Carbon Basicity[1a]

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Using the term "basicity" to refer to equilibrium measurements, equations are derived for calculating from thermochemical and other data the basicities, relative to the reference base hydroxide ion, of various species toward methyl, hydroxymethyl, phenyl, and acetyl cations, and other carbon acids. The methyl basicities of carbanions and thiolate anions exceed their hydrogen basicities by factors between 10^8 and 10^{16} in aqueous solution at 25°. The relatively high basicity of these reagents toward saturated carbon is explained, at least in part, in terms of the dependence of bond energies on the differences in electronegativity between the atoms bonded; the diminished relative basicity of these reagents toward α-hydroxyalkyl, phenyl, and acetyl cations is explained in terms of the various stabilizing influences that operate in the products of the attachment of the reference base hydroxide ion to such cations. It is pointed out that hydroxymethyl basicities of a series of bases change with the polar character of substituents in the same quantitative manner that their hydrogen basicities do, whereas the acetyl basicities of a (different) series of bases are much more sensitive to the polar character of substituents than their hydrogen basicities are. This is explained in terms of the fact that the polar character of hydroxymethyl and hydrogen substituents are similar but that acetyl is a much more strongly electron-withdrawing substituent. Although the correlation of carbon nucleophilicity with carbon basicity appears to be much better than the correlation with hydrogen basicity, it is still quite imperfect. The fact that alkylthiolate and arylthiolate anions appear in general to be more basic toward saturated carbon than are the analogous oxygen compounds provides a partial explanation for the greater carbon nucleophilicity of the sulfur-containing nucleophiles. The greater carbon nucleophilicity of unsubstituted primary alkoxide ions compared to hydroxide ions would be expected in view of their greater carbon basicity. Evidence is described that reagents whose high carbon nucleophilicity has been correlated in terms of the α-effect are also highly basic toward saturated carbon. Nucleophilicities toward aromatic and acyl carbon atoms are rationalized in terms of double bond–no bond resonance and basicities toward saturated carbon.

Introduction

Swain and Scott suggested that the term "basicity" be reserved for application to equilibrium measurements and "nucleophilicity" to rate measurements.[2] Parker suggested the useful elaboration that "carbon basicity" should be employed in cases where the equilibrium involves the formation by the base of a bond to carbon, with other terms, such as "hydrogen nucleo-

philicity" following logically.[3] As Parker pointed out, "there has been little discussion or measurement of carbon basicity."[3] Parker referred to two studies of equilibria involving halide ions and simple alkyl halides and to Bunnett, Hauser, and Nahabedian's observation that hydroxide ions are around 1000 times as basic as thiophenoxide ions toward 9-phenyl-10-methylacridinium ions in 37.6% (weight) acetone–water at 25°,[4] and reported his own measurements on equilibria between halide, azide, and thiocyanate ions as bases toward butyl and methyl bromide.

Subsequently, it was noted that the carbon basicities of sulfur bases are usually greater relative to their hydrogen basicities than is the case with the corresponding oxygen bases,[5a] and Miller showed that the methyl basicity of the sulfur atom of the $(PhO)_2POS^-$ anion is more than 10^4 times as large as that of the oxygen atom in spite of the fact that the hydrogen basicities of the two atoms are about the same.[6] Pearson has discussed acidity and basicity in general with a little specific attention to carbon,[7] and Bunnett has treated carbon basicity in a review on nucleophilicity.[8] Hall has determined equilibrium constants for the displacement of hydroxide ions from formaldehyde hydrate by substituted dinitromethide anions,[9] and Jencks and coworkers have studied equilibria in a number of transacetylation reactions.[10–11a]

It may be that the general topic of carbon basicity has not received more attention because of a belief that thermodynamic affinity for carbon parallels that for hydrogen, or perhaps it is not realized how much data is already available that reveals the relative basicities of many species toward carbon. Discussions of relative basicity toward carbon will be complicated by solvent effects (including ion pairing), etc., just as relative basicities toward hydrogen are,[12] and in addition it is

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(2) C. G. Swain and C. B. Scott, *ibid.*, 75, 141 (1953).

(3) A. J. Parker, *Proc. Chem. Soc.*, 371 (1961).

(4) J. F. Bunnett, C. F. Hauser, and K. V. Nahabedian, *ibid.*, 305 (1961).

(5) J. Hine, "Physical Organic Chemistry," 2nd Ed., McGraw-Hill Book Co., Inc., New York, N. Y., 1962: (a) section 11-2a; (b) p. 87; (c) section 4-1; (d) p. 97; (e) p. 161.

(6) B. Miller, *Proc. Chem. Soc.*, 303 (1962).

(7) R. G. Pearson, *J. Am. Chem. Soc.*, 85, 3533 (1963).

(8) J. F. Bunnett, *Ann. Rev. Phys. Chem.*, 14, 271 (1963).

(9) T. N. Hall, *J. Org. Chem.*, 29, 3587 (1964).

(10) W. P. Jencks and M. Gilchrist, *J. Am. Chem. Soc.*, 86, 4651 (1964).

(11) J. Gerstein and W. P. Jencks, *ibid.*, 86, 4655 (1964).

(11a) NOTE ADDED IN PROOF. A valuble discussion of facts and theories relevant to carbon basicity may be found in a chapter on carbonyl reaction mechanisms, which had previously escaped our attention: W. P. Jencks, *Progr. Phys. Org. Chem.*, 2 (1964).

(12) In whatever solvent (if any) the pK values 19 and 40 listed[13] for *t*-butyl alcohol and triphenylmethane apply, triphenylmethide ions are 10^{21} times as basic as *t*-butoxide ions toward hydrogen. In dimethyl sulfoxide, however, potassium *t*-butoxide reacts with triphenylmethane to give a red color whose intensity does not seem to be increased significantly by increasing the excess of butoxide,[14] showing that *t*-butoxide ions are more basic than triphenylmethide ions in this solvent. The use of dimethyl sulfoxide thus changes the relative hydrogen basicities of the two bases by a factor larger than 10^{21}. However, to the extent to which this effect is due to ion solvation, the carbon basicities of the two bases would change by exactly the same factor.

to be expected that there will also be variations in relative basicities toward carbon, depending on the state of hybridization of the carbon atom in question and on the nature of the other substituents attached to it. Nevertheless, we believe that, just as data on hydrogen basicity have been of great utility in theoretical organic chemistry, data on carbon basicity may also be useful. A knowledge of carbon basicities should not only permit an estimate of equilibrium constants for many reactions, it should also be useful in discussions of reaction rates; i.e., product stabilities are often reflected in transition-state stabilities. Therefore in the present paper information on carbon basicities will be extracted from the literature (quantitatively, where possible), and in addition new data designed to fill some of the many gaps in the available information will be described. Carbon basicities will be compared with hydrogen basicities and their significance will be discussed briefly.

Definitions and Equations

The equilibrium constant for reaction 1 could be

$$H^+ + A^- \rightleftharpoons HA \tag{1}$$

used as a measure of the Brønsted basicity or hydrogen basicity of A^-, but such a usage is accompanied by the inconvenient fact that such an equilibrium, involving two ions as reactants and an electrically neutral species as product, should be very solvent dependent. Furthermore, in all the available measurements in solution the proton is not bare as shown but covalently bonded to some other base. It seems more convenient to measure the hydrogen basicity of A^- relative to that of some other species. Unless stated otherwise, all basicities referred to in this paper will be relative to the hydroxide ion; the property measured by the equilibrium constant for reaction 2 will be referred to simply as the hydrogen

$$H_2O + A^- \xrightarrow{K_A} HA + OH^- \tag{2}$$
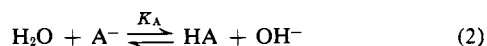
basicity of A^-.

If R^+ is some cation other than a proton, the equilibrium constant for reaction 3 measures the R basicity

$$ROH + A^- \xrightarrow{K_A{}^R} RA + OH^- \tag{3}$$

of A^-. There is a tendency for $K_A{}^R$ values to vary with the structure of A^- in somewhat the same way that K_A values do, but this correlation is far from perfect. The quotient $K_A{}^R/K_A$ is a measure of the imperfection of this correlation. If the R basicity of A^- were the same for every R as it is for hydrogen, this quotient would always have the value 1.0. This quotient is simply the equilibrium constant for reaction 4. $K_{HA}{}^{RA}$ measures

$$ROH + HA \xrightarrow{K_{HA}{}^{RA}} RA + H_2O \tag{4}$$
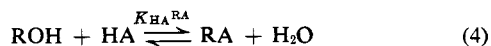
the R basicity of A^- relative to its hydrogen basicity. It may be noted that when the atom in the group A by which bonds are formed to H and R is oxygen, the same equilibrium constant may be used to determine two $K_{HA}{}^{RA}$ values. For example, when A is methoxy and R is ethyl, eq. 4 has the same form as when A is ethoxy and R is methyl; that is, $K_{HOMe}{}^{EtOMe}$ is identi-

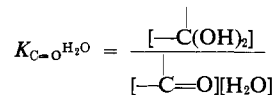cal with $K_{HOEt}{}^{MeOEt}$. From the relation

$$K_{HA}{}^{RA} = K_A{}^R/K_A \tag{5}$$

any one of the three K values may be obtained if the other two are known. In addition, calculations may be made indirectly, from equilibrium constants for addition to carbonyl compounds, for example. If

$$K_{C=O}{}^{HA} = \frac{[-\overset{|}{C}(OH)A]}{[-\overset{|}{C}=O][HA]}$$

and $\tag{6}$
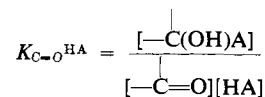
$$K_{C=O}{}^{H_2O} = \frac{[-\overset{|}{C}(OH)_2]}{[-\overset{|}{C}=O][H_2O]}$$

then

$$\frac{K_{C=O}{}^{HA}}{K_{C=O}{}^{H_2O}} = \frac{[-\overset{|}{C}(OH)A][H_2O]}{[-\overset{|}{C}(OH)_2][HA]} = K_{HA}{}^{RA} \tag{7}$$

If the compound $-\overset{|}{C}=O$ is $R'CHO$, the R group referred to in $K_{HA}{}^{RA}$ is the $R'CHOH$ group.

The values of $K_{HA}{}^{RA}$, $K_A{}^R$, and K_A used should be corrected for symmetry effects.[15]

Values of $K_{HA}{}^{RA}$ and $K_A{}^R$

In Table I are listed enthalpies and free energies of reaction in the gas phase at 25° for some reactions of the type represented by eq. 4. These data were calculated from experimental enthalpies of formation (except for t-butyl hydroperoxide, where an estimated value was used), and experimental and estimated entropies.[17] Although data were not available for many reactions of interest, Table I does not include all the reactions for which data were available. Most of the $K_{HA}{}^{RA}$ values listed were chosen to illustrate various points to be treated in the discussion; the tabulation is largely restricted to $K_{HA}{}^{RA}$ values for HA's whose ionization constants in water are known, so that carbon basicities ($K_A{}^R$ values) may be calculated in a common medium. For a number of the reactions, involving carefully studied compounds, the data given are probably reliable within a few tenths of a kilocalorie; very few values are thought to be in error by as much as 2 kcal. In the formation of dimethyl ether, the only one of the reactions listed for which we have found equilibrium constants determined at several temperatures, the free-energy change at 25° (extrapolated) is reported to be -4.4 kcal./mole,[18] in satisfactory agreement with the value calculated from thermochemical data. Values of $K_{HA}{}^{RA}$ (corrected for symmetry effects[15]) calculated from these free energies of reaction are listed in Table II.

To calculate values of $K_{HA}{}^{RA}$ in solution from the gas-phase values listed in Table II, the proper activity co-

(13) D. J. Cram, Chem. Eng. News, 41 (33), 92 (1963).
(14) G. G. Hammer, unpublished observations from this laboratory.

(15) Corrected values are obtained by multiplying the uncorrected values by the product of the symmetry numbers of the products and dividing by the product of the symmetry numbers of the reactants.[16] Inasmuch as this procedure gives the corrected constant only if the reactants and products are individual species, it is also necessary to multiply by two if there is an optically active reactant and divide by two if there is an optically active product.
(16) S. W. Benson, J. Am. Chem. Soc., 80, 5151 (1958).
(17) Sources of data and methods of estimation are described in the Appendix.
(18) P. H. Given, J. Chem. Soc., 589 (1943).

Table I. Enthalpies and Free Energies of Reaction in the Gas Phase at 25°[a]

Reaction						$\Delta H°$, kcal./mole	$\Delta G°$, kcal./mole
2MeOH			→	Me₂O	+ H₂O	−5.6	−3.9
2EtOH			→	Et₂O	+ H₂O	−5.6	−3.7
2i-PrOH			→	i-Pr₂O	+ H₂O	−3.4	−0.3
MeOH	+	PhOH	→	MeOPh	+ H₂O	−5.3	−4.4
t-BuOH	+	H₂O₂	→	t-BuOOH	+ H₂O	−9.0	−9.0
t-BuOH	+	t-BuOOH	→	t-Bu₂O₂	+ H₂O	−9.0	−8.1
MeOH	+	H₂S	→	MeSH	+ H₂O	−10.4	−10.2
MeOH	+	MeSH	→	Me₂S	+ H₂O	−13.2	−11.8
MeOH	+	PhSH	→	MeSPh	+ H₂O	−12.9	−11.6
PhOH	+	MeSH	→	MeSPh	+ H₂O	−5.8	−5.2
MeOH	+	HCN	→	MeCN	+ H₂O	−19.9	−19.3
i-PrOH	+	HCN	→	i-PrCN	+ H₂O	−18.0	−17.3
MeOH	+	HCH₂Ac	→	MeCH₂Ac	+ H₂O	−16.4	−16.1
i-PrOH	+	HF	→	i-PrF	+ H₂O	+3.5	+3.6
MeOH	+	HCl	→	MeCl	+ H₂O	−7.3	−7.0
MeOH	+	HBr	→	MeBr	+ H₂O	−9.6	−9.3
MeOH	+	HI	→	MeI	+ H₂O	−11.0	−10.8
MeOH	+	H₂	→	MeH	+ H₂O	−27.6	−27.9

[a] See ref. 17.

Table II. K_{HA}^{RA} Values in the Gas Phase at 25°[a]

R	A	K_{HA}^{RA}	R	A	K_{HA}^{RA}
Me	OMe	3×10^3	Et	OEt	2×10^3
Me	OPh	3×10^3	i-Pr	OPr-i	6
Me	SH	3×10^7	i-Pr	CN	1×10^{13}
Me	SMe	2×10^9	i-Pr	F	4×10^{-3}
Me	SPh	6×10^8	t-Bu	OOH	4×10^6
Me	CN	3×10^{14}	t-Bu	OOBu-t	3×10^6
Me	CH₂Ac	2×10^{11}	Ph	OMe	3×10^3
Me	Cl	3×10^6	Ph	SMe	1×10^4
Me	Br	1×10^7			
Me	I	2×10^8			
Me	H	1×10^{21}			

[a] See ref. 15.

efficient ratio is needed. We calculated values in aqueous solution from relation 8 where the subscripts

$$(K_{HA}^{RA})_w = (K_{HA}^{RA})_g \frac{(c/p)_{RA}(c/p)_{H_2O}}{(c/p)_{ROH}(c/p)_{HA}} \quad (8)$$

w and g refer to the aqueous and gas phases, respectively, and where the c/p ratio for each of the four species involved in eq. 4 is the ratio of the concentration (c) of the species in a dilute aqueous solution to the partial pressure (p) of the species over the same solution. In some cases we used data from solutions that were not as dilute as might be desired. In the cases of compounds whose mutual solubilities with water are small we assumed that the partial pressure of the compound is the same when it is saturated with water as when it is pure. In some cases the data shown for 25° were obtained by interpolation or extrapolation from data at other temperatures. These approximations should result in uncertainties that are small compared to those due to uncertainties in the thermodynamic data used (a 1.4-kcal. error in $\Delta G°$ will result in a tenfold error in K_{HA}^{RA}). The solubility and vapor pressure data, partly from the literature and partly determined in the present investigation, are summarized in Table III. These activity coefficients were used with eq. 8 to calculate 12 of the values of K_{HA}^{RA} listed in Table IV. Additional values calculated from equilibrium constants that have been determined in aqueous solution

for other reactions of the type of eq. 4 are also included. Also listed in Table IV are values of K_{HA}^{RA} calculated by use of eq. 7 from the equilibrium con-

Table III. Activity Coefficients in the Gas Phase Referred to Infinite Dilution in Water at 25°[a]

Compd.	Concn., M	Partial pressure, mm.	c/p
H₂O	55.3[b]	23.8[c]	2.33
MeOH	1.09	3.85	0.283
EtOH	1.33	6.3	0.211
i-PrOH	0.352	1.55	0.227
Me₂O	0.99[b,d]	760	0.00130
Et₂O	0.80[b]	537[c]	0.00149
i-Pr₂O	0.02[b]	151[c]	0.00013
PhOH	0.213	0.333	0.640
PhOMe	0.0013[b]	4.16	0.00031
H₂S	0.102[b]	760	0.000134
MeSH	0.330[b,d]	760	0.000434
Me₂S	0.353[b,d]	485[c]	0.000728
PhSH	0.0076[b,d]	1.92[c]	0.0040
PhSMe	0.0041[b,d]	0.76[c]	0.0054
HCN	1.83	150	0.0122
MeCN	1.59	42	0.038
Me₂CO	0.17	41	0.0041
MeCOEt	0.47	50	0.0094
H₂	0.00078[b]	760	1.03×10^{-6}
MeH	0.00143[b]	760	1.88×10^{-6}

[a] For sources of data see the appendix. [b] Saturated solution. [c] Vapor pressure of the pure compound. [d] Determined in the present investigation.

stants for additions to aldehydes and ketones given in Table V.

Discussion

K_{HA}^{RA} **Values.** Some of the major variations in the enthalpies and free energies of reaction listed in Table I and in the K_{HA}^{RA} values listed in Tables II and IV may be explained in terms of electronegativities. According to Pauling's equation,[19] the bond energy of the A–B bond (in kcal./mole) is equal to the average of the A–A and

(19) L. Pauling, "The Nature of the Chemical Bond," 3rd Ed., Cornell University Press, Ithaca, N. Y., 1960, pp. 88–105.

Table IV. Values of K_{HA}^{RA}, K_A, and K_A^R in Water at 25°[a]

R	A	K_{HA}^{RA}	K_A	K_A^R
Me	OMe	1.1×10^2	1.1×10^{-1b}	1.2×10
Me	OPh	1.4×10	9.0×10^{-7c}	1.3×10^{-5}
Me	SH	8×10^8	1.0×10^{-9d}	8×10^{-1}
Me	SMe	2×10^{10}	1.9×10^{-6e}	4×10^4
Me	SPh	7×10^9	3.0×10^{-10e}	2
Me	CN	7×10^{15}	1.5×10^{-7f}	1.0×10^9
Me	CH₂Ac	4×10^{12}		
Me	H	1.5×10^{22}		
Et	OEt	1.7×10^2	9×10^{-1b}	1.5×10^2
Et	OAc	6.8^g	2.6×10^{-12h}	1.8×10^{-11}
i-Pr	OPr-i	4×10^{-2}	8^i	3×10^{-1}
CF₃CH₂	OAc	2.6×10^{-2g}	2.6×10^{-12h}	7×10^{-14}
HOCH₂	OCH₂OH	4.6^j	3.3×10^{-3k}	1.5×10^{-2}
HOCH₂	C(NO₂)₂Me	1.1×10^{6l}	6.1×10^{-12l}	6.7×10^{-6}
HOCH₂	C(NO₂)₂Cl	1.0×10^{8l}	2.9×10^{-13l}	2.8×10^{-7}
HOCH₂	C(NO₂)₂Br	1.9×10^{8l}	1.3×10^{-13l}	2.5×10^{-7}
HOCH₂	C(NO₂)₃	1.4×10^{6l}	5.2×10^{-17l}	7.3×10^{-11}
HOCH₂	C(NO₂)₂CN	6.3×10^{5l}	2.7×10^{-23l}	1.7×10^{-17}
MeCHOH	CN	6.5×10^{5m}	1.5×10^{-7f}	9.8×10^{-2}
Me₂COH	CN	4×10^{5m}	1.5×10^{-7f}	6×10^{-2}
Me₂COH	CH₂Ac	4×10^{2m}		
N-Methyl-9-phenyl-9-acridyl	SPh	2.5×10^{6n}	3.0×10^{-10e}	7.4×10^{-4}
Ph	OMe	1.4×10	1.1×10^{-1b}	1.5
Ph	SMe	6×10^5	1.9×10^{-6e}	1.1
Ph	OAc	4.3×10^{-4o}	2.6×10^{-12h}	1.1×10^{-15}
p-O₂NC₆H₄	OAc	1.3×10^{-5o}	2.6×10^{-12h}	3.4×10^{-17}
Ac	OEt	6.8^g	9×10^{-1b}	6.1
Ac	OCH₂CH₂OMe	2.8^g	6×10^{-2p}	1.7×10^{-1}
Ac	OCH₂CH₂Cl	9.2×10^{-1g}	1.8×10^{-2p}	1.7×10^{-2}
Ac	OCH₂CH₂NMe₃⁺	7.9×10^{-1g}	9×10^{-3o}	7×10^{-3}
Ac	OCH₂CF₃	2.6×10^{-2g}	2.1×10^{-4p}	5.5×10^{-6}
Ac	OC₆H₄OMe-p	1.6×10^{-3o}	1.5×10^{-6c}	2.4×10^{-9}
Ac	OC₆H₄Me-p	9.8×10^{-4o}	1.6×10^{-6c}	1.6×10^{-9}
Ac	OPh	4.3×10^{-4o}	9.0×10^{-7c}	3.9×10^{-10}
Ac	OC₆H₄Cl-p	3.0×10^{-4o}	2.4×10^{-7c}	7.2×10^{-11}
Ac	OC₆H₄NO₂-m	6.0×10^{-5o}	2.2×10^{-8c}	1.3×10^{-12}
Ac	OC₆H₄NO₂-p	1.3×10^{-5o}	1.3×10^{-9c}	1.7×10^{-13}
Ac	OPO₃²⁻	1.4×10^{-3o}	4.5×10^{-5q}	6.3×10^{-8}
Ac	ON(Me)Ac	3.2×10^{-3o}	6.4×10^{-8o}	2.0×10^{-10}
Ac	SCH₂CH₂NHAc	5.9×10^{-2o}	2.7×10^{-7o}	1.6×10^{-8}
Ac	NC₃H₃N[r]	1.2×10^{-5o}	1.5×10^{-2s}	2×10^{-7}

[a] All values have been corrected for symmetry effects. See ref. 15. All K_{HA}^{RA} values were obtained by applying activity corrections from Table III to vapor phase K_{HA}^{RA} values from Table II, unless otherwise noted. [b] Data from J. Murto, *Ann. Acad. Sci. Fennicae AII*, No. 117 (1962). [c] A. I. Biggs and R. A. Robinson, *J. Chem. Soc.*, 388 (1961). [d] M. M. Kreevoy, E. T. Harper, R. E. Duvall, H. S. Wilgus, III, and L. T. Ditsch, *J. Am. Chem. Soc.*, **82**, 4899 (1960). [e] M. M. Kreevoy, B. E. Eichinger, F. E. Stary, E. A. Katz, and J. H. Sellstedt, *J. Org. Chem.*, **29**, 1641 (1964). [f] R. M. Izatt, J. J. Christensen, R. T. Pack, and R. Bench, *Inorg. Chem.*, **1**, 828 (1962). [g] Data from ref. 10. [h] H. C. Brown, D. H. McDaniel, and O. Häfliger, "Determination of Organic Structures by Physical Methods," E. A. Braude and F. C. Nachod, Ed., Academic Press Inc., New York, N. Y., 1955, Chapter 14. [i] J. Hine and M. Hine, *J. Am. Chem. Soc.*, **74**, 5266 (1952). It is assumed that this value of K_A is the same in water as in isopropyl alcohol. [j] P. S. Skell and H. Suhr, *Chem. Ber.* **94**, 3317 (1961). [k] R. P. Bell and D. P. Onwood, *Trans. Faraday Soc.*, **58**, 1557 (1962). [l] Data from ref. 9. [m] Obtained by applying eq. 7 to data from Table V. [n] From data in 37.6 wt. % acetone–62.4 wt. % water.[4] [o] Data from ref. 11. [p] P. Ballinger and F. A. Long, *J. Am. Chem. Soc.*, **82**, 795 (1960). [q] I. M. Kolthoff, *Rec. trav. chim.*, **46**, 350 (1927). [r] 1-Imidazolyl. [s] H. Walba and R. W. Isenee, *J. Org. Chem.*, **26**, 2789 (1961).

Table V. Equilibrium Constants for Additions to Aldehydes and Ketones in Water at 25°[a]

Carbonyl compd.	HA	K_{C-O}^{HA}
MeCHO	H₂O	1.1×10^{-2b}
MeCHO	HCN	7.1×10^{3c}
Me₂CO	H₂O	2×10^{-5d}
Me₂CO	HCN	7.1^e
Me₂CO	HCH₂Ac	9×10^{-3f}

[a] All K values have been corrected for symmetry effects. See ref. 15. [b] R. P. Bell and J. C. Clunie, *Trans. Faraday Soc.*, **48**, 439 (1952). [c] W. F. Yates and R. L. Heider, *J. Am. Chem. Soc.*, **74**, 4153 (1952). [d] R. W. Redding, unpublished results (at 35°) from this laboratory. [e] D. P. Evans and J. R. Young, *J. Chem. Soc.*, 1310 (1954). [f] K. Koelichen, *Z. physik. Chem.*, **33**, 129 (1900).

B–B bond energies plus 23 times the square of the difference in electronegativities of A and B (eq. 9). Because

$$BE_{AB} = \frac{BE_{AA} + BE_{BB}}{2} + 23(X_A - X_B)^2 \qquad (9)$$

of the second-power dependence on electronegativity differences, reactions of the type under consideration will be exothermic when, of the four bonds being formed and broken, the bond between the atoms with the largest difference in electronegativities is in one of the products, and endothermic when this bond is in one of the reactants. Inasmuch as an O–H bond is formed in all the reactions in question, there will be a bond with

a greater electronegativity difference in the reactants only in the case where the A group in eq. 4 is fluorine. Hence only in this case does the Pauling equation predict that the reaction will be endothermic. It is found that in the only case in which A is fluorine, the formation of isopropyl fluoride (Table I), the reaction is indeed endothermic. In all the cases in which the atom through which the group A forms bonds is less electronegative than oxygen the Pauling equation predicts that the reaction will be exothermic, and, if entropy effects are not too large, that K_{HA}^{RA} will be larger than 1.0. The data in Tables I, II, and IV show that such reactions are exothermic or K_{HA}^{RA} is larger than 1.0 in all cases where the group R is saturated or aromatic, although there are two exceptions (when A is SCH$_2$-CH$_2$NHAc and imidazolyl) when R is acetyl, which will be discussed later.

Although qualitative agreement with Pauling's equation is good in the cases where R is saturated, in the sense that all the reactions predicted to be exothermic are, and the only reaction predicted to be endothermic is, there are quantitative discrepancies of a magnitude sufficient to warrant discussion. A reaction whose net result may be described as breaking one C–H and one C–O bond and forming one O–H and one C–C bond (the nitrile- and ketone-forming reactions in Table I) is predicted by eq. 9 to be exothermic by 18.4 kcal./mole, in satisfactory agreement with the data shown. However, inasmuch as Pauling's electronegativities for sulfur and iodine are the same as that of carbon, the reactions involving the formation of C–S and C–I bonds are predicted to be equally exothermic, whereas actually they are considerably less exothermic. Such deviations would be expected, in view of the familiar tendency of carbon-bound sulfur and iodine to behave as if they are more electronegative than carbon (e.g., the Hammett *meta* substituent constants for CH$_3$, CH$_3$S, and I are −0.069, 0.15, and 0.352, respectively[5b]).

The 18.4-kcal. exothermic character predicted by eq. 9 for C–C bond-forming reactions of the type of eq. 4 would correspond to a K_{HA}^{RA} value of about 3×10^{13} at 25°, in the absence of entropy effects. The relevant gas-phase K_{HA}^{RA} values listed in Table II are reasonably near this figure, as are the K_{HA}^{RA} values for C–C bond-forming reactions in water listed in Table IV in those cases where R is a saturated hydrocarbon radical. In the cases where R bears an α-hydroxy substituent, however, K_{HA}^{RA} is much smaller. This effect of α-hydroxy substituents is no doubt partly due to the fact that the reference base is hydroxide ion; the combination of hydroxide ions with α-hydroxy alkyl cations results in the formation of a compound with two oxygen atoms attached to the same saturated carbon atom, a structural feature that is accompanied by an increased stability that amounts to about 7.0 kcal./mole and has been attributed to double bond–no bond resonance.[20] Such a 7-kcal. effect can explain about half of the approximately 10^{10}-fold decrease in K_{HA}^{RA} values brought about by the introduction of an α-hydroxy substituent into R (compare, in Table IV, the cases where A is CN and R is Me, MeCHOH, and Me$_2$COH, or where A is CH$_2$Ac and R is Me and Me$_2$COH). We have no satisfactory explanation for the other half of the effect of α-hydroxy groups.

(20) J. Hine, ref. 1a.

For those A groups in which the atom by which A is attached to H and R in eq. 4 is an oxygen atom, eq. 9 predicts a heat of reaction of zero and, in the absence of entropy effects, a K_{HA}^{RA} value of 1.0. The data in Tables I, II, and IV include a number of major deviations from this prediction. In Table II, for example, it may be seen that the carbon basicities, or more specifically the *t*-butyl basicities, of the hydroperoxide anion and the *t*-butyl hydroperoxide anion are more than 10^6 times as large as their hydrogen basicities (these data refer to the gas phase, but it would require an activity coefficient effect far larger than any observed in the present study to prevent the *t*-butyl basicity of these peroxy anions from being larger than their hydrogen basicities in water as well as in the gas phase). This observation provides information about the "α-effect" of Edwards and Pearson, who discussed the high nucleophilicity of bases whose nucleophilic atoms have as an α-substituent an atom with an unshared electron pair.[21] Gerstein and Jencks have already noted that in nucleophilic attack on acyl carbon atoms the α-effect is not only a kinetic but a thermodynamic effect.[11] The present data show that it is also a thermodynamic effect in the attack of nucleophiles on saturated carbon.
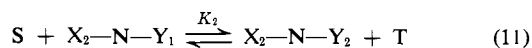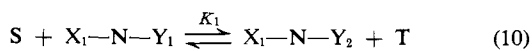
It may be seen from the K_{HA}^{RA} values in Table IV that, although the methyl basicity of the thiomethylate anion is 2×10^{10} times as large as its hydrogen basicity, its phenyl basicity is only 6×10^5 times as large as its hydrogen basicity. This decrease in carbon basicity is presumably due to the relatively small amount of resonance interaction between a phenyl group and a divalent sulfur atom attached to it (compared to the amount of resonance interaction between phenyl and hydroxyl, the reference base). Toward the acetyl group, where the amount of resonance interaction with attached oxygen is even greater, the carbon basicity of the sulfur base is actually smaller than its hydrogen basicity, as Gerstein and Jencks[11] and others have pointed out in somewhat different terms.

It is noteworthy that in one series of reactions for which data is given in Table IV substituents in A change the carbon basicity in the same manner that they change the hydrogen basicity, so that K_{HA}^{RA} remains essentially constant, whereas in another series, substituents in A change the carbon basicity to a much greater extent than they change the hydrogen basicity. Thus, the hydroxymethyl basicities of various dinitromethyl anions remain within a factor of two of 10^6 times as large as their hydrogen basicities over a range of (five) substituents whose presence changes either hydroxymethyl basicity or the hydrogen basicity by a factor of about 10^{12}. On the other hand substituents that change the hydrogen basicities of a series of alkoxide and aryloxide anions by about 10^9 change the acetyl basicities by more than 10^{14}, or more than 10^5 times as much. These facts may be rationalized in the following terms.

In a generalized derivation that in specific cases leads to the Hammett and Taft equations, it has been shown[5c,22] for the reaction

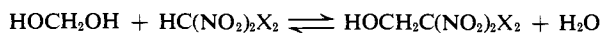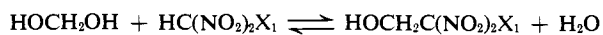(21) J. O. Edwards and R. G. Pearson, *J. Am. Chem. Soc.*, **84**, 16 (1962).

(22) In the derivation referred to,[5c] A was the common reactant and B was the common product in the two reactions. They have been replaced by S and T in the present discussion in order to avoid confusion with other A's and B's used in this paper. In this derivation[5c] the left-hand sides of eq. 4–4, 4–6, 4–8, and 4–9 should be prefaced by a minus sign.

$$S + X_1\text{---}N\text{---}Y_1 \xrightleftharpoons{K_1} X_1\text{---}N\text{---}Y_2 + T \qquad (10)$$

$$S + X_2\text{---}N\text{---}Y_1 \xrightleftharpoons{K_2} X_2\text{---}N\text{---}Y_2 + T \qquad (11)$$

that

$$\log \frac{K_1}{K_2} = \tau_N(\sigma_{X_2}{}^N - \sigma_{X_1}{}^N)(\sigma_{Y_2}{}^N - \sigma_{Y_1}{}^N) \qquad (12)$$

where the σ^N values are the polar substituent constants for the substituents denoted by subscripts when attached to the group N, and τ_N is a measure of the efficiency of transmittal of polar substituent effects through the group N in a given solvent at a given temperature. If in eq. 10 and 11 S is formaldehyde hydrate, T is water, N is the dinitromethylene group, Y_1 is hydrogen, Y_2 is the hydroxymethyl group, and X_1 and X_2 are two of the five substituents studied by Hall,[9] we have the equilibria

$$HOCH_2OH + HC(NO_2)_2X_1 \rightleftharpoons HOCH_2C(NO_2)_2X_1 + H_2O$$

$$HOCH_2OH + HC(NO_2)_2X_2 \rightleftharpoons HOCH_2C(NO_2)_2X_2 + H_2O$$

whose equilibrium constants[15] are the $K_{HA}{}^{RA}$ values that measure the hydroxymethyl basicities of the two $C(NO_2)_2X^-$ anions relative to their hydrogen basicities. According to eq. 12, the relative magnitudes of two such $K_{HA}{}^{RA}$ values will be proportional to $\sigma_{CH_2OH}{}^N - \sigma_H{}^N$, the difference between the polar substituent constants of the hydroxymethyl and hydrogen substituents (as substituents on a dinitromethylene group). If the Taft substituent constants σ^* are regarded as satisfactory measures of these substituent constants, it may be seen that the known values (0.49 and 0.56 for the hydrogen and hydroxymethyl substituents, respectively[5d]) are very close to each other. Similarly, the Hammett *para* substituent constants for hydrogen (0.00) and hydroxymethyl (-0.01)[23] substituents are equal, within the experimental uncertainty (no σ_m appears to have been determined for the hydroxymethyl substituent). Therefore the term $\sigma_{CH_2OH}{}^N - \sigma_H{}^N$ would be expected to be small and the values of $K_{HA}{}^{RA}$ in this series of reactions would be expected to be relatively insensitive to the electron-withdrawing power of the various X-substituents. Because of various uncertainties, such as the notoriously poor behavior of the hydrogen substituent in certain correlations, we could not have predicted that the changes in $K_{HA}{}^{RA}$ would be hardly larger than the experimental error.

When S is acetic acid, T is water, N is oxygen, Y_1 is hydrogen, Y_2 is acetyl, and X_1 and X_2 are two of the XOH compounds whose acetylation was studied by Gerstein and Jencks, eq. 10 and 11 assume the form

$$AcOH + HOX_1 \rightleftharpoons AcOX_1 + H_2O$$

$$AcOH + HOX_2 \rightleftharpoons AcOX_2 + H_2O$$
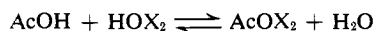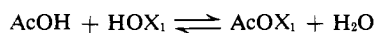
whose equilibrium constants[15] are the $K_{HA}{}^{RA}$ values that measure the acetyl basicities of the two XO^- anions relative to their hydrogen basicities. According to eq. 12, the relative magnitudes of two such $K_{HA}{}^{RA}$ values will be proportional to $\sigma_{Ac}{}^N - \sigma_H{}^N$, the difference between the polar substituent constants of the acetyl and hydrogen substituents (as substituents on oxygen). The substituent constants for hydrogen and acetyl are seen to differ considerably, regardless of whether one chooses σ^* values (0.49 and 1.65, respectively),[5d] σ_m

(23) O. Exner and J. Jonaš, *Collection Czech. Chem. Commun.*, **27**, 2296 (1962).

values (0 and 0.376),[5b] or σ_p values (0 and 0.502)[5b]; as cases in which hydrogen and acetyl are attached to oxygen the σ_m values 0.121 and 0.39 for hydroxy and acetoxy, respectively, or the corresponding σ_p values -0.37 and 0.31 may be quoted.[5b] Thus, $\sigma_{Ac}{}^N - \sigma_H{}^N$ will be a positive number much larger in magnitude than $\sigma_{CH_2OH}{}^N - \sigma_H{}^N$ (for the hydroxymethylation reaction) and, according to eq. 12, $K_{HA}{}^{RA}$ values will decrease as the electron-withdrawing power of X increases (τ-values are always positive), as they are seen to do in Table IV.

It is interesting that in all the examples listed in Tables II and IV the carbon basicities of methoxide and ethoxide ions are greater than their hydrogen basicities. The generalization that the carbon basicities of most simple primary alkoxide ions are greater than their hydrogen basicities also offers an explanation for the fact that the equilibrium constants for hemiacetal formation by aliphatic aldehydes in alcohol solution are considerably larger (often more than ten times as large) than the equilibrium constants for the hydration of the same aldehydes in aqueous solution,[24,25] although such a comparison is complicated by the fact that the reactions were carried out in different solvents. Secondary and tertiary alcohols add to aldehydes to a smaller extent than primary alcohols do (although secondary alcohols often add to a greater extent than water does).[24,25] This is presumably due to steric hindrance, as is the small value for $K_{HA}{}^{RA}$ in the case where R is isopropyl and A is isopropoxy (*cf.* Table IV); in fact, the formation of di-*t*-butyl ether from the corresponding alcohol is significantly endothermic (4.8 kcal./mole),[26] unlike any of the ether formations shown in Table I. The explanation for the relatively high carbon basicity of primary alkoxide ions is less obvious, however. Steric hindrance would tend to make the carbon basicities of all alkoxide ions smaller than their hydrogen basicities. The $K_{HA}{}^{RA}$ values that are relevant in the present case are the equilibrium constants for the splitting out of a small molecule, water, between two larger alcohol molecules to give a still larger ether molecule. The fact that this reaction is accompanied by favorable enthalpy and free-energy changes recalls the similar situation in the case of the isosteric hydrocarbons; *e.g.*, see Table VI.[27] Pitzer and Catalano have

Table VI

⌐——— Reaction ———⌐	ΔH°, kcal./mole	ΔG°, kcal./mole
$2MeCH_3 \rightarrow Me_2CH_2 + CH_4$	-2.24	-2.03
$2EtCH_3 \rightarrow Et_2CH_2 + CH_4$	-3.25	-2.91

suggested that the favorable energy changes in these hydrocarbon reactions are due to London forces (electron correlation energies).[29]

(24) W. Herold, *Z. physik. Chem.*, **18B**, 265 (1932).

(25) I. L. Gauditz, *ibid.*, **48B**, 228 (1941).

(26) G. Pilcher, A. S. Pell, and D. J. Coleman, *Trans. Faraday Soc.*, **60**, 499 (1964).

(27) Enthalpies and free energies of reaction were calculated from the compilation of data by Rossini and co-workers.[28]

(28) F. D. Rossini, K. S. Pitzer, R. L. Arnett, R. M. Braun, and G. C. Pimentel, "Selected Values of Physical and Thermodynamic Properties of Hydrocarbons and Related Compounds," Carnegie Press, Pittsburgh, Pa., 1953.

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

$K_A{}^R$ *Values and Nucleophilicity.* If in a series of related reactions a structural change results in the formation of a more stable product, this increased stability may be reflected in the transition state. Although structural changes do not *always* change reaction rates in the same direction that they change equilibrium constants, they *usually* do. It is often implied that the fairly numerous exceptions to this generalization include those cases in which the less basic (toward hydrogen) of two species is the more nucleophilic (toward carbon). Actually such a case will be an exception to the general rule only if a species that is less basic toward a given carbon atom under a given set of conditions is also more nucleophilic toward the same carbon atom under the same conditions. Although there does not appear to be enough data available to permit a very general discussion of the correlation between carbon basicity and carbon nucleophilicity, the present data warrant some comment.

The $K_{HA}{}^{RA}$ values in Table IV show that the methyl basicities of thiolate anions are around 10^{10} times as great as their hydrogen basicities. Observations that various reactions of the type

RSH + R'OR'' (or R'OH) $\longrightarrow$ RSR' + R''OH (or H_2O)
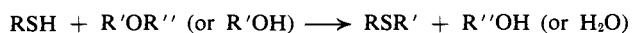
give good yields of sulfides[30,31] support the qualitative conclusion that thiolate anions are more basic toward saturated carbon than toward hydrogen.

The $K_A{}^R$ values in Table IV show that the methyl basicity of thiomethylate and thiophenylate anions is 10^3 to 10^5 times as great as that of the corresponding oxygen species. Qualitatively, similar conclusions follow from observations under conditions other than aqueous solution at 25°. For example, Hughes and Thompson reported that 1 mole of anisole, 1 mole of thiophenol, and 1.5 moles of potassium hydroxide in ethanol at 200° give quantitative yields of phenol and thioanisole,[32] showing that the following equilibrium lies almost entirely to the right. In view of such ob-

PhS⁻ + PhOMe $\rightleftharpoons$ PhSMe + PhO⁻
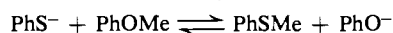
servations it seems probable that in hydroxylic solvents[33] the basicity of alkylthiolate and arylthiolate anions toward saturated carbon[34] will be greater than that of the corresponding alkoxide and aryloxide anions. Thus the qualitative fact that alkoxide and aryloxide anions are usually less nucleophilic toward saturated carbon but more basic toward hydrogen than the corresponding thiolate anions is not an exception to the generalization that structural changes in the reactant tend to cause rates to change in the same direction that equilibrium constants do. There are many exceptions to this generalization to be found in the field of nucleophilic displacement reactions, however. In the area of nucleophilic displacements on hydrogen, deviations from the Brønsted catalysis equation[35] provide a number of such exceptions. Bunnett and

Baciocchi have described an interesting case in which the relative rates at which thioethylate and methoxide anions attack benzyldimethylcarbinyl derivatives by the E2 mechanism is reversed as the leaving group is changed from dimethyl sulfide to the methanesulfinate anion.[36] The observation of McCleary and Hammett that iodide ions are more nucleophilic but less basic than hydroxide ions toward ethyl *p*-toluenesulfonate in aqueous dioxane[37] provides an exception in the area of nucleophilic displacements on carbon; other examples could be given.

Inasmuch as the $K_{CN}{}^{Me}$ value listed in Table IV shows that the methyl basicity of cyanide ions is 10^9 times as large as that of hydroxide ions the reactivity of cyanide ions toward methyl iodide in 50% aqueous dioxane might have been expected to exceed that of hydroxide ions by more than the 28-fold factor observed.[38]

Rate–equilibrium correlations tend to improve as the differences in structure between the compounds whose reactions are being compared are decreased. For this reason a correlation between basicity and nucleophilicity of hydroxide ions and alkoxide ions would be expected to be a better correlation than if the hydroxide ions were being compared with carbanions or thiolate anions. Murto's estimate that methoxide ions react with methyl iodide five times as rapidly as hydroxide ions do in aqueous methanol at 20°[39] is thus qualitatively correlated with the $K_{OMe}{}^{Me}$ value in Table IV that shows the methyl basicity of methoxide ions to be some twelve times that of hydroxide ions. Bender and Glasson[40] and England and co-workers,[41,42] among others, have also pointed out the greater nucleophilicity of methoxide ions compared to hydroxide ions. Judging from the $K_A{}^R$ values in Table IV, other simple alkoxide ions would also be expected to be more basic toward carbon than hydroxide ions are, although in some cases steric effects will bring about exceptions to this rule.

It might be expected that the nucleophilicities of various bases in nucleophilic aromatic substitution reactions and in nucleophilic attack on such acyl derivatives as acid anhydrides, acid halides, esters, etc., would be correlated with their aryl basicities (*e.g.*, *p*-nitrophenyl basicities), and acyl basicities (*e.g.*, acetyl basicities). However, most such reactions proceed by a stepwise mechanism in which a reactive intermediate is formed by the addition of the nucleophile to an sp^2 carbon atom, changing its hybridization to sp^3. Aryl basicities and acyl basicities are measures of the stability of the products, in which the nucleophile has become bonded to the sp^2 carbon of an aryl or acyl group. Regardless of whether the first or second step of the reaction is rate controlling, the transition state will ordinarily lie nearer to the reactive intermediate than to the reactants or products,[43,44] and when the first step is rate controlling, as it usually is in the reactions that have been

(30) G. Illuminati and H. Gilman, *J. Am. Chem. Soc.*, 71, 3349 (1949).
(31) M. E. Cain, M. B. Evans, and D. F. Lee, *J. Chem. Soc.*, 1694 (1962).
(32) G. K. Hughes and E. O. P. Thompson, *Nature*, 164, 365 (1949).
(33) In such solvents as dimethyl sulfoxide, where the basicity of alkoxide ions (toward hydrogen, at least) is markedly increased, this generalization may not hold.
(34) This generalization may fail when the carbon atom in question bears α-alkoxy or other substituents that would permit double bond–no bond resonance interactions with a hydroxy group.
(35) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, Chapter X.

(36) J. F. Bunnett and E. Baciocchi, *Proc. Chem. Soc.*, 238 (1963).
(37) H. R. McCleary and L. P. Hammett, *J. Am. Chem. Soc.*, 63, 2254 (1941).
(38) M. F. Hawthorne, G. S. Hammond, and B. M. Graybill, *ibid.*, 77, 486 (1955).
(39) See Table IV, footnote *b*.
(40) M. L. Bender and W. A. Glasson, *J. Am. Chem. Soc.*, 81, 1590 (1959).
(41) R. G. Burns and B. D. England, *Tetrahedron Letters*, No. 24, 1 (1960).
(42) I. R. Alet and B. D. England, *J. Chem. Soc.*, 5259 (1961).
(43) J. E. Leffler, *Science*, 117, 340 (1953).
(44) G. S. Hammond, *J. Am. Chem. Soc.*, 77, 334 (1955).

investigated, the product is not even being formed in the rate-controlling step of the reaction. Hence, although rates of nucleophilic aromatic substitution and nucleophilic attack on acyl carbon atoms may not be correlated well with any kind of carbon basicities, they would be expected to be correlated better with basicities toward saturated carbon than with basicities toward unsaturated carbon. In attempting any such correlations, however, it should be remembered that relative basicities toward saturated carbon vary with the nature of the substituents on the carbon atom in question; complications attributable to double bond–no bond resonance are common and important, as already pointed out in the previous section.

Double bond–no bond resonance should not significantly complicate correlations of nucleophilicity and basicity in the case of alkoxide ions because alkoxy groups should participate in such resonance to essentially the same extent that the reference group hydroxy does. Therefore, since primary alkoxide ions are usually more basic toward saturated carbon than hydroxide ions are, they would be expected to be more reactive in nucleophilic aromatic substitution reactions, and indeed methoxide ions have been estimated to be 185 times as reactive as hydroxide ions toward p-dinitrobenzene,[39] 38 times as reactive toward o-dinitrobenzene,[39] and 20 and 33 times as reactive toward 2,4-dinitrochlorobenzene.[42,45]

Toward activated aromatic chlorides, bromides, and iodides thiophenylate anions usually show the increased reactivity (compared to alkoxide and hydroxide ions) that characterizes their reactions with aliphatic halides.[46] Toward the corresponding fluorides (and sulfonate esters, etc.) the hydroxide and alkoxide ions have the advantage of yielding intermediates that should be stabilized by double bond–no bond resonance. This fact provides an explanation for the diminished relative reactivity of thiophenylate ions toward aromatic fluorides noted by Bunnett (and explained in terms of London forces).[47]

Double bond–no bond resonance (or whatever the factor is that results in the particular stability of compounds with several oxygen or fluorine atoms attached to the same saturated carbon atom) should be of even greater importance in influencing nucleophilicity in attack on acid anhydrides, acyl halides, esters, etc. Reactions of this type involve the formation of an intermediate that always has at least one oxygen atom and may have as many as four oxygen, fluorine, and/or nitrogen atoms attached to the carbon atom at which nucleophilic attack took place. For this reason bases such as carbanions, thiolate anions, etc., whose addition to a carbonyl group would give a species with much less stabilization by double bond–no bond resonance than the species formed by addition of the reference base hydroxide ion, will show greatly diminished basicity toward carbon atoms of the type under consideration and therefore will probably show greatly diminished nucleophilicity in attacking acyl carbon atoms.

Interpretation of the available experimental data in terms of the generalization made in the preceding paragraph is complicated by the fact that the rate-controlling step varies from one case to another, and in many cases proton-transfer reactions are of importance in determining the observed reaction rate. Nevertheless, these generalizations seem to be supported by a number of observations, only a few of which will be cited here. Unsubstituted primary alkoxide ions are more nucleophilic in attacking acyl carbon, just as they are in attacking alkyl and aryl carbon. For example, Murto has estimated that methoxide ions attack acetic anhydride 14 times as rapidly as hydroxide ions do.[39] The following sequence of reactivities toward ethyl chloroformate, reported by Green and Hudson:[48,49] $Me_2C\!\!=\!\!NO^- > OH^- > PhO^- > NO_2^- > N_3^- > F^- > Br^-$, I^-, SCN^-, OCN^-, ClO_4^-, and NO_3^-, shows that reagents such as iodide and thiocyanate ions, which are usually more nucleophilic toward saturated carbon than hydroxide ions are,[5e] display greatly diminished relative reactivity. These reagents ordinarily use as their nucleophilic atom an atom of high atomic weight, which cannot enter significantly into double bond–no bond resonance interactions as can the oxygen, nitrogen, and fluorine atoms that are present in all the six nucleophiles that are reasonably reactive toward ethyl chloroformate. The hydrogen basicities of these six species stand in the order OH^-[50] $> Me_2C\!\!=\!\!NO^-$[51] $> PhO^-$[50] $> N_3^-$[52] $> F^-$[53] $\sim NO_2^-$[54], but the effect of electronegativities on bond energies should cause the carbon basicity of the azide ion to be higher than its hydrogen basicity and the carbon basicity of the fluoride ion to be lower than its hydrogen basicity. In addition, the carbon basicities of the acetoxime, azide, and nitrite[55] anions should be increased, relative to their hydrogen basicities, by the α-effect. It is therefore possible that the order of nucleophilicities observed is the same as the order of basicities toward the carbon atom in question.

A particularly striking example of the tendency of fluorine and/or oxygen atoms to cluster around the same saturated carbon atom is found in the report of Bradley, Redwood, and Willis that the higher alkali metal fluorides react with carbonyl fluoride to give stable solid salts of trifluoromethanol.[56] A striking

$$F_2CO + KF \longrightarrow F_3COK$$
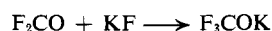
example of the α-effect in an equilibrium process is the observation of Zinner and Ritter that N,O-dimethylhydroxylamine gives aldehyde adducts so stable that they may be distilled without decomposition.[57]

$$MeNHOMe + PrCHO \longrightarrow PrCH\!-\!NOMe$$
$$\qquad\qquad\qquad\qquad\quad | \quad\;\; |$$
$$\qquad\qquad\qquad\qquad\;\; OH \;\; Me$$

Experimental

In order to determine gas solubilities, a 200-ml.; three-necked flask was more than 90% immersed in a

(45) J. F. Bunnett and G. T. Davis, *J. Am. Chem. Soc.*, 76, 3011 (1954).

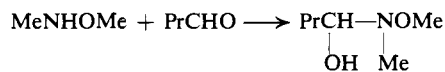(46) *Cf.* J. F. Bunnett, *Quart. Rev.* (London), 12, 1 (1958).

(47) J. F. Bunnett, *J. Am. Chem. Soc.*, 79, 5969 (1957).

(48) M. Green and R. F. Hudson, *Proc. Chem. Soc.*, 149 (1959).

(49) R. F. Hudson and M. Green, *J. Chem. Soc.*, 1055 (1962).

(50) See appropriate footnotes in Table IV.

(51) C. V. King and A. V. Marion, *J. Am. Chem. Soc.*, 66, 977 (1944).

(52) N. Yui, *Bull. Inst. Phys. Chem. Research* (Tokyo), 20, 390 (1941); *Chem. Abstr.*, 36, 1230⁶ (1942).

(53) H. H. Broene and T. De Vries, *J. Am. Chem. Soc.*, 69, 1644 (1947).

(54) H. Schmid, R. Marchgraber, and F. Dunkl, *Z. Elektrochem.*, 43, 337 (1937).

(55) In the present discussion we refer to the basicity of the oxygen atoms of the nitrite ion.

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(57) G. Zinner and W. Ritter, *Angew. Chem. Intern. Ed. Engl.*, 2, 399 (1963).

$25 \pm 2°$ water bath, fitted with a calibrated dropping funnel, and attached to a vacuum manifold and a 100-ml. gas buret with a water jacket kept at $25 \pm 2°$. Also attached to the manifold were a vacuum pump, a McLoed gauge, a rubber balloon, and a cylinder of the gas whose solubility was to be measured. The level of the confining liquid (mercury) in the gas buret was raised to the stopcock at the top of the buret; this stopcock and the stopcock on the dropping funnel were then closed and the remainder of the system (flask, manifold, gauge, and tubing leading to the gas cylinder and balloon) was evacuated to a pressure of 0.1 mm. or less. The stopcocks leading to the vacuum pump and gauge were closed and gas was admitted to the system until the balloon showed that the internal pressure exceeded the external pressure. The stopcock leading to the gas buret was then opened, and when the buret was partly full of gas the internal and external pressures were equalized by use of the leveling bulb. Next, the stopcock between the flask and the manifold was closed, and a measured volume of freshly degassed water was added through the dropping funnel to the flask, where it was stirred with a magnetic stirrer.

In the measurements on methyl mercaptan the level of the mercury in the gas buret was then raised so as to keep the system at atmospheric pressure (or at a known pressure near atmospheric). With the more soluble dimethyl ether the pressure was allowed to drop to as little as 450 mm. (determined by measuring the difference in mercury levels between the gas buret and the leveling bulb and subtracting from the barometric pressure). In each case after the system had reached equilibrium, more water was added and the process was repeated.

The volume of the flasks and tubing leading to the surrounding stopcocks was determined (by filling with water and measuring the volume of water required) to be 260 ml. The amount of methyl mercaptan or dimethyl ether present in the vapor phase was calculated by use of the ideal gas laws with a correction for the pressure of the water vapor, which was assumed to saturate the contents of the flask but to be absent from the gas buret. Both gases were so soluble in water that deviations from ideality or even the correction for the vapor pressure of water would not greatly change the results obtained. The concentration of methyl mercaptan or dimethyl ether in the aqueous phase was calculated from the volume of water added and the amount of solute that had disappeared from the vapor phase. In five experiments on dimethyl ether the ratio of concentration of ether in the aqueous phase to partial pressure of ether (in mm.) in the vapor phase was $(13.0 \pm 0.2) \times 10^{-4}$. Three experiments on methyl mercaptan gave the ratio $(4.34 \pm 0.07) \times 10^{-4}$.

The solubilities of dimethyl sulfide, thiophenol, and thioanisole in water were determined by ultraviolet measurements on their diluted saturated solutions. The liquid in question was stirred vigorously with water for at least 4 hr. in an erlenmeyer flask surrounded by a water bath at $25 \pm 2°$. In the case of dimethyl sulfide, the cloudy suspension separated into two clear layers rather shortly after stirring was discontinued. In the cases of thiophenol (where all experiments were carried out under nitrogen) and thioanisole, the cloudy suspension was centrifuged (still at $25 \pm 2°$) until at least

the aqueous layer was clear. In each case a sample of the clear, aqueous layer was taken by use of a syringe and diluted volumetrically by a factor that preliminary experiments had shown would give a solution with an absorbance in the range 1.0–2.0 at the wave length(s) at which measurements were to be made. Dilutions were made by adding a known volume of the more concentrated solution to a volumetric flask that already contained an amount of water such that it was filled almost to the mark by the added concentrated solution. This procedure avoided the loss of solute vapors. To determine the needed extinction coefficients, standard methanolic solutions of the compounds were diluted volumetrically with water in such a manner that the final solutions upon which spectral measurements were made contained no more than 1% methanol. Water containing the same concentration of methanol as the sample solution was used as the reference solution. Although dimethyl sulfide absorbs fairly strongly below about 2200 Å., no absorption maximum was seen above 2000 Å. Extinction coefficients, increasing from 242 to 1576 M^{-1} cm.$^{-1}$, were measured at ten wave lengths ranging from 2300 to 1975 Å. Measurements on the diluted saturated solution, using a Cary spectrophotometer, Model 14, gave the value 0.353 ± 0.004 M for the solubility. In the cases of thioanisole and thiophenol, measurements were made at the absorption maxima at 2500 and 2360 Å., respectively, where extinction coefficients of 9060 and 7400 M^{-1} cm.$^{-1}$, respectively, had been determined, yielding values for the solubility of 4.07×10^{-3} and 7.56×10^{-3} M in water at 25°. Sakodynskii and Babkov reported aqueous solubilities of $(8.5 \pm 1.4) \times 10^{-3}$ M and $(11.1 \pm 0.8) \times 10^{-3}$ M for thiophenol at 20 and 40°, respectively.[58]

Appendix

Enthalpies of formation, entropies, and free energies of formation for most of the organic oxygen compounds were obtained from the review by Green,[59] and the values for the elements and for most of the other compounds with no more than two carbon atoms were obtained from the compilation by Rossini and co-workers.[60] When either the enthalpy of formation or the entropy was obtained from any other source the free energy of formation was calculated in the present investigation. Other sources were used for the enthalpies of formation for methyl mercaptan,[61] thiophenol,[61] thioanisole,[61] dimethyl sulfide,[61] dimethyl ether,[26] diethyl ether,[26] diisopropyl ether,[26] t-butyl hydroperoxide (an estimated value),[62] di-t-butyl peroxide,[62] hydrogen peroxide,[63] and isobutyronitrile.[64] The gas-phase enthalpies of formation of methyl ethyl ketone and anisole were calculated from the liquid-phase values,[59] using the reported heat of vaporization (8.31 kcal./mole) of methyl ethyl ketone and a value (10.96 kcal./mole) for anisole estimated by the method

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of Klages.[65]   To calculate the enthalpy of formation of isopropyl fluoride, the enthalpy of hydrogenation of isopropyl fluoride to propane and hydrogen fluoride at 248°[66] was used. The heat capacities of hydrogen,[60] hydrogen fluoride,[60] propane,[28] and isopropyl fluoride[67] at 25° were used to calculate the enthalpy of hydrogenation at 25°.[68] This value (-20.69 kcal./mole) led to the value -68.33 kcal./mole for the heat of formation of isopropyl fluoride. Entropies of diethyl ether, diisopropyl ether, and methyl ethyl ketone were calculated from the Benson and Buss rule of additivity of group properties and those of anisole,[69] t-butyl hydroperoxide, di-t-butyl peroxide, thiophenol,[69] thioanisole,[69] isobutyronitrile,[70] and isopropyl fluoride from their rule of additivity of bond contributions.[63] The entropy values listed by Benson and Buss were used for hydrogen peroxide, methyl mercaptan, and dimethyl sulfide.[63]

Reported values for the solubility of diethyl ether,[71] diisopropyl ether,[72] anisole,[73] hydrogen sulfide,[74] hy-

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(67) The value 19.48 cal. deg.$^{-1}$ mole was calculated by the method of adding bond contributions.[63]
(68) The use of constant heat capacities over the temperature range 25–248° is based on the approximation that the heat capacities of propane and isopropyl fluoride will increase by the same amount over this range. Changes in the relative heat capacities of hydrogen and hydrogen fluoride will be negligible.
(69) Since the Ph-H and Ph–C bond contributions are 1.2 and 1.0 e.u. lower than the C–H and C–C bond contributions, it was assumed that the Ph-O and Ph–S bond contributions are 1.1 e.u lower than the C–O and C–S contributions, respectively. With the Ph–O contribution thus obtained the entropy of phenol may be calculated with an error of only 0.56 e.u.
(70) This value (74.8 e.u.) was calculated by adding to the entropy of acetonitrile[60] the contributions for two more C–C bonds and four more C–H bonds and making the symmetry number correction.
(71) J. Timmermans, "The Physico-Chemical Constants of Binary Systems in Concentrated Solutions," Vol. 4, Interscience Publishers, Inc., New York, N. Y., 1960.
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drogen,[75] and methane[76] in water at 25°, and for the vapor pressures of pure water, diethyl ether,[71] diisopropyl ether,[77] and dimethyl sulfide[78] at 25° were used. The vapor pressure of thiophenol was calculated from an equation derived from data at higher temperatures,[79] and that of thioanisole from its boiling point[80] and Dreisbach's Cox chart No. 10.[81] For methanol and ethanol, solutions of the concentrations shown are reported to have the partial pressures of alcohol shown in Table III.[71] It was assumed that the partial pressure of hydrogen cyanide over a 1.83 M solution at 18°[71] increases by the same factor that the vapor ·pressure of pure hydrogen cyanide does[71] when the temperature is increased to 25°. The partial pressure of acetonitrile was calculated by interpolation and extrapolation from data on solutions of similar concentration at 20 and 30°.[71] Data on the partial pressures of isopropyl alcohol,[82] phenol,[71] acetone,[71] and methyl ethyl ketone[71] at concentrations near those shown in Table III and temperatures in the area 35–90° were adjusted to a common concentration and a plot of log p vs. $1/T$ was prepared. From the resultant slightly curved lines the partial pressure at 25° was estimated by extrapolation.

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The Volume of Activation in Elimination Reactions

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Volumes of activation have been measured for El and E2 reactions of neutral and ionic substrates. The transition states for elimination and substitution are almost equal in volume for every combination of charge-type and mechanism. The transition states for the formation of Hofmann and Saytzeff products from a common starting material are also equal within experimental error. The results permit inferences concerning the nature of the bonding in the transition states.

Introduction

In recent years there has been great interest in the detection of the structural details of transition states

in olefin-forming elimination reactions. Two relatively new and promising methods of investigation are the solvent isotope effect[1] and heavy element isotope effects.[2] Still another research tool as yet not applied to elimination reactions is the determination of volumes of activation by measurement of the effect of hydrostatic pressure on reaction rates. The application of this technique to the study of organic reaction mechanisms has been recently reviewed.[3]

The work reported here was directed to three prin-

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