

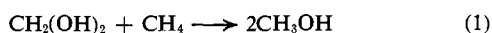
Structural Effects on Rates and Equilibria. XVIII. Thermodynamic Stability of Ortho Esters^{1a}

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Abstract: Enthalpies of -1.70 , -1.70 , -5.91 , and -6.64 kcal/mol have been measured for the reactions of liquid trimethyl orthoformate, triethyl orthoformate, trimethyl orthoacetate, and tetramethyl orthocarbonate, respectively, with excess 65% tetrahydrofuran–35% water in the presence of acid at 25° to give the corresponding simple esters and methanol or ethanol. Enthalpies of formation of -136.8 , -164.2 , -146.0 , and -183.4 kcal/mol are calculated for the respective liquid ortho esters by combining the enthalpies of hydrolysis with enthalpies of solution and measured (or, in the case of dimethyl carbonate, estimated) ΔH_f° values for the reactants and products. From estimated ΔH_f° values for the vapor phase, interaction parameters for an Allen correlation and group contributions for a Benson correlation of ΔH_f° values are calculated. The marked stabilization that accompanies the attachment of several alkoxy groups to the same saturated carbon atom may be illustrated by the disproportionation of dimethyl ether to tetramethyl orthocarbonate and methane, which is exothermic by 52 kcal/mol of the ortho ester. Possible reasons for such stabilization are discussed.

The tendency of fluorine, oxygen, and nitrogen atoms to cluster around the same saturated carbon atom has been the subject of earlier articles in this series.^{2,3} In correlating thermodynamic properties by use of an Allen-type scheme, this tendency appears in the form of stabilizing interactions of pairs of atoms attached to a given saturated carbon atom. The most strongly stabilizing interaction for which there is experimental evidence appears to be that of two oxygen atoms attached to the same carbon atom, which contributes about -13 kcal/mol to the enthalpy of formation of a compound in the gas phase at 25°. ⁴⁻⁶ A moderately simple *ab initio* molecular orbital calculation to the same level of approximation on a number of simple compounds, many of which have never been isolated, gives similar parameters, which are called "bond separation energies," and the largest (15.2 kcal/mol) is for reaction 1.⁹ For these reasons it was of interest to



learn more about this stabilizing interaction by studying compounds with three and four oxygen atoms attached to the same saturated carbon atom. The enthalpy of hydrolysis determinations that we therefore

made on four ortho esters should also give us information about the stabilities of species with three or four oxygen atoms attached to the same carbon atom that are formed as intermediates in ester hydrolysis and related reactions. After the completion of our work we learned that enthalpies of formation of two of the compounds we studied had been determined by combustion calorimetry.¹⁰

Results

The enthalpies of hydrolysis of trimethyl orthoformate, triethyl orthoformate, trimethyl orthoacetate, and tetramethyl orthocarbonate in 65% (by volume) tetrahydrofuran–35% water (65% THF) containing 0.001 *M* perchloric acid were measured at $25 \pm 2^\circ$ using a calorimeter similar to that described by Arnett and coworkers¹¹ as modified by Rogers.¹² According to the rate constant for the acid hydrolysis of triethyl orthoformate in water at 25° (interpolated from data at 10° and 30°)¹³ the half-time for reaction at our acidity would be about 0.5 sec. If added tetrahydrofuran increases the reaction rate, as added dioxane does,¹⁸ then hydrolysis should certainly be complete in the several minutes over which the evolution of heat was measured. Trimethyl orthoformate was assumed to hydrolyze at a rate at least comparable to that of its ethyl analog; since triethyl orthoacetate is about 40 times as reactive as triethyl orthoformate,¹³ trimethyl orthoacetate should also be more reactive. Hence, the hydrolysis of these ortho esters should also proceed essentially to completion. Since the hydrolytic reactivity of tetraethyl orthocarbonate is only about one-sixth that of triethyl orthoformate, there seemed a possibility that the hydrolysis of tetramethyl orthocarbonate in the presence of 0.001 *M* perchloric acid would be slow enough to complicate our results slightly. Hence, this ester was also studied in the presence of 0.01 *M* perchloric acid, where no difference in the results was detected.

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(6) In the Allen scheme⁸ the enthalpy of formation is expressed as the sum of a contribution from every bond (B_{CH} for the C–H bond), every pair of atoms attached to a common atom (Γ_{FC} for a chlorine atom and a fluorine atom attached to the same carbon atom), and every trio of atoms attached to a common atom (Δ_{CCO} for two carbon atoms and an oxygen atom attached to the same nitrogen atom). If any member of a pair or of a trio is hydrogen, then Γ or Δ is defined as zero. The smaller stabilizing interaction of two oxygen atoms attached to the same carbon atom calculated previously² was calculated on a different basis.

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The half-life for the hydrolysis of methyl formate in the presence of 0.001 *M* aqueous acid at 25° may be estimated from literature data^{14,15} to be about 50 hr. Direct determination by titration of the formic acid produced showed that about 0.4% hydrolysis of the methyl formate took place during the 30 min after initiation of reaction that the average reaction was followed. Since ethyl formate is slightly less reactive,^{16,17} methyl acetate is definitely less reactive,¹⁷ and dimethyl carbonate is much less reactive^{18,19} than methyl formate, hydrolysis of these esters under our conditions should be even less significant.

The enthalpies measured on dissolving the ortho esters in the acidic reaction solution, which are the enthalpies of solution plus the enthalpies of hydrolysis in solution, are listed in Table I. The enthalpies of

Table I. Enthalpies of Hydrolysis of Esters^a at 25°

Ester	No. of runs	-Δ <i>H</i> , cal/mol ^b		
		Measured	In soln	Pure liquids
Trimethyl orthoformate	12	1703 ± 23	2358 ± 23	2292 ± 28
Triethyl orthoformate	6	1705 ± 14	2797 ± 20	3168 ± 19
Trimethyl orthoacetate	4	5910 ± 64	6194 ± 65	6290 ± 65
Tetramethyl orthocarbonate	4	6638 ± 41	7482 ± 43	7425 ± 41
Methyl formate ^c	4	12348 ± 571		
Ethyl formate ^c	2	13038 ± 215		

^a In acidic 65% THF unless otherwise noted. ^b The uncertainties listed are standard deviations. ^c In 0.02 *M* aqueous sodium hydroxide.

Table II. Enthalpies of Solution in 65% THF at 25°

Compound	No. of runs	Δ <i>H</i> , cal/mol ^a
Trimethyl orthoformate ^b	2	655 ± 1
Triethyl orthoformate ^b	2	1092 ± 14
Trimethyl orthoacetate ^b	2	284 ± 10
Tetramethyl orthocarbonate ^c	2	844 ± 13
Methyl formate	2	1143 ± 15
Ethyl formate	4	1303 ± 12
Methyl acetate	6	934 ± 8
Dimethyl carbonate	4	1341 ± 4
Methanol	6	-394 ± 2
Ethanol	4	-37 ± 2
Water	14	-234 ± 3

^a The uncertainties listed are standard deviations. ^b In 65% THF containing 0.005 *M* sodium hydroxide. ^c In 65% THF containing 0.001 *M* sodium hydroxide.

solution of the ortho esters in 65% THF were measured by using solvent containing dilute sodium hydroxide to prevent hydrolysis. Subtraction of the resulting values, which are listed in Table II, from the enthalpies measured in acidic solution gives the enthalpies of hydrolysis of the ortho esters dissolved in 65% THF to the

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products in the same solvent, which are listed in the next to the last column of Table I. Enthalpies of solution of all the other reactants and products in the hydrolysis reactions are listed in Table II. From these values, the enthalpies of reaction of liquid ortho ester with liquid water to give liquid alcohol and liquid simple ester, which are listed in the last column of Table I, were calculated.

In order to obtain enthalpies of formation for methyl formate and ethyl formate, the reaction of these two esters with 70–200% excess 0.02 *M* sodium hydroxide in aqueous solution was also studied calorimetrically. Rate constants for the basic hydrolysis of these two esters under the given conditions²⁰ show that in no case would more than 0.01% of the ester remain after 30 sec.

Discussion

The enthalpies of hydrolysis we have measured may be combined with other data and estimates to give enthalpies of reaction and of formation in the gas phase. Calorimetrically determined enthalpies of vaporization at 25° of 10.52, 8.91, and 10.11 kcal/mol were used for water, methanol, and ethanol, respectively.²¹ Values of Δ*H*_v at the boiling points²² were combined with the generalization that *C*_p for a nonassociated liquid is about 15 cal/(mol deg) larger than for its vapor²³ to give Δ*H*_v values at 25° of 6.78, 7.69, 7.95, and 8.87 kcal/mol for methyl formate, ethyl formate, methyl acetate, and dimethyl carbonate, respectively. A plot of these and the eight Δ*H*_v (25°) values determined by Wadsö for carboxylic acid esters²¹ vs. the boiling points of the esters showed that no value deviated from eq 2 by more than 0.2 kcal/mol.

$$\Delta H_v(25^\circ) = 5.6 + 0.037t_{bp} \quad (2)$$

No enthalpies of vaporization seem to have been determined for ortho esters, so we relied on the generality of relationships like eq 2 for given families of compounds. A plot of Δ*H*_v vs. boiling point for diethyl ether,²⁴ tetrahydrofuran,²⁵ diisopropyl ether,²⁶ tetrahydropyran,²⁷ di-*tert*-butyl ether,²⁶ and di-*n*-butyl ether²⁸ gave a straight line with a least-squares intercept of 5.20 kcal/mol and a slope of 0.0367 kcal/(mol deg). An analogous plot for the dimethyl and diethyl acetals of formaldehyde^{29,30} and acetaldehyde^{4,31} and for (C₂H₅OCH₂)₂O³⁰ gave an intercept of 5.28 kcal/mol and a slope of 0.0379 kcal/(mol deg). Since the plots for simple ethers and acetals are thus identical, within the experimental uncertainty, the latter was used to calculate Δ*H*_v values of 9.13, 10.81, 9.37, and 9.56 kcal/mol for trimethyl orthoformate, triethyl orthoformate, tri-

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methyl orthoacetate, and tetramethyl orthocarbonate, respectively. From the preceding values of ΔH_v , the enthalpy of hydrolysis of trimethyl orthoformate in the gas phase is $-2.292 - 10.52 - 9.13 + 6.78 + 2(8.91)$ or 2.658 kcal/mol. This and the values for the other esters are listed in Table III. Combination of the gas-

Table III. Enthalpies of Formation and of Gas-Phase Hydrolysis of Esters at 25°^a

Ester	ΔH_f° , hydrol gas	$-\Delta H_f^\circ$	
		Gas	Liq
Trimethyl orthoformate	2.7	127.7	136.8
Triethyl orthoformate	3.4	153.4	164.2
Trimethyl orthoacetate	-0.4	136.6	146.0
Tetramethyl orthocarbonate	-0.8	173.9	183.4
Methyl formate	5.8	86.6	93.4
Ethyl formate	6.2	95.2	102.9

^a In kcal/mol. The values for the ortho esters refer to hydrolysis to 2 mol of alcohol and one of simple ester.

or liquid-phase enthalpy of hydrolysis with the gas- or liquid-phase value of ΔH_f° (25°) for water (-57.796 or -68.315 kcal/mol³²), methanol (-48.07 or -57.01 kcal/mol³³), or ethanol (-56.24 or -66.42 kcal/mol³³) and the appropriate simple ester gives ΔH_f° for the ortho ester in that phase. Modern values of ΔH_f° have been reported for liquid methyl acetate and methyl formate (-106.57 and -92.28 kcal/mol, respectively³⁴) but apparently not for ethyl formate or dimethyl carbonate. The enthalpies of basic hydrolysis of methyl and ethyl formate may be combined with the enthalpy of neutralization of formic acid by aqueous sodium hydroxide at 25° (-13.63 ± 0.04 kcal/mol)³⁵ to give values of 1.28 ± 0.57 and 0.59 ± 0.22 kcal/mol for the reactions of liquid methyl and ethyl formate with water to give dilute aqueous solutions of formic acid and of methanol and ethanol, respectively. Combination with ΔH_f° for water and for formic acid, methanol, and ethanol in dilute aqueous solution³² gives the values of ΔH_f° for the liquid formates listed in Table III. The value for methyl formate is 1.1 kcal/mol more negative than that reported recently by Hall and Baldt³⁴ and 4.8 kcal/mol more negative than an older value.³⁷ Our value of ΔH_f° for methyl formate was used in calculating the ΔH_f° values for trimethyl orthoformate shown in Table III.

The enthalpy of formation of dimethyl carbonate was estimated on the basis of a value for diethyl carbonate. Månsson's value (-152.47 kcal/mol in the gas phase at 25°)³⁸ was used in preference to a value about 10 kcal/mol more negative reported in 1971.³⁹ The 1971 report is implausible for the reasons given by Månsson, be-

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(35) This refers to <0.01 M aqueous acid reacting with excess sodium hydroxide at concentrations of 0.004–0.02 M, with no significant trend being observed with changes in base concentration.³⁶

(36) W. J. Canady, H. M. Popée, and K. J. Laidler, *Trans. Faraday Soc.*, **54**, 502 (1958).

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cause it reported ethylene carbonate to be 23 kcal/mol more stable than stated elsewhere,³³ and because the difference between the ΔH_f° values reported for ethylene carbonate and propylene carbonate is 10 kcal/mol smaller than would be expected from a group additivity scheme.⁴⁰ Subtraction of twice the $[(C(H)_2(C)(O))]$ group contribution⁴⁰ from the value for diethyl carbonate gives -136.3 kcal/mol as the estimate of $\Delta H_f^\circ(g)$ for dimethyl carbonate at 25°. An independent method of relating ΔH_f° for dimethyl carbonate to that for diethyl carbonate can be based on the work of three investigators, each of whom studied both of these esters before the modern era of thermochemistry. For the ratio of the heat of combustion of the liquid diethyl ester to that of the dimethyl ester values of 1.903 (corrected from data on the gaseous esters by use of the heats of vaporization given herein),⁴¹ 1.902,⁴² and 1.891⁴³ may be calculated. Combination of the average value (1.899) with Månsson's heat of combustion of diethyl carbonate gives an estimate of 341.7 kcal/mol for the dimethyl ester. This gives the value -135.0 kcal/mol for $\Delta H_f^\circ(g)$ at 25°, in good agreement with the alternative estimate, -136.3 kcal/mol, which was used in calculating the ΔH_f° values for the orthocarbonate in Table III.

Our value of ΔH_f° for liquid trimethyl orthoformate is 0.7 kcal/mol less negative and our value for triethyl orthoformate is 1.4 kcal/mol more negative than the respective values of Pihlaja and Tuomi. Considering the uncertainties in the enthalpies of formation of reference compounds as well as our experimental uncertainties the agreement is about as good as could be expected.

In an Allen correlation the gas-phase enthalpies of atomization may be expressed in terms of eq 3 for non-

$$\Delta H_a(C_nH_{2n+2}O_m) = (2n + 2)B_{CH} + 2mB_{CO} + (n - m - 1)B_{CC} + b_1\Gamma_{CCC} + b_2\Gamma_{CCO} + b_3\Gamma_{COO} + b_4\Gamma_{OCO} + c_1\Delta_{CCC} + c_2\Delta_{CCO} + c_3\Delta_{COO} + c_4\Delta_{OOO} - S \quad (3)$$

hydroxylic acyclic organic oxygen compounds containing only single bonds.⁴⁴ The B parameters are bond contributions. Pairwise interactions are covered by the Γ parameters. For example, Γ_{COO} is the interaction energy of two carbon atoms attached to the same oxygen and b_3 is the number of such interactions. Similarly, Γ_{CCO} is the interaction energy of a carbon and an oxygen attached to the same carbon atom. The Δ parameters refer to the interaction of the trio of atoms denoted by the subscript across a carbon atom. Thus, in $CH_3CH(OCH_3)_2$, b_2 and b_3 are each 2, b_4 and c_3 are 1, and b_1 , c_1 , c_2 , and c_4 are all zero. The parameter S is the amount of steric destabilization. In evaluating this parameter Pilcher and Fletcher neglected any gauche interaction between an oxygen atom and a methylene group attached to adjacent carbon atoms as well as any gauche interaction between two methylene groups

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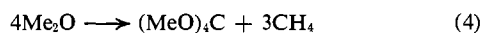
(43) W. Louguinine, *Ann. Chim. (Paris)*, [6] **8**, 128 (1886).

(44) When the properties correlated are enthalpies of formation, the values of the B parameters may change in magnitude and algebraic sign, but the values of the Γ and Δ parameters change only in sign.

attached to a carbon and an adjacent oxygen atom.⁴ Pihlaja and Kankare, on the other hand, used parameters for each of these types of gauche interactions,⁵ but Pihlaja modified their scheme in a way we do not understand, which allows for destabilizing steric interactions in isopropyl and *tert*-butyl alcohols, for example.⁴⁵ Conformational analysis of derivatives of tetrahydropyran and dioxanes shows that a gauche interaction between an oxygen atom and a methylene group is not very large but that a gauche interaction between two methylene groups may be larger when they are attached to adjacent carbon and oxygen atoms than when they are attached to two adjacent carbon atoms.

Setting *S* equal to zero and using the values of Pilcher and Fletcher for all the parameters in eq 3 except Δ_{OOO} , for which they had no value, our results on trimethyl orthoformate, triethyl orthoformate, trimethyl orthoacetate, and tetramethyl orthocarbonate yield Δ_{OOO} values of -7.4 , -5.7 , -6.9 , and -6.6 kcal/mol, respectively.⁴⁶ Three new group contributions to ΔH_f° (g) of -28.5 , -29.2 , and -43.1 kcal/mol may be calculated for $[\text{C}(\text{H})(\text{O})_3]$, $[\text{C}(\text{C})(\text{O})_3]$, and $[\text{C}(\text{O})_4]$ using the most recently compiled Benson group contributions for organic oxygen compounds.⁴⁰ None of the strain interactions listed⁴⁰ refer to strains that are compulsory in any of our compounds (although some of our compounds may have significant gauche strains).

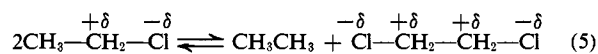
From the appropriate enthalpies of formation the disproportionation reaction shown in eq 4 may be cal-



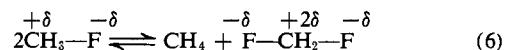
culated to be exothermic by 52 kcal/mol in the gas phase at 25°, in spite of the fact that there are exactly 24 C-H bonds and 8 C-O bonds in the reactants and in the products. This is much larger than the 36 kcal/mol given off in the disproportionation of cyclohexene to cyclohexane and benzene, which is the type of result that has simulated a great deal of discussion of the concept of aromaticity. A sufficiently rigorous quantum mechanical calculation would presumably reproduce the observed enthalpy of reaction in eq 4, but it might be equally useful to devise a simple qualitative rationalization of such deviations from an unadorned bond energy correlation.

Before discussing possible rationalizations, it should be made clear that to maintain a consistent qualitative theory of structural effects on stability the net stabilizing interactions reflected in the parameters of an Allen-type scheme must be treated as the resultants of simple polar interactions, which are destabilizing in the cases presently of interest, and larger stabilizing interactions. Disproportionation reactions, such as that of bromobenzene to give benzene and dibromobenzenes⁴⁷ and of ethyl chloride to give ethane and ethylene chloride, tend to proceed so as to keep the electron-withdrawing substituents in separate molecules or relatively far apart in the same molecule. This fact, which can be used as a basis for the derivation of such relationships as the Hammett and Taft equations,⁴⁸ may be explained in terms of a simple electrostatic argument. In the dis-

proportionation of ethyl chloride, for example, the two carbon-chlorine dipoles, which are in separate molecules in the reactant, are brought into the same molecule with an unfavorable relative orientation in the products (*cf.* eq 5). A simple electrostatic model has



been said to be capable of rationalizing the tendency of several fluorine atoms to cluster around the same saturated carbon atom.⁴⁹ It is true that, in terms of eq 6,



bringing the positive end of each carbon-fluorine dipole nearer the negative end of the other will give a stabilizing interaction considerably larger than the destabilization resulting from bringing the negative ends closer together. However, the largest interaction, which has been neglected in some discussions,⁴⁹ must be the destabilization resulting from placing the positive ends of both dipoles on the same carbon atom. The point charge treatment of bond dipoles, from which an infinite destabilization would be calculated, cannot be used, but it seems clear that the simple electrostatic result of the process shown in eq 6 would be destabilization, even though saturation effects should make the δ 's in the products smaller than those in the reactants. In spite of the difficulty in evaluating the electrostatic destabilization quantitatively, a qualitative tendency for it to decrease with decreasing electronegativity of the interacting atoms is predictable. For this reason it can be seen that there is a stabilizing interaction between two fluorine atoms attached to the same saturated carbon atom that exceeds Γ_{FCF} by a larger amount than the corresponding stabilizing interaction between two oxygen atoms exceeds Γ_{OOO} .

One rationalization of the stabilizing interaction that has been suggested is double bond-no bond (db-nb) resonance.² The "anomeric effect"⁵⁰⁻⁵² (the tendency of 2-oxy-substituted tetrahydropyrans to have their oxy substituents axial, for example) operates in the direction to be expected from db-nb resonance. The possibility that the anomeric effect is a manifestation of db-nb resonance has been considered,⁵³ but a number of observations, including the dependence of the magnitude of the effect on solvent polarity, show that electrostatic interactions are probably the principal reason for the anomeric effect. In any event the anomeric effect, which amounts to no more than about 1.5 kcal/mol for 2-alkoxytetrahydropyrans,^{50,53} could not be identified with more than a minor part of the stabilizing interaction that results in the observed values of Γ_{OOO} . Pople and coworkers used a molecular orbital equivalent of db-nb resonance to explain the calculated relative stabilities of the various conformers of many of the species they treated.⁹ However, most of these relative stabilities are qualitatively the same as would be expected from a simple treatment in terms of electrostatic interactions, which should be maximal since the calculations refer to the gas phase.

(49) *Cf.* D. Holtz, *Progr. Phys. Org. Chem.*, **8**, 1 (1971).

(50) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Wiley, New York, N. Y., 1965, Sections 6-4 and 6-6.

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(52) R. U. Lemieux, *Pure Appl. Chem.*, **25**, 527 (1971).

(53) E. L. Eliel and C. A. Giza, *J. Org. Chem.*, **33**, 3754 (1968).

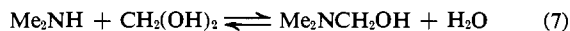
(45) K. Pihlaja, *Acta Chem. Scand.*, **25**, 451 (1971).

(46) Note that in the case of tetramethyl orthocarbonate b_4 is 6 and c_4 is 4.

(47) J. Hine and H. E. Harris, *J. Amer. Chem. Soc.*, **85**, 1476 (1963).

(48) J. Hine, "Physical Organic Chemistry," 2nd ed, McGraw-Hill, New York, N. Y., 1962, Section 4-1.

A strong argument that the clustering effect cannot be explained solely in terms of db–nb resonance or of interactions between unshared electron pairs on non-bonded atoms⁵⁴ may be found in data on the basicities of α -hydroxyalkylamines. From the Allen parameters listed by Cox and Pilcher, the equilibrium constant for eq 7,⁵⁵ and the assumption that ΔS is zero for eq 7, the



parameter Γ_{NCO} may be calculated to be 8.4 kcal/mol plus the destabilization energy of the gauche interaction in the product.⁵⁶ In terms of db–nb resonance more than half of this large amount of stabilization would be expected to come from interaction of the more polar carbon–oxygen bond with the more available unshared pair of electrons on nitrogen. Yet, the basicity of α -hydroxytrimethylamine⁵⁵ is lower than that of trimethylamine by only 1.85 pK units, which is essentially the amount that would be calculated from ρ^* for the basicity of tertiary amines (3.30)⁵⁷ and σ^* for the hydroxymethyl group (0.56).⁵⁸ Since the loss of the unshared pair is thus not accompanied by any otherwise unexpected loss of stability, it is difficult to attribute the particular stability of a compound with an amino group and a hydroxy group on the same saturated carbon atom to an interaction involving the unshared pair. Additional arguments against the major importance of db–nb resonance have been described by Holtz and others.^{3,49}

Another possible rationalization of these stabilizing interactions is that they are electron correlation energy effects. The relatively small stabilizing interaction of two unhindered alkyl groups attached to the same carbon atom (~ 2.6 kcal/mol) has been discussed in these terms.⁵⁹ There is evidence that when bond separation energies are derived from *ab initio* calculations that are carried close enough to the Hartree–Fock limit, electron correlation energies largely cancel.⁶⁰ If this is so, and if the calculations of Pople and coworkers, which led to a number of bond separation energies (*i.e.*, Γ values) larger than 10 kcal/mol, are in this category, electron correlation energies do not provide a plausible general explanation for the interactions we are discussing.

In summary, we feel that no simple qualitative explanation for the clustering effect has yet been put on a firm basis.

Experimental Section⁶¹

Reagents. Methyl formate and ethyl formate were distilled over phosphorus pentoxide on a spinning-band column and no impurities were found upon glpc at 90° on a Carbowax 20M column. The ortho esters were all fractionally distilled over sodium; just before their analysis by glpc, about 3 μ l of propyl-

amine was put through the instrument to minimize acid-catalyzed breakdown. Trimethyl orthoformate showed no impurities. Triethyl orthoformate appeared to contain about 0.6% ethanol and 0.01% ethyl formate (on a Carbowax 20M column at 90°), but the ethanol peak was so broad as to suggest that it resulted from decomposition. Under analogous conditions at 70° tetramethyl orthocarbonate was found to contain 0.1% methanol. Trimethyl orthoacetate appeared to decompose on the column to give methanol and methyl acetate even at 45°. Therefore, the material was analyzed by quantitative infrared measurements at 1750 and 3530 cm^{-1} . Various samples that were used contained 0.01–0.45 mol % methanol and 0.30–0.78 mol % methyl acetate for a total of 0.55–0.96 mol % impurities. Ethanol was refluxed over sodium ethoxide and diethyl phthalate and methanol over magnesium. After fractionation neither showed any impurity on a Porapak Q-S column. Tetrahydrofuran was distilled over sodium–benzophenone. The “65% THF” was prepared by adding 65% of the nominal volume of tetrahydrofuran to a volumetric flask and then filling to the mark with water and aqueous perchloric acid.

Calorimetric Measurements. The calorimeter used was based on the design of Arnett and coworkers,¹¹ as modified by Rogers to give a twin calorimeter system.¹² Before and after each run the chart paper was calibrated by passing a known amount of current through the calibrated resistance heater for a measured interval of time. The two calibrations agreed with a standard deviation of 0.4%. The postreaction calibration was usually larger (in joules per chart division), perhaps because the reactant in the syringe before injection did not reach the temperature of the solution in the calorimeter during the heating period of the prereaction calibration. The apparatus was also calibrated by ten measurements of the enthalpy of reaction of tris(hydroxymethyl)aminomethane with 0.1 M hydrochloric acid in aqueous solution at 25° [corrected from results in the range $25.3 \pm 0.5^\circ$ by use of a factor of 41.6 cal/(mol deg)], which gave 7114 ± 31 cal/mol in comparison with the literature result of 7109 ± 1 cal/mol,⁶² and by four measurements of the enthalpy of solution of ethanol in water, which gave 2432 ± 15 cal/mol in comparison with 2451 and 2415 ± 20 cal/mol.⁶³

Runs were begun by stirring 150–175 ml of solvent in each of the dewar flasks for 2–4 hr with the heater power supply on and the recorder on stand-by. Then the drift was measured on the recorder, which registers the difference in temperature between the two flasks, and, if necessary, one flask was heated to minimize the drift. The liquid to be added was weighed into each of the 2.5-ml plastic sample syringes, which had been fitted with a thin (No. 22) needle and wrapped with Teflon tape at the joint with the needle. The needles were filled with air to prevent premature transfer of the liquid, and a syringe was inserted into the hole in the lid in each flask. After a further equilibration period and electrical calibration of each flask, the sample was injected smoothly into the first flask and the solution was drawn into the syringe and reinjected into the flask to rinse out the last of the sample. After the recorder trace had become linear, the procedure was repeated in the second flask and the postreaction calibration was carried out. The recorder deflections brought about by the electrical heating and by adding the samples were determined from the recorder trace by the method of Dickinson.⁶⁴

All the measurements were made at $25 \pm 2^\circ$. For methyl formate, the most volatile (bp 32°) liquid used, the sample introduction method described in the preceding paragraph was not satisfactory, and a sealed syringe system similar to the solid delivery apparatus of Arnett and coworkers¹¹ was used. Sample sizes were 4–9 mmol, except in the case of methanol and ethanol, where 13–15 mmol were used, and in the reactions of methyl and ethyl formates with aqueous sodium hydroxide, where 1–2 mmol were used. The results obtained with the orthoacetate and the orthocarbonate were corrected (never by as much as 1%) for the impurities found on analysis.

Reaction Products. Gas–liquid partition chromatography on several columns showed only the corresponding alcohols and simple esters as products of the hydrolysis of the ortho esters. Since the most plausible side reaction we could think of was one yielding the corresponding dialkyl ether, evidence for the formation of such ethers was sought with particular care. A column with diisodecyl phthalate on 60–80 mesh Chromosorb W was used at

(54) Cf. N. D. Epiotis, *J. Amer. Chem. Soc.*, **95**, 3087 (1973).

(55) R. G. Kallen and W. P. Jencks, *J. Biol. Chem.*, **241**, 5864 (1966).

(56) The major uncertainty in this calculation is probably the fact that the equilibrium constant refers to aqueous solution and the Allen parameters to the gas phase. To the extent to which the enthalpies of vaporization of the products from the aqueous solution are matched by those of the reactants, this uncertainty will vanish.

(57) H. K. Hall, Jr., *J. Amer. Chem. Soc.*, **79**, 5441 (1957).

(58) R. W. Taft, Jr., “Steric Effects in Organic Chemistry,” M. S. Newman, Ed., Wiley, New York, N. Y., 1956, Chapter 13.

(59) K. S. Pitzer and E. Catalano, *J. Amer. Chem. Soc.*, **78**, 4844 (1956).

(60) L. C. Snyder and H. Basch, *J. Amer. Chem. Soc.*, **91**, 2189 (1969).

(61) All glpc analyses were carried out on an F & M gas chromatograph, Model 720, using 6-ft columns. Concentrations were taken to be proportional to peak areas, as calculated from heights and widths at half-height.

(62) J. O. Hill, G. Ojelund, and I. Wadsö, *J. Chem. Thermodyn.*, **1**, 111 (1969).

(63) F. Franks and B. Watson, *J. Sci. Instrum.*, **1**, 940 (1968).

(64) H. C. Dickinson, *Nat. Bur. Stand. (U.S.), Bull.*, **11**, 189 (1951).

58°. Although the calorimetric measurements were made on ortho esters at concentrations of 0.02–0.05 *M*, when no side reactions could be detected in such reaction solutions, concentrations around 0.1 *M* were used for glpc analysis. A 6- μ l sample of a reaction mixture from trimethyl orthoformate gave no observable peak for dimethyl ether; although if such a peak had had 0.3% of the area of the methyl formate peak, it would have been 1 mm high and 2 mm wide and would have been clearly visible. (The retention time was well separated from that of other peaks and the noise level was on the order of 0.2 mm.) Analogous results were obtained with tetramethyl orthocarbonate. With trimethyl orthoacetate there appeared to be a peak about 0.2 mm high at the retention time for dimethyl ether. The reaction mixture from the hydrolysis of

triethyl orthoformate showed no peak at the retention time for diethyl ether although addition of enough diethyl ether to correspond to a 1% yield gave a peak 4.5 mm high and 3 mm wide. On the basis of this evidence the hydrolysis of all the ortho esters was assumed to proceed without side reactions.

The extent of the hydrolysis to formic acid that took place during the hydrolysis of trimethyl orthoformate was determined by potentiometric hydrolysis.

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A Comparative Study of the Rates and Mechanisms of Conformational Interconversion in Derivatives of Cyclohexanone and Methylene-cyclohexane¹

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Abstract: The cyclohexanone derivatives **2a**, **3a**, **4a**, and **5a** were studied by variable temperature pmr and their behavior was compared to that of the analogous methylenecyclohexane derivatives **2b**, **3b**, **4b**, and **5b**. All compounds except **4a** gave temperature-dependent spectra which by means of computer spectral simulations allowed the determination of the activation parameters characteristic of chair inversion. An interconversion map which allows a simple description of all inversion mechanisms possible is devised and the different trends observed for the two series of compounds are explained in terms of a mechanism in which the most energetical conformation of the inversion profile is different for each series.

The investigation of the conformational properties of cyclic and acyclic molecules has been considered a very important area of fundamental chemical experimentation^{2–7} and, among the systems studied, six-membered rings, by virtue of their abundance and importance as structural units of many natural products, have received greatest attention. Furthermore, nuclear magnetic resonance has revealed itself to be among the best suited experimental techniques for the study of both static and dynamic properties of molecular conformations.

Although only a few classes of molecules have been studied, it has been observed that carbocyclic derivatives of cyclohexane containing sp² hybridized ring carbon atoms are appreciably more flexible than the parent cyclohexane molecule. For example, the dnmr method^{3–6} has been applied to cyclohexene^{8,9} and its

derivatives^{10–12} and to derivatives of cyclohexane-1,4-dione¹³ and 2,2,5,5-tetramethylcyclohexane-1,3-dione,¹⁴ all of which contain two sp² ring carbon atoms.

Even fewer reports have been concerned with cyclohexane derivatives containing only one sp² ring carbon atom. Authors of previous works state unanimously that the barrier to ring inversion for cyclohexanone (**1a**) is much smaller than that of methylenecyclohexane¹⁵ (**1b**) whose barrier to chair–chair interconversion is 8.4 kcal/mol. Estimates of ΔG^\ddagger were published for cyclohexanone-2,2,6,6-*d*₄ (~ 4.9 kcal/mol)¹⁵ and for 4,4-difluorocyclohexanone (~ 2.3 kcal/mol),¹⁶ even though no characteristic spectral change was observed for both cases. In fact, until the recent publication by Anet,¹⁷ the only accurate inversion barrier for a cyclo-

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