterized by dynamic NMR. The characteristic geometric elements are: a two-fold symmetry axis passing through the carbonyl group, and a two-by-two equivalence of the tertibutyl groups bonded to the α carbons. This is coherent with the crystallographic study and the theoretical calculation of the geometry. The exalted values of the valence angle and of the C-C bond lengths of the module $\text{>C}<\begin{smallmatrix} \text{tBu} \\ \text{tBu} \end{smallmatrix}$ (gem-persubstituted 3 effect) should be noted.

Ortho-tolyldi-tertio-butylcarbinol: If internal strain characterized the influence of a radical, then it is important to follow a hindered "module" during a chemical change.

The chemistry of hexasubstituted ketones allows the transfer of very hindered ketones into other structures, thanks to the easy addition of organolithium compounds. In ortho-tolyldi-tertio-butylcarbinol obtained in this manner from hexamethylacetone, the steric hindrance is such that the rotations around the simple bonds are very hindered. We were thus able to separate easily the syn and anti atropisomers (37).



For the calculations, by replacing the hydroxyl function by a methyl group, we obtain a good approximation of the real data; however, the bonds are still rather short and the angles too open (Fig. 16) (38).

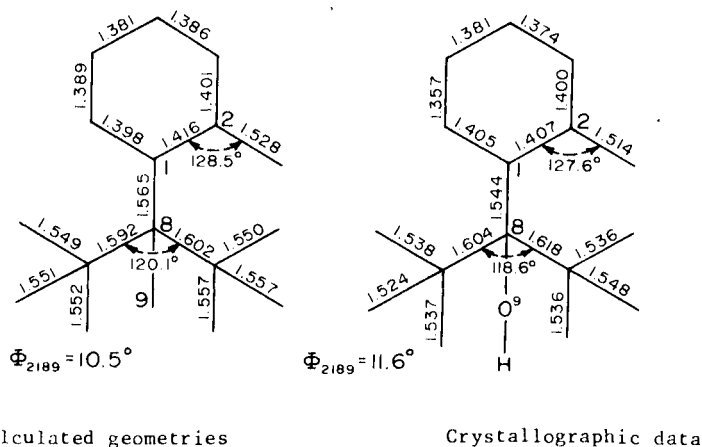


Fig. 16. Syn-ortho-tolyldi-tert-butylcarbinol: structural data

CONCLUSION

Taken alone, the spectral properties of ketones were hard to interpret; however, the overall results considered in terms of progressively established models has led to an improvement in correlating these properties with both the ketone structures and conformations.

The interest that lies in crystallographic structural determinations, a slow but sure means, is not questioned; however, it should be noted that satisfactory results obtained by structure calculation methods are going to permit studying these problems in a faster and more systematic manner, once sufficiently significant "crystallographic data/calculated value" correlations have been obtained. While the parallels drawn in this presentation for geminated and bis-geminated alkyl groups are encouraging, it is nonetheless necessary to envisage improving the molecular mechanics methods by adapting their parameters to the study of hindered ketones. These efforts will be directed towards a surer attribution of certain specific reference conformational assignments from which the conformations and molecular dimensions of numerous other ketones will be deduced by filiation methods.

In short, the power of the methodology, that we have used herein to account for a very large set of data, is based on certain structural assignments of ketones. It should be noted that the optimization of molecular mechanics methods, which we shall undertake, is valid for other types of strained molecules, viz. hydrocarbons and olefins.

Acknowledgment - The author wishes to express his appreciation to his co-workers, whose names appear in the references.

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STEREOCHEMISTRY OF DISSOLVING METAL REDUCTION OF KETONES

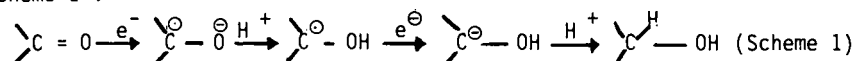
André RASSAT

Université Scientifique et Médicale de Grenoble, E.R.A. n° 20, Laboratoire de Chimie Organique Physique du Département de Recherche Fondamentale du C.E.N.G., 85, F. 38041 GRENOBLE CEDEX.

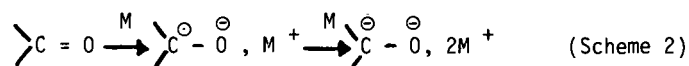
Abstract - Experimental results on the reduction of ketones by metals in liquid ammonia are summarized. The product yields are very dependent upon the choice of experimental conditions. Theoretical results are presented on some intermediate or products involved in these reductions. Ketyl radical-anions are non planar in their equilibrium conformation. Protonation on oxygen is favoured. The composition of equilibrium mixture of epimers can be calculated to a good approximation.

The reduction of ketones by dissolving metals and the related electrochemical reductions have been much studied. House (1) has summarized the recent work. The main features of these reactions are relatively well understood. The first step is the formation of a ketyl, and the ratio of the two epimeric alcohols obtained is not necessarily the equilibrium ratio. However, it is still impossible to make quantitative prediction on the steric course of these reactions. In this talk, I would like to present some experimental results which show the complexity of the reactions and theoretical treatments of two related problems: the structure of the ketyl radical-ion and the stability of epimeric alcohols.

The most common dissolving-metal reduction is probably the sodium-and-alcohol reaction (1), an heterogeneous reaction. We preferred to study the homogeneous reaction in liquid ammonia (2-12). Other workers (e.g. 13-17 and ref. therein) have also studied this reaction. Every component of the reaction mixture, the solvent (liquid ammonia), the ketone to be reduced, the electron donor (the metal) and a proton donor are necessary, as may be seen in reaction scheme 1 :



A co-solvent may be used if the ketone is not soluble in liquid ammonia. Various procedures may be found in the literature (1), the ketone, the metal and the proton donor being added in different order to the liquid ammonia. We have chosen two extreme types A and B : A) The ketone and proton donors (ethanol under standard conditions) are dissolved in liquid ammonia and the metal is added to this solution. The rate of reduction is apparently controlled by the metal dissolution. B) The metal is first dissolved in liquid ammonia, care being taken that no proton donor be present at this stage. The ketone is added to the blue solution. After 30 minutes, a proton donor (ethanol under standard conditions) is added before work-up. It is hoped that in case A all the steps of scheme 1 can occur, while in case B protonation is forbidden and scheme 2 is now to be considered before protonation.



(in this scheme 2, ionic structures are given, but different ion-pairs of various degrees of aggregation are possible (1)). Other procedures may be considered as intermediate : for instance, adding the metal to the ketone in liquid ammonia may be a type A reaction at the beginning, if some water is present in liquid ammonia, and then type B, when the proton donor is added after the A type reaction is over.

The experimental results can be summarized in the following way : In monocyclic cyclohexanone derivatives (15), A-type reduction gives the more stable equatorial epimer in a larger than 9:1 ratio to the less stable epimer. In polycyclic ketones, various ratios of stable to unstable epimer have been found (1-24). In some cases (3-9, 13-18, 23), pinacols are formed, sometimes in 90% yield. (It may be noted that a symmetrical ketone gives one alcohol and one pinacol only, a prochiral ketone gives one racemic alcohol and two different pinacols (meso and *dℓ*), an optically active ketone gives two epimeric alcohols (α and β) and three different pinacols ($\alpha\alpha$, $\alpha\beta$ and $\beta\beta$), while the corresponding racemic ketone may give two racemic epimeric alcohols and six different pinacols (racemic- and meso- , $\alpha\alpha$, $\alpha\beta$ and $\beta\beta$). Two different pinacols have been obtained from d-camphor 1 (3, 17) and from A-nor-cholestan-2-one 2 (4), but it is difficult to determine their stereochemistry. A series of pinacols has been obtained from norcamphor 3 (8, 9, 11, 15)).

These experimental data (yields of pinacols and of alcohols, and ratio of the two epimeric alcohols) may sometimes strongly depend upon the experimental conditions and on the nature of the metal used. Since some contradictory results have appeared in the literature, I would like to illustrate this dependence :

a) Cases have been found where the products are insensitive to the reaction conditions : For fenchone 4, reduction gives no pinacol and less than 5% *exo* epimer and more than 95% *endo* epimer (6), whatever the metal or the type of reaction. The equilibrium mixture is probably 30% *exo* - 70% *endo* (6).

b) The ratio of epimers may be insensitive to the reaction conditions but the relative yields of pinacols and of alcohols change : In androstan-17 one 5, less than 5% androstan-17 α -ol is obtained (in the α + β alcohol mixture) (the equilibrium mixture is 35% α ,65% β) but the yield of pinacol (Table I) varies between 35% and 2% depending upon the metal used and the type of reduction (11, 12).

TABLE I

| | Cs | K | Na | Li | Ba | Sr | Ca |
|--------|----|----|----|----|----|----|----|
| A type | | 13 | 34 | 6 | | | |
| B type | 3 | 6 | 17 | 28 | 10 | 12 | 0 |

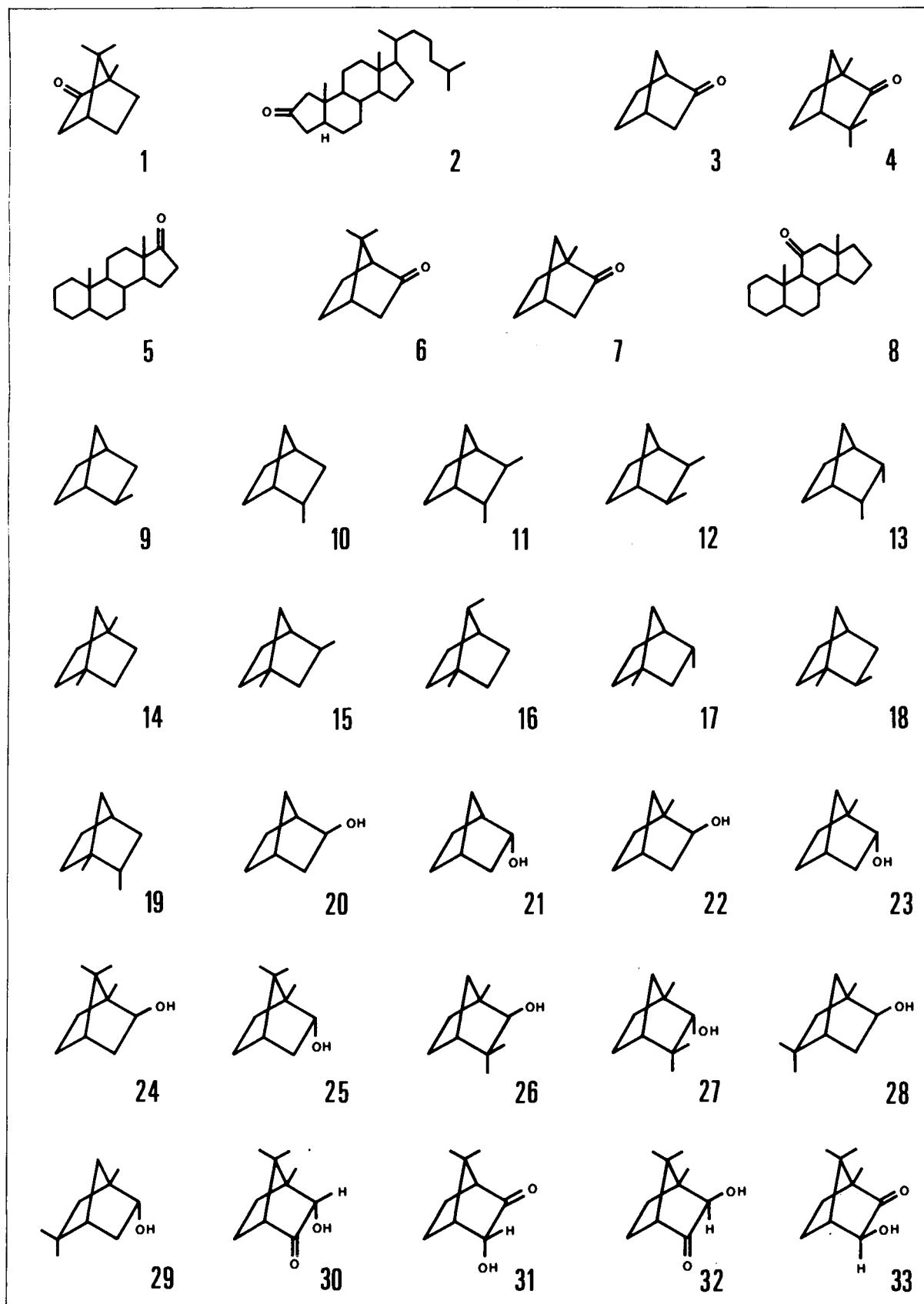
Yield of pinacols obtained in the reductions of androstan-17 one

Similar results have been obtained for α -fenchocamphorone 6, 1-methyl norcamphor 7, the most abundant epimer being the most stable for 6 and the less stable for 7.

c) The ratio of epimers and the pinacols-yield vary with the metal used and do not vary much with the type of reduction : This is the case for A-norcholestan-2-one 2 (4) ; Table II gives the percentage (*r*) of α -epimer obtained in the alcohols mixture, and the pinacols yield (*y*) :

TABLE II

| | | K | Na | Li |
|--------|----------|----|----|----|
| A type | <i>r</i> | 14 | 33 | 33 |
| | <i>y</i> | 55 | 52 | 41 |
| B type | <i>r</i> | 20 | 33 | 43 |
| | <i>y</i> | 47 | 32 | 27 |



d) The ratio of epimers does not change much with different metals but changes drastically with the type of reduction : This is the case of androstan-11 one 8 (5, 12) for which table III gives the % of epimer in the alcohol mixture.

TABLE III

| | Cs | K | Na | Li | Ba | Sr | Ca |
|--------|----|----|----|----|----|----|----|
| A type | | 5 | 6 | 4 | | | 7 |
| B type | 42 | 42 | 42 | 43 | 35 | 42 | 21 |

The α epimer is probably the most stable (5,12).

e) It is now possible to discuss some conflicting results in the litterature : Reduction of norcamphor 3 has been studied by A. COULOMBEAU (8-11) in our group and by J.W. HUFFMANN and J.T. CHARLES (15) :

Table IV gives the yield of pinacols obtained under standard conditions in A-type or B-type reductions a) by our group, b) by HUFFMANN and CHARLES.

TABLE IV

| | $N(Et)_4^*$ | Cs | Rb | K | Na | Li | Ba | Sr | Ca |
|---|-------------|----|----|----|----|----|----|----|----|
| A | a | | | 12 | | 15 | | | |
| | b | | 0 | 0 | 0 | 0 | | | |
| B | a | 0 | 48 | 54 | 57 | 61 | 53 | 38 | 34 |
| | b | | | 0 | 0 | 0 | 28 | | |

* In this reduction, the metal (barium) has been precipitated by $N(Et)_4Cl$

These discrepancies are difficult to explain. However, in our hand, the recovery of material was quantitative, while HUFFMANN and CHARLES results account for less than 50% of the material. We may also notice that in our hands, the pinacol yield varies between 25 and 100%, in the B-type reduction with lithium (8-11). The discrepancies are less for the percentage of epimer : Table V gives the % of exo alcohol in the alcohols mixture.

TABLE V

| | $N(Et)_4^*$ | Cs | Rb | K | Na | Li | Ba | Sr | Ca |
|---|-------------|----|----|----|----|----|----|----|----|
| A | a | | | 11 | | 19 | | | |
| | b | | 9 | 10 | 15 | 15 | | | |
| B | a | 10 | 17 | 17 | 22 | 30 | 30 | 30 | 25 |
| | b | | | 9 | 20 | 29 | 27 | | |

* In this reduction, the metal (barium) has been precipitated by $N(Et)_4Cl$

The case of camphor is important : We had first noticed that a) the alcohol mixture obtained by the dissolving metal reductions was different from the equilibrium mixture (2); b) In liquid ammonia, the ratio of epimer obtained (2) and the pinacol yield (3) changed drastically with the conditions and the metal used. This was confirmed in a detailed study (7-11) by A. COULOMBEAU. At the same time, HUFFMANN and CHARLES (15) could not reproduce some of our results. However, this point was studied later by MURPHY and SULLIVAN (17) who confirmed our previous results :

TABLE VI

| $N(ET)_4^*$ | | Cs | Rb | K | Na | Li | Ba | Sr | Ca |
|-------------|---|----|----|---|----|----|----|----|----|
| A | a | | | 0 | 0 | 28 | 0 | | 0 |
| | b | | | | | | | | |
| | c | | | 0 | 0 | 0 | | | |
| B | a | 0 | 0 | 0 | 20 | 60 | 0 | | 0 |
| | b | | 0 | 0 | 20 | 70 | 0 | 0 | 0 |
| | c | | | 0 | 0 | 17 | | | |

* see Table IV

Table VI gives the pinacols yield obtained under standard conditions A and B by : a) our group, b) MURPHY and SULLIVAN, c) HUFFMANN and CHARLES, in the reductions of camphor.

TABLE VII

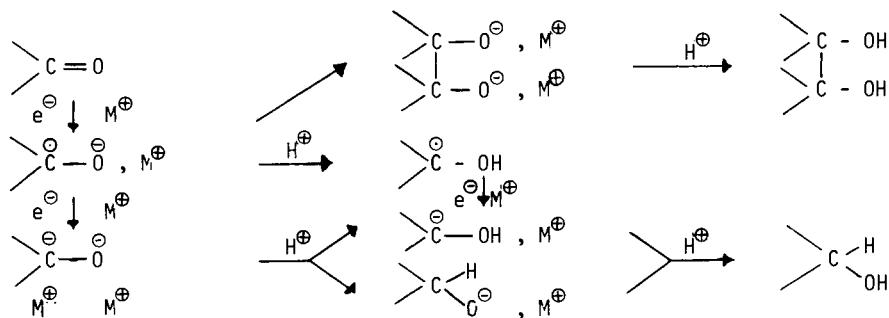
| $N(ET)_4^*$ | | Cs | Rb | K | Na | Li | Ba | Sr | Ca |
|-------------|---|----|----|----|----|----|----|----|----|
| A | a | | | 42 | 23 | 15 | 30 | | 20 |
| | b | | | | | | | | |
| | c | | | 13 | 13 | 11 | | | |
| B | a | 39 | 82 | 77 | 60 | 42 | 23 | 32 | 28 |
| | b | | 78 | | 58 | 40 | 20 | 29 | 30 |
| | c | | | 22 | 19 | 16 | | | |

* see Table IV

Table VII gives the % exo epimer in the alcohol mixture found by : a) our group, b) MURPHY and SULLIVAN, c) HUFFMANN and CHARLES, under standard conditions A and B.

It is apparent that under standard conditions, the reductions in liquid ammonia give reproducible results. Although the origin of the reported discrepancies may be trivial, one may speculate that some more subtle influences such as differences in magnetic field (25) play a role.

The experimental data on these reductions are thus mainly yields and isomer ratio. From these data, various mechanisms have been proposed (1, 3, 10, 11, 15, 17). It is generally accepted that products formation is kinetically controlled and that some of the steps of scheme 3 are involved. However, no quantitative data can be given on the relative rates of the different processes, on the reversible nature of some steps, on the structure of the ion pairs involved, and on their degree of aggregation. Detailed kinetic and physico-chemical studies of all the intermediates and all the steps are probably beyond our present capacities (See also (26) for a detailed study of the reduction of α -diketones.)



Scheme 3

We have chosen to study two problems : the *structure of the ketyl radical-ion* formed in the first step, since its conformation may have some implication on the stereochemistry of the products, and the difference of *stability of the epimeric alcohols* formed in the last step.

The structure of ketyl radicals :

Drs. J. DOUADY, Y. ELLINGER and R. SUBRA, from this laboratory, in collaboration with Dr. G. BERTHIER, have studied the simple ketyl H_2CO^- (For references to previous work, see (27)). Its equilibrium geometry has been studied by energy minimisation as a function of distances and angles, α being the out-of-plane angle between CO and H_2C plane. Two methods have been used :

A perturbation method, (to 3rd order) with Configuration Interaction using Localized Orbitals (PCILO), in the semi-empirical CNDO approximation. The original PCILO method (28) has been modified (29, 30) for open-shell molecules and in order to take into account the CO three-electrons bond.

An ab-initio method, the spin-restricted LCAO-SCF method of Roothaan with some Configuration Interaction (27). Two basis of Gaussian-type orbitals were used : Basis I : (7s, 3p/3s) contracted to (3s, 2p/1s) ; Basis II was basis I plus polarization functions (3s, 2p, 1d/1s, 1p).

Table VIII gives the optimized geometry for H_2CO^- in its equilibrium conformation and the barrier to inversion, calculated as difference between the energy for $\alpha = 0$ and α at equilibrium.

TABLE VIII : Calculated equilibrium conformational barrier to inversion using PCILO (a), and ab initio SCF method with basis I (b) or II (c).

| <u>Geometrical parameters</u> | <u>PCILO (a)</u> | <u>SCF I (b)</u> | <u>SCF II (c)</u> |
|---------------------------------|------------------|------------------|-------------------|
| CO (Å) | 1.33 | 1.33 | 1.30 |
| CH (") | 1.13 | 1.03 | 1.09 |
| HCH (°) | 114 | 117.5 | 116.5 |
| α (°) | 30 | 24 | 27 |
| Barrier to inversion, kcal/mole | 1.63 | 0.446 | 0.875 |

The CO bond is significantly longer than in H_2CO (31). As usual, the CNDO parameterisation gives too large a barrier. The 0.875 kcal/mole barrier is probably a better estimate. In H_2NO , the inversion barrier has been calculated (27) to be smaller (0.064 kcal/mole) and the stable conformation of stable nitroxides is found by diffraction methods to be planar for symmetrical and bent for non symmetrical molecules (32). By comparison, it is concluded that ketone radical-ions are bent, the out of plane angle being ca 30° and the inversion barrier slightly less than 1 kcal/mole. If this is correct, the stereochemistry of the reduction may be discussed in terms of a bent radical-ion (1, 10, 17).

The protonation step in the reduction may also be considered: What is the more favored process in ketyls, protonation at O or at C? Although this may strongly depend upon solvation and/or complexation by the counter ion, we have tried to answer this question for a free ketyl: Using the electrostatic potential technique (33) it is possible, from the SCF wave function, to draw the H_2CO^- electrostatic potential (34). Since the species is negatively charged, the potential is attractive for a proton and rather spherical at large distances. It is more attractive around oxygen (ca -200 kcal/mole), than around C (ca -100 kcal/mole). A minimum (-249 kcal/mole) is found at the expected direction of an oxygen lone pair, at ca 1 Å from O. What is the meaning of this result? The electrostatic potential approach gives only the first term of the interaction energy between H_2CO^- and H^+ , in a perturbation development. $\text{H}_2\text{COH}^\cdot$ has been calculated (35) and found to have a stable geometry corresponding to the minimum of the electrostatic potential of H_2CO^- . We believe that the protonation of H_2CO^- occurs at oxygen first (as expected from simple electronegativity consideration). This step is probably reversible, while protonation at carbon, if any, is probably irreversible and may be a step controlling the stereochemistry of products. Further discussion seems still more speculative.

We shall now turn to the study of relative stability of the reduction products. It was originally thought that dissolving metal reactions give the equilibrium mixture of alcohols (1). This is not the case, and the reaction is kinetically controlled. However, we have studied the stability of these alcohols. Experimentally, we have used acetone-isopropyl alcohol-potassium to equilibrate the potassium alcoholates (4, 6, 8). Some results are reported in Table X. In order to investigate all the reduction steps, it may be necessary to know the relative stability of unstable epimeric species (radicals or anions). Such an experimental determination may be impossible and calculation may be necessary. In order to test the methods, we have tried to calculate the relative stability of epimeric alcohols, for which experimental data were available. It is possible to measure the composition of an equilibrium mixture at different temperature T and to obtain the free energy difference ΔG° between isomers, from which the enthalpy and entropy differences ΔH° and ΔS° are calculated. These values are related to the experimental conditions and take solvation into account. In order to calculate these values, it is reasonable to identify the enthalpy of formation ΔH to the energy of formation calculated for one molecule. However, the calculation is done for an isolated molecule and solvation cannot be explicitly taken into account.

In order to calculate the energy of formation, it is necessary to start from the geometry of minimal energy. Because quantum methods are too expensive for a complete optimization, we have calculated this geometry by a standard molecular mechanics program. The initial geometries were taken from photographic projections of molecular models (36) and the minimisation of energy was searched by a simplex method (37). Using this optimised geometry, the energy of formation for each isomer was calculated (38) using PCIL0 method (28) in the CNDO approximation, for each isomer, thus giving the enthalpy differences. These differences

are not equal to those calculated using a non-optimized geometry (39, 40). The entropy differences between isomers were estimated (41) as arising mainly from entropy of rotation and entropy of mixing (42). The first term is a symmetry term, the second depends on the possibility of different conformers. These conformers were estimated (38, 41) by changing one or two torsional angles in the optimized molecule, calculating the energy as a function of this internal coordinate to find conformers secondary minima. Their relative proportion x_i is then estimated assuming a Boltzmann distribution, and the entropy of mixing is calculated as $RT \sum_i x_i \log x_i$. Having ΔH° and ΔS° , the ΔG° can be calculated, as well as the relative percentages of isomers at different temperatures. This procedure has been applied to three groups of bicyclo-[2,2,1] heptane derivatives. Hydrocarbons (38), alcohols (38-41) and ketols (41) : Monomethyl and dimethyl hydrocarbons have been equilibrated by other workers (43). The calculated and experimental values are given in Table IX.

TABLE IX : Calculated and experimental energy values and % at equilibrium for bicycloheptane hydrocarbon derivatives.(a) ref. (43).

| Compounds | | ΔG° kcal/mole | | | | |
|-------------------------------------|-----------|----------------------------|------------|------------------|---------|-----------|
| | | calc. | | exp.(a) | % calc. | % exp (a) |
| Methylnorbornane at 300°C | <u>9</u> | 0 | | 0 | 63.3 | 68 |
| | <u>10</u> | 0.62 | ± 0.30 | +0.89 ± 0.05 | 36.7 | 32 |
| Dimethyl- norbornane at 160°C | <u>11</u> | 0 | | 0 | 83.6 | 91 |
| | <u>12</u> | 1.71 | ± 0.30 | 2.28 ± 0.06 | 11.4 | 7 |
| | <u>13</u> | 2.43 | ± 0.30 | 3.3 ± 0.3 | 5 | 2 |
| | <u>14</u> | 0 | | 0 | 53.8 | 58.1 |
| Dimethyl- norbornanes at 25°C | <u>15</u> | 0.72 | ± 0.30 | 0.78 ± 0.04 | 15.8 | 15.4 |
| | <u>16</u> | 0.98 | ± 0.30 | 1.02 ± 0.05 | 10.2 | 10.4 |
| | <u>17</u> | 1.26 | ± 0.30 | 1.38 ± 0.08 | 6.4 | 5.6 |
| | <u>18</u> | 1.09 | ± 0.30 | 1.42 ± 0.08 | 8.5 | 5.3 |
| | <u>19</u> | 1.39 | ± 0.30 | 1.43 ± 0.08 | 5.3 | 5.2 |
| | | | | | | |

Table X gives our experimental and calculated results for bicyclic alcohols. The role of the optimized geometry is shown by including results obtained without optimisation (40). Table XI gives the results for 4 epimeric ketols 30, 31, 32, 33, without optimisation of geometry (41).

TABLE X : Calculated and experimental ΔG° for epimeric bicycloheptanol derivatives : a) non-optimized geometry (40), b) Optimized geometry (38), c) experimental values, d) ref.44, e) ref.45.

| Compounds. (X=exo, N=endo) | | ΔG° calc. | ΔG° calc. | ΔG° | ΔG° calc. | ΔG° calc. | ΔG° |
|-------------------------------|----|------------------------|------------------------|------------------------------|------------------------|------------------------|-------------------------------|
| | | at 25°C (a) | at 25°C (b) | Equilibration at 25°C (c) | at 170°C (a) | at 170°C (b) | Equilibration at 170°C (c) |
| Norbornéol X | 20 | 1.28 | 0.46 | -1.10 | 1.33 | 0.37 | -0.97 |
| Norborneol N | 21 | | | | | | |
| Me-1 Norborneol X | 22 | 1.19 | -0.45 | | 1.40 | -0.26 | -0.36 |
| Me-1 Norborneol N | 23 | | | | | | |
| Isoborneol X | 24 | 0.72 | 0.62 | 0.73 | 0.84 | 0.73 | 0.61 |
| Borneol N | 25 | | | | | | |
| β -Fenchol X | 26 | 0.67 | 0.86 | | 0.67 | 0.94 | 0.81 |
| α -Fenchol N | 27 | | | | | | |
| α -Isopenchol X | 28 | 0.96 | 0.84 | | 1.12 | 0.96 | (d)(e) |
| β -Isopenchol N | 29 | | | | | | |

TABLE XI : Calculated and experimental energy and entropy differences for the equilibrium between ketols 30, 31, 32, 33.

| Isomer | | <u>30</u> | <u>31</u> | <u>32</u> | <u>33</u> |
|--------------------------------------|-------|-----------|-----------|-----------|-----------|
| ΔH° (kcal/mole) | exp. | 0 | +0.48 | +1.44 | +2.24 |
| | calc. | 0 | +0.84 | +1.81 | +2.02 |
| ΔS° (u.e.) | exp. | 0 | -0.5 | + 0.6 | +0.8 |
| | calc. | 0 | -0.22 | +0.24 | +0.29 |
| ΔG° (kcal/mole) at 65° | exp. | 0 | +0.66 | +1.24 | +2.0 |
| | calc. | 0 | +0.91 | +1.73 | +1.93 |
| ΔG° (kcal/mole) at 100° | exp. | 0 | +0.68 | +1.23 | +1.98 |
| | calc. | 0 | +0.92 | +1.72 | +1.92 |
| ΔG° (kcal/mole) at 165° | exp. | 0 | +0.70 | +1.17 | +1.93 |
| | calc. | 0 | +0.93 | +1.70 | +1.89 |

The following conclusions can be drawn : The experimental results are very well reproduced for hydrocarbons, hindered alcohols and ketols. (These last molecules are hindered and also show internal hydrogen bonding (26)). Discrepancies are noticed specially for norborneols 20 21, the least hindered alcohols. It is possible that the method we have used is satisfactory when solvation is negligible and that inclusion of solvation may give a fully satisfactory way to calculate the equilibrium ratios in isomeric mixtures.

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THE HYDROLYSIS OF PHOSPHATE ESTERS

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Abstract. The hydrolysis of a phosphate, phosphonate or phosphinate ester generally takes place either through a trigonal bipyramidal hydroxyphosphorane as intermediate (with expansion of the coordination number of phosphorus from four to five) or (at least for phosphates) through a monomeric metaphosphate as intermediate (with contraction of the coordination number of phosphorus from four to three). These processes parallel the principal mechanisms for the hydrolysis of carboxylic esters, which require either the formation of a tetrahedral intermediate or that of an acylium cation.

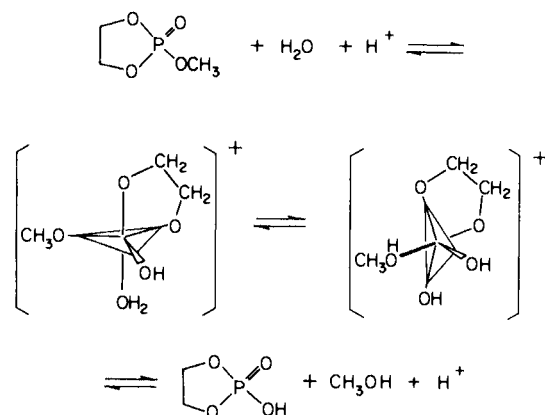
INTRODUCTION

The hydrolyses of phosphate esters parallel to a remarkable degree those of esters of carboxylic acids. The major pathway for the hydrolysis of an ordinary ester requires the formation of a tetrahedral intermediate; the major pathway for the hydrolysis of a phosphate, phosphonate or phosphinate ester requires the formation of a trigonal bipyramidal intermediate. Kinetics (1), isotope exchange (2) and other chemistry (3) provide evidence that a tetrahedral intermediate, as contrasted to a tetrahedral transition state, is required in the hydrolysis of a carboxylic acid ester; the evidence for a true intermediate in the hydrolysis of some phosphate esters, from kinetics, product formation and stereochemical studies is equally convincing.

A second mechanism for the hydrolysis of organic esters proceeds through acylium ions such as CH_3CO^+ (4, 5, 6). A comparable mechanism for the hydrolysis of phosphate esters involves the intervention of monomeric metaphosphates, such as CH_3OPO_2 and PO_3^- . Just as nmr spectroscopy has provided solid evidence for acylium ions, so several recent developments have provided evidence for monomeric metaphosphates.

PHOSPHORANES

Phosphoranes from cyclic phosphates. Convincing evidence that trigonal bipyramidal structures are intermediates, rather than transition states, in the hydrolysis of cyclic phosphate esters was offered in 1966 (7). The hydrolysis of methyl ethylene phosphate occurs both with ring opening and with loss of the exocyclic methyl group (8); the rates for both processes are about 10^6 times that for trimethyl phosphate. Hydrolysis of methyl butylphosphonate (9) occurs rapidly, but nearly exclusively with ring cleavage (7), whereas the hydrolysis of methyl tetramethylenephosphinate is slow. These facts could be reconciled (7) on the assumptions that (a) nucleophilic attack on an ester to form a phosphorane, and subsequent loss of a leaving group from a phosphorane, occur preferentially to and from apical positions of a trigonal bipyramid, (b) five-membered heterocycles containing phosphorus are strained (10), (c) when a phosphorane is formed as intermediate in hydrolysis, the strain is relieved by placing the small ring in one apical and one equatorial position, (d) in phosphoranes, the polarity rules are obeyed, e.g. electron withdrawing groups preferentially occupy apical positions, while electron donating groups preferentially occupy equatorial positions (11) (this rule has now been modified; see Trippett (12)). (e) The final assumption is that phosphoranes may undergo ligand reorganization ("pseudorotation") under the limitations of the strain rule and the polarity rule given above. For example, the exocyclic cleavage of methyl ethylene phosphate most probably occurs as follows:



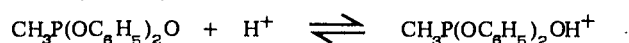
The general scheme, represented by the principles (a) - (e) above, and illustrated with the mechanism of hydrolysis of methyl ethylene phosphate, has proved to have considerable predictive capability, and has been verified by numerous investigators (13).

Acyclic aryl phosphates. The acid catalyzed hydrolysis of triaryl phosphates shows a maximum in the rate vs. acidity curve (14, 15, 16). This maximum has been ascribed to the decrease in the activity of water with increasing concentration of acid.

The hydrolysis of amides shows a maximum rate at about 3M acid, and a decrease in rate at higher acidity; this decrease in rate has likewise been ascribed to a decrease in the availability of water at high acidity (17). But amides show a pK in the neighborhood of -1 to -2, so that in acid more concentrated than 2M (where $H_0 < -1$) they are substantially protonated. A further increase in acid cannot cause much additional acid catalysis; consequently, the decrease in the activity of water that accompanies an increase in acidity can be responsible for a decrease in rate. However, the pK of triphenyl phosphate (16, 18) is probably around -5, so that in the acidity range where $H_0 > -3$, less than 1% of the ester is protonated. If the rate maximum, and fall in rate at high acidity, occurs because water is insufficiently available for hydrolysis, then a decrease in water activity must be great enough to overcompensate for the increase in concentration of protonated species with increasing acidity. The case thus does not strictly parallel that of amides.

Aryloxyphosphonium salts. The new chemistry discussed here relates to studies with aryloxyphosphonium salts. These salts serve as models for protonated esters; that is to say, the cation,

$\text{CH}_3\text{P}(\text{OC}_6\text{H}_5)_3^+$, should serve as a model for $\text{CH}_3\text{P}(\text{OC}_6\text{H}_5)_2\text{OH}^+$; the latter in turn is the protonation product of diphenyl methylphosphonate.



In our previous communication (19), we proposed a mechanism for the hydrolysis of aryloxyphosphonium salts and of aryl phosphates. Further investigation has now shown that the mechanisms previously advanced cannot be completely correct, and may in fact be seriously in error. At the present time, we are unable to specify the hydrolytic mechanism with confidence. Nevertheless, some alternatives can be examined, and tentative conclusions reached. In any event, the chemistry of the aryloxyphosphonium salts, as it develops, should help elucidate that of the aryl phosphates.

Compounds such as $\text{CH}_3\text{P}(\text{OC}_6\text{H}_5)_3^+$, CF_3SO_3^- undergo rapid hydrolysis. The rate in acetonitrile increases more or less with the third power of the water content of the solvent, and exceeds the limits of the stopped-flow apparatus (i. e. $k > 1000 \text{ sec}^{-1}$) at about 8% water. However, the hydrolysis of methyltri(2,6-dimethylphenoxy)phosphonium ion can be followed up to 60% water, where the rate levels off. Since the effect of water on the hydrolyses of the two salts is similar, a reasonable extrapolation of the rate of hydrolysis of the methyltriphenoxyphosphonium salt to high water concentration can be made. The appropriate graphical presentation of the data is given in Figs. 1 and 2 (19).

Whatever the mechanism of hydrolysis of the aryloxy salt, the same mechanism should obtain, with (perhaps) a similar rate constant, for the hydrolysis of the protonated ester. In the region of acidity where the phosphate ester is only slightly protonated, the rate of hydrolysis of the ester should be proportional to the hydrogen ion concentration (or to some other acidity function).

Under these conditions, and almost regardless of mechanism, if the rate constant for the hydrolysis of the protonated ester is the same as that for the corresponding aryloxy salt, then we expect that

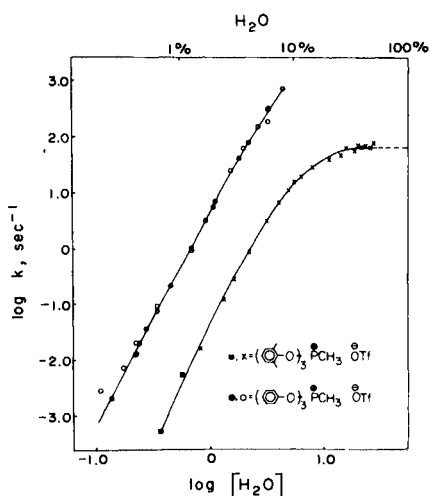


Fig. 1 Rate constants in inverse seconds for the hydrolysis of methyltri-phenoxyphosphonium triflate and of methyl tri(2,6-dimethylphenoxy)phosphonium triflate at 25°. Open circles and X's: measurements with a Durham-Gibson stopped-flow apparatus; filled circles and squares: measurements with a Cary 15 spectrophotometer. (Reprinted with permission from J. Amer. Chem. Soc.)

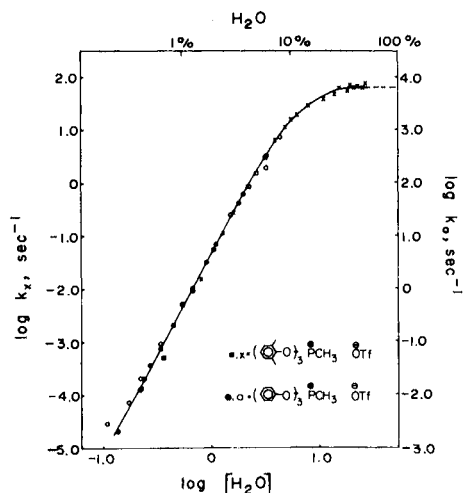


Fig. 2 Rate constants in inverse seconds for the hydrolysis of methyltri-phenoxyphosphonium triflate (right-hand scale) and for the hydrolysis of methyltri(2,6-dimethylphenoxy)phosphonium triflate (left-hand scale), at 25°. (Reprinted with permission from J. Amer. Chem. Soc.)

$$k^{\text{ester}} = k^{\text{salt}} (\text{H}^+) / K_1 \quad (1)$$

(It will be shown later that this equation does not lead to a good approximation for k^{ester} , and the assumptions underlying the model will be reexamined.)

Effect of triflic acid. The rates of the hydrolyses drop sharply with increase in acid concentration. The data for the two salts in 6% water - 94% acetonitrile and for the sterically hindered salt in 34% water - 66% acetonitrile are shown below. The rate falls off with something like the 3.6th power of the concentration of added triflic acid (19).

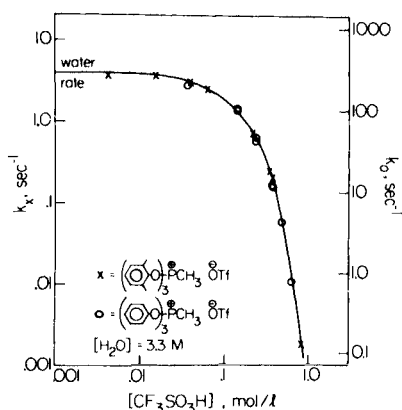


Fig. 3 Rate constants in inverse seconds for the hydrolysis of methyltri-phenoxyphosphonium triflate (right hand scale) and for the hydrolysis of methyltri(2,6-dimethylphenoxy)phosphonium triflate (left hand scale) in 6% aqueous acetonitrile at 25°. (Reprinted with permission from J. Amer. Chem. Soc.)

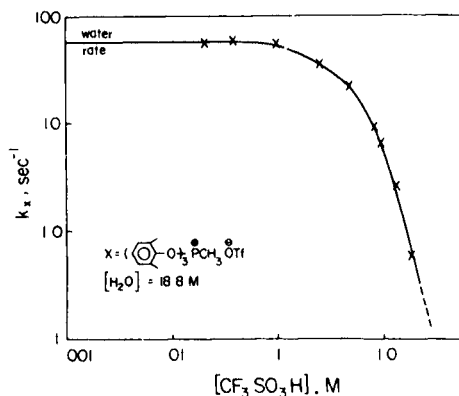
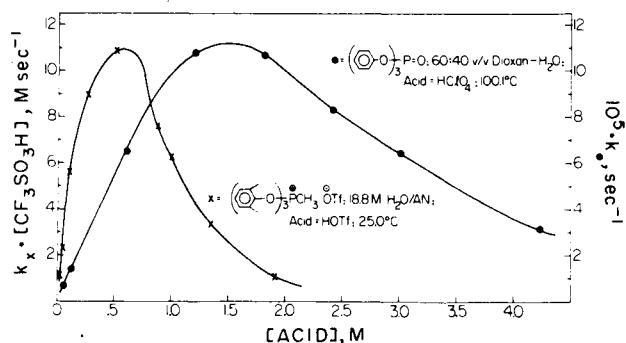


Fig. 4 Rate constants in inverse seconds for the hydrolysis of methyltri(2,6-dimethylphenoxy)phosphonium triflate, in 34% aqueous acetonitrile as solvent. (Reprinted with permission from J. Amer. Chem. Soc.)

When $k^{\text{salt}}(\text{H}^+)$ is plotted against hydrogen-ion concentration (in accordance with eq. [1]) a curve with approximately the correct shape is obtained but the rate maximum occurs at about 0.6 M acid, instead of at about 1.8 M acid, as observed for the hydrolysis of triphenyl phosphate; the two curves are shown together in Fig. 5.



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Fig. 5 pH-rate profile for the hydrolysis of triphenyl phosphate (after Barnard et al. (14) and calculated by eq. (1) from the data for the hydrolysis of methyltri-(2,6-dimethylphenoxy)phosphonium triflate.

However, when the absolute rate for the hydrolysis of the ester is calculated from equation (1), the calculated rate exceeds that observed (note a) by a large factor, probably about 1,000. The determination of this factor depends, of course, on the $\text{p}K$ of -5 assigned to the conjugate acid of triphenyl phosphate (16, 18). This value may not be the appropriate one to use; as Arnett (20) has pointed out, the particular acidity function chosen in any specific example should be measured with indicators similar in structure to the substrate. Further problems arise because different solvents have been used in different investigations. But if (as seems probable) a large discrepancy still exists when these factors have been properly taken into account, then some further explanation must be sought; a possible explanation is presented later.

The hydrolysis of aryloxyphosphonium salts is subject to an unusually large salt effect. The rate constant for the hydrolysis of methyltri(2,6-dimethylphenoxy)phosphonium triflate in 66% acetonitrile - 34% water is only about 1/30 as great in the presence of 1.8 M lithium triflate as in its absence. Further, triflic acid is much less effective in decreasing the rate of hydrolysis of this phosphonium cation at constant high ionic strength (Fig. 6) than in the absence of salt (Fig. 4). Moreover, since the additional effect of acid, over and beyond that of salt, is relatively small, the possibility remains open that the apparent effect of acidity at high ionic strength is an artifact, arising from a difference in salt effects between triflic acid and lithium triflate. In our previous publication (19), we had suggested that, at high acid concentration, the rates of hydrolysis of our aryloxyphosphonium salts vary inversely as the second power of the acidity. The new data show that this is not correct. A major part, and perhaps all of the diminution in rate in the presence of acid is probably caused by a diminution in the availability of water, sequestered by the added salts or acid; this is the explanation previously advanced by Haake (14) and Bunton (15) for the rate maximum in the hydrolysis of aryl phosphates and phosphonates.

But how can one explain a diminution in rate of hydrolysis by a factor of 30 caused by only 1.8 M salt? Jordan has suggested (22) that the acidity of solutions in aqueous acetonitrile can be estimated by calculating the concentration of acid as if the acetonitrile were not present. In other words, 1.8 M lithium triflate in 34% aqueous acetonitrile may be the equivalent of 5.4 M lithium triflate in water. At such high concentrations, a large salt effect becomes reasonable, although a factor of 30 is still large even compared to the effect of high concentration of salt on H_2O (23).

If this line of thinking is correct, why then does 2.4 M salt diminish the rate of hydrolysis of triphenyl phosphate in 60% dioxane - 40% water by a factor of only 2.4? Possibly the difference lies in the

Note a. The rate constant originally reported for the acid-catalyzed hydrolysis of diphenyl methylphosphonate (21) is less than that for triphenyl phosphate by a factor of about 100. More recently, however, Professor Hudson (21b) has informed us, in a private communication, that the correct rate constant for the hydrolysis of this ester at 110° in 60% DME - 40% water in the presence of 1 M triflic acid is $4.15 \times 10^{-5} \text{ M}^{-1} \text{ sec}^{-1}$, quite comparable to the corresponding rate constant for the hydrolysis of triphenyl phosphate.

solvent; dioxane may coordinate cations well enough to "protect" the water, whereas acetonitrile does not. But possibly the relatively modest diminution in rate of hydrolysis of the ester in the presence of salt arises in part as the resultant of two opposing effects: an increase in the concentration of protonated ester caused by a decrease in H_0 in salt solutions (23), coupled with a large decrease in the rate of hydrolysis of the cations similar to that found here for aryloxyphosphonium salts.

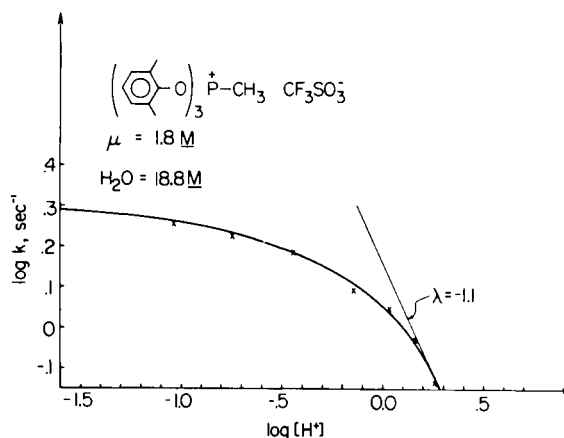
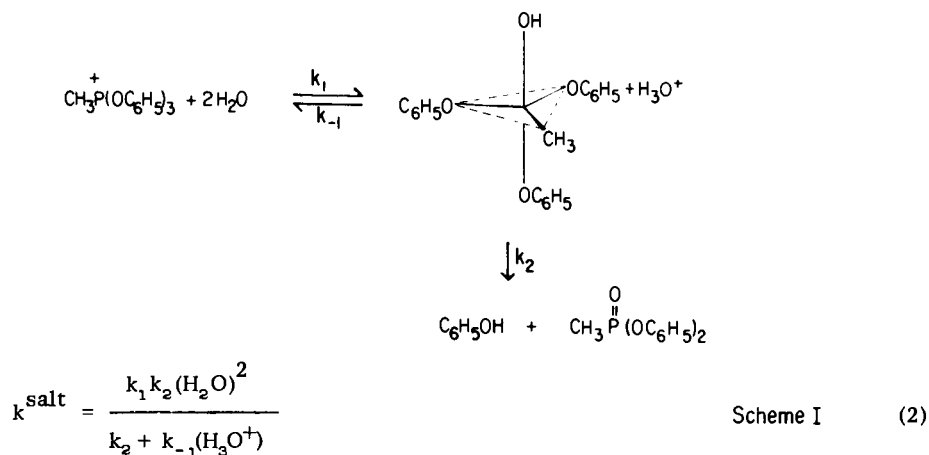


Fig. 6 Rate constants in inverse seconds for the hydrolysis of methyltri(2,6-dimethylphenoxy)phosphonium triflate in aqueous acetonitrile at an ionic strength of 1.8 M.

Scheme I shows a mechanism for the hydrolysis of aryloxyphosphonium salts that leads to equation (2).



Equation 2 leads to the conclusion that, at low acidity, the addition of water to the phosphonium salt is rate limiting; further, the addition of water might prove rate limiting at all reasonable acid concentrations, since the data are not yet available (note b) to evaluate the relative values of k_{-1} and k_2 . If this scheme is correct, then a parallel mechanism (preceded, of course, by protonation of the ester) applies to ester hydrolysis. The postulated hydroxyphosphorane (25) has already been shown to decompose rapidly, although the details of the mechanism have not yet been elucidated. Further, in the event that the decrease in rate at high acidity proves significant, and not an artifact, equation (2)

Note b. The rate constant for the ionization of methyltetraphenoxyphosphorane in acetonitrile at 25° is 7.5 sec^{-1} (24); this sets a lower limit for k_2 , but the value for the hydroxyphosphorane in the more polar solvent may be substantially higher.

would accommodate the data.

Despite some attractive features, Scheme I coupled with equation (1) has major defects. First, as previously noted, the absolute rate constant, calculated on the basis of the assumption that an aryloxyphosphonium salt is a good model for the corresponding protonated ester, is about 1000 times as great as that observed in acid for the hydrolysis of triphenyl phosphate or for diphenyl methylphosphonate. Perhaps the uncertainty in the pK of triphenyl phosphate (see above) is important, or the differences in solvent are significant. Perhaps, however, the phenoxy group is not a good surrogate for the hydroxyl group. Both because the hydroxyl group can accommodate positive charge better than a phenoxy group, and because the former will be hydrogen bonded to the solvent, it may drain more of the positive charge from phosphorus than the latter. A less electropositive phosphorus atom would hydrate less rapidly. Whether such an effect is large enough to account for the observed rate ratio cannot yet be decided.

A second defect is that the kinetic scheme requires that, at high acidity, the addition of water to an aryloxyphosphonium salt, or to a protonated ester, be reversible. This requirement would at first glance seem to demand that oxygen exchange into the ester accompany acid-catalyzed hydrolysis, whereas Bunton and Farber (16) found that very little oxygen exchange accompanies the hydrolysis of triphenyl phosphate in 0.5 M acid at 100° in 75% dioxane - 25% water. But of course if the rate-limiting step in the hydrolysis (according to Scheme I) is the addition of water to the phosphonium cation, subsequent steps would occur too rapidly to permit oxygen exchange. Even if it should develop that the apparent inhibition by acid, shown in Fig. 6, is mechanistically important, oxygen exchange still need not accompany hydrolysis. If, in the mechanism here suggested, the phenoxy group is very much more apicophilic than the hydroxyl group, then pseudorotation would be required for oxygen exchange, but not for ester hydrolysis. In the dihydroxyphosphorane formed as an intermediate, one hydroxyl group is apical and one equatorial; only the apical one will protonate, and pseudorotation is required to make the two equivalent. Pseudorotation, although rapid, has proved rate-limiting in other cases (26). Quite obviously, the mechanism will have to be much more firmly established before such subtle effects are worth consideration.

Finally, it must be admitted that Scheme I is not the only mechanistic pathway consistent with the experimental data. On the assumption that the diminution of rate with increasing acid concentration at constant ionic strength is an artifact, a mechanism that ejects phenol from the cations,

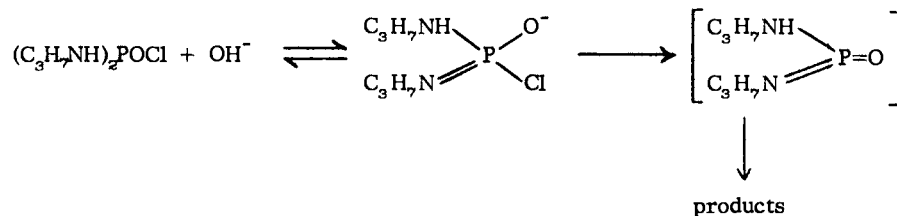


would also fit the data for the hydrolysis of the aryloxyphosphonium salt and those for the corresponding phosphonate ester. In fact, even a mechanism that involves a displacement by water from the cations could be considered. Such a mechanism would necessarily be concerted with proton transfer, to yield hydronium ion, a phosphonium ion and phenolate ion; unless it were concerted, the product would violate the adjacent charge rule. While these latter mechanisms appear relatively unlikely, with the evidence at hand they cannot be positively excluded. Although many problems of the hydrolysis of the aryl phosphates are still unsolved, investigations of the chemistry of the aryloxyphosphonium salts should enhance and facilitate the determination of mechanism.

MONOMERIC METAPHOSPHATES

The hydrolysis of sterically hindered carboxylic acids in strong acid may take place by way of acylium ions. These highly electrophilic ions were first detected by cryoscopic measurements in sulfuric acid solution (4), but subsequently these and other carbonium ions were seen in nmr spectroscopy by Deno (5) and Olah (6) and their collaborators.

The comparable chemistry of phosphate esters takes place by way of the strongly electrophilic monomeric metaphosphate ion and the corresponding esters. The anion, PO_3^- , was postulated twenty years ago on the basis of kinetic evidence (27). Subsequently a number of other studies (28, 29) strongly suggested monomeric metaphosphates in the hydrolysis of certain phosphate esters. The nitrogen analogs of monomeric metaphosphates, the monomeric metaphosphorimidates, were also postulated (30) as intermediates in the hydrolysis of phosphoramidic halides. Since these hydrolyses proceed as much as 10^8 times as rapidly when a hydrogen atom is attached to an amide nitrogen atom as when the nitrogen atoms are fully substituted (31), reaction via metaphosphorimidates seemed indicated (32), e. g.

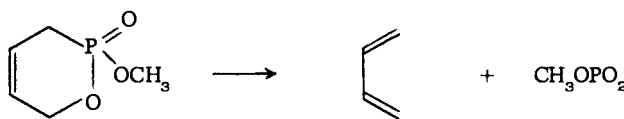


The postulate of monomeric metaphosphorimidates has also been supported by stereochemical evidence (33), and by the preparation of silylated imidates (34) such as $(\text{CH}_3)_3\text{Si}-\text{N}=\text{P}[\text{NSi}(\text{CH}_3)_2]$ and analogous alkylideneoxyphosphoranes.

Three phase test. Recently two other methods of preparing and/or observing monomeric metaphosphates have been reported: the three-phase test, introduced by J. Rebek (35) and the pyrolysis of phosphonates from our laboratory (36).

Rebek has attached to one type of polymer beads a compound that is expected to decompose to a monomeric metaphosphate, and a possible receptor to another type of beads. The beads are then mixed in a solvent (dioxane) and treated with a catalyst needed to produce the unstable intermediate. Transfer of the monomeric metaphosphate or metaphosphorimidate from one bead to another cannot occur by way of a bimolecular reaction, and therefore requires the transfer of an unstable intermediate through the solvent. When a fully substituted phosphoramidate (i.e. with no ionizable hydrogen atom) is attached to the polymer beads, no phosphorimidate can be formed, and no reaction occurs. Rebek has also demonstrated PO_3^- by the three phase test.

Pyrolysis. The pyrolysis of methyl butenylphosphonate yields butadiene and monomeric methyl metaphosphate (36).



The pyrolysis is carried out at about 600° and 20μ pressure of inert gas, with a contact time of the order of a few hundredths of a second. The product gases impinge on the surface of a stirred solution of some trapping agent dissolved in butyl benzene at -80° . Monomeric methyl metaphosphate was first trapped with N-methylaniline to yield compound A.

A more significant test comes from the reaction of monomeric methyl metaphosphate with diethylaniline, which results in electrophilic substitution into the aromatic ring to yield B.



The formation of the electrophilic substitution product serves to identify monomeric metaphosphates.

The pyrolysis technique has also been used to make phosphonobenzene, $\text{C}_6\text{H}_5\text{PO}_2^-$, and phosphonomesitylene. Pyrolysis of methyl ethylene phosphite produces monomeric methyl metaphosphate, along with ethylene.

The evidence for the existence of monomeric metaphosphate is then comparable to that for the existence of acylium ions. Kinetic evidence is always required, however, to decide whether monomeric metaphosphates participate in specific chemical or biochemical processes.

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