[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Quantitative Correlation of Relative Rates. Comparison of Hydroxide Ion with Other Nucleophilic Reagents toward Alkyl Halides, Esters, Epoxides and Acyl Halides[1]

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A two-parameter equation is found to correlate the relative rates of 47 reactions (11 new, 36 from the literature) of various nucleophilic reagents (water, chloride ion, hydroxide ion, aniline, etc.) with various organic substrates (alkyl halides, esters, epoxides, acyl halides and a sulfonium ion) in water solution with a mean median deviation of only a factor of 1.5, although the mean variation in relative rates from water to the most nucleophilic reagent measured for each substrate is more than a factor of 10^5. This equation is $\log(k/k^0) = sn$ where k^0 is a rate constant for reaction with water, k is the corresponding rate constant for reaction with any other nucleophilic reagent, s (the substrate constant) is characteristic of only the substrate and defined as 1.00 for methyl bromide in water at 25° and n (the nucleophilic constant) is characteristic of only the nucleophilic reagent and defined as 0.00 for water. Typical nucleophilic constants are 2.7 for acetate ion, 3.0 for chloride ion, 4.0 for azide ion, 4.2 for hydroxide ion, 4.5 for aniline, 5.0 for iodide ion and 6.4 for thiosulfate ion. Typical substrate constants are 0.66 for ethyl tosylate, 0.77 for β-propiolactone, 0.95 for β-chloroethylethylenesulfonium ion, 1.00 for 2,3-epoxypropanol, and 1.43 for benzoyl chloride. Contrary to previous belief, the nucleophilic reactivity of hydroxide ion toward epoxides or acyl halides is not abnormally low (based on methyl bromide as a standard substrate). A four-parameter equation allows for variations in the electrophilic reagent (water, phenol, hydrogen ion, mercuric bromide, etc.) as well. The Brönsted catalysis laws, Grunwald–Winstein correlation and the two-parameter equation are corollaries of the four-parameter equation.

A polar displacement reaction of an uncharged organic molecule (S) may generally be abbreviated as

$$\mathrm{N} + \mathrm{S} + \mathrm{E} \rightleftarrows \text{[transition state]} \longrightarrow \text{products}$$

where N is a nucleophilic reagent and E is an electrophilic reagent.[2] The over-all rate constant (k) for this reaction may then be compared with the corresponding rate constant (k^0) where water acts as both N and E in the same medium at the same temperature.

$$\mathrm{H_2O} + \mathrm{S} + \mathrm{H_2O} \rightleftarrows \text{[different transition state]} \longrightarrow$$

The linear free-energy relationship correlating these rates would be

$$\log(k/k^0) = sn + s'e \qquad (1)$$

where the nucleophilic constant, n, is a quantitative measure of the nucleophilic reactivity[3] of N ($n = 0$ for H_2O), the electrophilic constant, e, measures the electrophilic reactivity of E ($e = 0$ for H_2O) and the substrate constants, s and s', measure the discrimination of S among different N and E reagents.

Although equation 1 is new, three of the simpler corollaries derivable from it are well known and useful quantitative relationships between structure and reactivity. If N and S are fixed and e is proportional to the logarithm of the acid ionization constant of E (*i.e.*, $e = (-\alpha/s')(pK_a)$), the Brönsted catalysis law for acids[4] results.

$$\log(k_a/k_{a'}) = \alpha \log(K_a/K_{a'})$$
$$\log k_a = \alpha \log K_a + C$$
$$k_a = G_a K_a^{\alpha}$$

If S and E are fixed and n is proportional to the logarithm of the basic ionization constant of N (*i.e.*, $n = (-\beta/s)(pK_b)$), the Brönsted catalysis law for bases[4] results.

$$k_b = G_b K_b^{\beta}$$

If sn is negligibly small compared to $s'e$, then

$$\log k/k^0 = s'e \qquad (2)$$

For the special subcase where E is the solvent, if one substitutes $s' = m$ ($m = 1$ for $t\text{-}C_4H_9Cl$) and $e = Y$ ("solvent ionizing power"), the Grunwald–Winstein correlation of solvolysis rates results.[5]

$$\log k/k^0 = mY$$

A fourth corollary, of equal importance, appears to have been neglected. If $s'e$ is negligibly small compared to sn, then

$$\log k/k^0 = sn \qquad (3)$$

In this work, the applicability and accuracy of equation 3 have been evaluated using only water as E, hydroxide ion, aniline, water and other nucleophilic reagents as N, and alkyl halides, esters, epoxides and acyl halides as S in water solutions at 25°. Since $e = 0$ for water, the $s'e$ term of equation 1 vanishes.[6]

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[1] Paper X in the series, Concerted Displacement Reactions. Paper IX, C. G. Swain, THIS JOURNAL, **74**, 4108 (1952). This work was supported by the Office of Naval Research, contract no. N5-ori-07838, project no. NR056-198. For full experimental data for all runs, see C. B. Scott, Ph.D. Thesis, M.I.T., Jan., 1952.

[2] C. G. Swain and R. W. Eddy, *ibid.*, **70**, 2989 (1948); C. G. Swain, *ibid.*, **72**, 4583 (1950); *Record of Chemical Progress*, **12**, 21 (1951); C. G. Swain and W. P. Langsdorf, Jr., THIS JOURNAL, **73**, 2816 (1951); C. G. Swain and J. F. Brown, Jr., *ibid.*, **74**, 2538 (1952); C. G. Swain, *ibid.*, **74**, 4108 (1952).

[3] Both "nucleophilic" and "basic" mean having a tendency to supply an unshared pair of electrons to form a new covalent bond. However, nucleophilic is used in discussion of *rate*, whereas basic refers to *equilibrium* conditions. Thus thiosulfate and other thiols are more nucleophilic in displacements on carbon than would have been anticipated from their basicity (toward H_3O^+) in water solution. Electrophilic and acidic are the corresponding antonyms. For the noun meaning nucleophilic reactivity, character, power or strength (analogous to basicity), "nucleophilicity," "nucleophilia" and "nucleophilyl" have been suggested, but none has been widely adopted.

[4] J. N. Brönsted and K. J. Pedersen, *Z. physik. Chem.*, **108**, 185 (1924); J. N. Brönsted, *Chem. Revs.*, **5**, 320 (1928).

[5] E. Grunwald and S. Winstein, THIS JOURNAL, **70**, 846 (1948); **73**, 2700 (1951). Actually these authors chose 20% water–80% ethanol rather than water as the standard solvent for which $k = k^0$ and $Y = 0$; this merely caused a shift in the abscissa scale of $Y - e = +3.56$. Note that equation 2 would also result if sn were large but constant or practically constant for any reason. This would correspond to choosing a different reaction, involving a constant amount of nucleophilic driving force (sn), as the standard reaction for which $k = k^0$ and $s' = 1$; this would merely cause a shift in the ordinate scale equal to sn.

[6] Equation 3 is formally similar to the Hammett equation, which correlates the effect of *m*- and *p*-substituents in compounds containing a phenyl group (L. P. Hammett, *ibid.*, **59**, 96 (1937); "Physical Or-

TABLE I

Log (k/k^0)

Substrate	CH_3COO^-	Cl^-	Br^-	N_3^-	HO^-	$C_6H_5NH_2$	SCN^-	I^-	$S_2O_3^=$
Ethyl tosylate[a]	..	2.26	2.61	...	3.00	...	..	3.11	...
Benzyl chloride[b]	2.51	..	..	...	3.59	...	..	...	...
β-Propiolactone[c]	2.49	2.26	2.77	...	6.08[d]	...	3.58	3.48	5.28
Epichlorohydrin[e]	2.54	2.82	3.55	...	...	...	4.56	4.76	...
Glycidol[e]	..	3.04	3.89	...	4.11[f]	...	4.77	5.08	...
Mustard cation[g]	2.72	3.04	..	...	5.62[d]	4.60[h]	4.54	4.54	6.15
Methyl bromide	..	..	..	4.00[i]	4.20[i]	4.49[j]	..	5.04[k]	6.36[l]
Benzenesulfonyl chloride[m]	..	..	..	...	5.87	5.15	..	...	...
Benzoyl chloride[m]	2.86	..	..	...	6.00	6.38	..	...	...

[a] H. R. McCleary and L. P. Hammett, THIS JOURNAL, **63**, 2254 (1941); in 39% water–61% dioxane at 50°. [b] G. W. Beste and L. P. Hammett, *ibid.*, **62**, 2481 (1940); in 39% water–61% dioxane at 50°. [c] P. D. Bartlett and G. Small, *ibid.*, **72**, 4867 (1950); in water at 25°. [d] Not used to calculate best line. [e] Reference 7a; in water at 20°. [f] In water at 20°. [g] Reference 9; from β,β'-dichlorodiethyl sulfide in 95% water–5% ethanol at 25°. [h] C. G. Swain, Ph.D. Thesis in Chemistry, Harvard University, 1944, p. 85. [i] In 99% water–1% acetone at 49.8°; in this solvent, $k/k^0 = 1.0 \times 10^4$ for N_3^-, 1.6×10^4 for HO^-. [j] In 50% water–50% acetone at 49.8°; in this solvent, $k/k^0 = 3.6 \times 10^4$ for N_3^-, 3.8×10^4 for HO^-, 3.1×10^4 for $C_6H_5NH_2$. [k] E. A. Moelwyn-Hughes, *Trans. Faraday Soc.*, **45**, 167 (1949); in water at 25°. [l] A. Slator and D. F. Twiss, *J. Chem. Soc.*, **95**, 93 (1909); in water at 25°. [m] In 50% water–50% acetone at 0.5°.

An auxiliary objective of this work was to compare the reactivity of hydroxide ion with that of other nucleophilic reagents. There has been considerable misunderstanding about the reactivity of hydroxide ion. In the reaction with ethylene oxides, it has been thought to be less reactive than chloride ion or even water.[7] In the Schotten-Baumann acylation procedure it also appears to be singularly unreactive.[8] Aniline and other amines are successfully acylated in spite of excess hydroxide ion. Yet with both the β-chloroethylethylenesulfonium ion[9] and triphenylcarbonium ion,[10] hydroxide ion is more reactive than water, chloride ion or aniline.

Much of the confusion is a result of insufficient data. In the present work, the relative reactivities of a sufficient number of nucleophilic reagents have been determined to show that, with minor variations, hydroxide ion actually fits very well into one reactivity series which holds over a wide range of organic compounds.

Substrate Constants and Nucleophilic Constants. Equation 3 was applied to all uncharged substrates for which data with four or more nucleophilic reagents in water solution was found in our own work or from the literature. All these data are included in the tables. In addition, data are included for the mustard ion (β-chloroethylethylenesulfonium ion), benzyl chloride and benzenesulfonyl chloride.

The relative rates of reaction with different nucleophilic reagents are unfortunately not perfectly independent of the solvent. This solvent effect often changes the relative rates by a factor of three or four for a change from 99% water–1% acetone to 50% water–50% acetone. A correction factor for the solvent should be determined, but in the absence of sufficient data, and with the recognition that a factor of four is small where relative reactivities of over a million are involved, the solvent effect has been neglected in calculating nucleophilic and substrate constants.

Table I lists the logarithms (common, base 10) of the relative rates. The *order* of reactivity of different nucleophilic reagents is remarkably constant considering the wide variation in structure of the substrates. However, the *spread* in relative rates, *i.e.*, the degree of discrimination or selectivity shown, varies widely from one substrate to another. For example, log (k_{OH^-}/k^0) is 3.0 for ethyl tosylate, 4.2 for methyl bromide, 6.0 for benzoyl chloride, 7.5 for acetyl fluoride,[11] 7.8 for benzoyl fluoride,[11] and 10.4 for ethyl acetate.[12]

Methyl bromide was chosen as a standard substrate for which $s = 1.00$.[13] Values of n for azide, hydroxide, iodide and thiosulfate ions and aniline were then defined by the equation

$$\log k/k^0 = n \qquad (4)$$

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ganic Chemistry," McGraw–Hill Book Co., Inc., New York, N. Y., 1940, Chapter VII; C. G. Swain and W. P. Langsdorf, Jr., THIS JOURNAL, **73**, 2813 (1951)). A large positive ρ is generally paralleled by a high s and low s', whereas if ρ is strongly negative, s is low and s' high. Thus ρ is strongly negative for reactions of trityl halides (the halides, not the carbonium ion), and the rate is not easily accelerated by hydroxide ion because s is so low that 1 M hydroxide ion cannot compete against 55 M water. This is more reasonable than the steric explanation which we previously suggested (*ibid.*, **70**, 1126 (1948), last paragraph).

Note that equation 3 should still hold, *i.e.*, log k/k^0 still should be a linear function of n, if no E is involved (as when S is a positive ion), or if $s'e$ is large but practically constant for any reason (as in a fixed nonaqueous medium); this would merely cause a shift in the ordinate scale equal to $s'e$. However, to apply the equation to a different medium, *e.g.*, to dry benzene solutions, new n values should be measured (based on suitable standards) in the new medium.

(7) J. N. Brönsted, M. Kilpatrick and M. Kilpatrick, *ibid.*, **51**, 428 (1929); L. P. Hammett, "Physical Organic Chemistry," McGraw–Hill Book Co., Inc., New York, N. Y., 1940, p. 302.

(8) L. P. Hammett, *ibid.*, p. 303.

(9) A. G. Ogston, E. R. Holiday, J. St. L. Philpot and L. A. Stocken, *Trans. Faraday Soc.*, **44**, 45 (1948); *cf.* also P. D. Bartlett and C. G. Swain, THIS JOURNAL, **71**, 1406 (1949).

(10) C. G. Swain, Carleton B. Scott and Karl H. Lohmann, *ibid.*, **75**, 136 (1953).

(11) C. G. Swain and C. B. Scott, *ibid.*, **75**, 246 (1953).

(12) E. M. Terry and J. Stieglitz, *ibid.*, **49**, 2216 (1927); A. Skrabal and A. Zahorka, *Monatsh.*, **53**, 562 (1929).

(13) Methyl bromide is chosen as a standard compound because of its simplicity, and because, in the future, additional n values can be more easily obtained from it than from compounds which have been scrutinized more in the past (mustard gas, trityl ion, ethylene oxides or β-propiolactone). Strictly speaking $s = 1$ for only one medium and only one temperature. We define pure water and 25° as these standard conditions. However, in practice the dependence of s on % water and on temperature is small from pure water to 50% water–50% acetone and from 25–50°; hence data from mixed sources and over this range of conditions are used to set up the n scale. A more refined treatment would extrapolate all data to pure water and to 25°. If the difference in entropy of activation for k and k^0 reactions is negligible, the change in s with temperature is given by $298\, s_{298} = T s_T$, where T is the absolute temperature. This corresponds to only an 8% decrease in s from 25 to 50°.

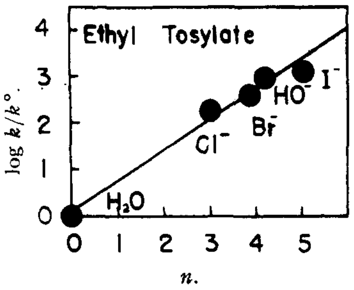

Fig. 1.

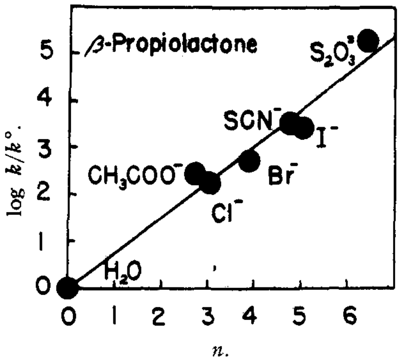

Fig. 2.

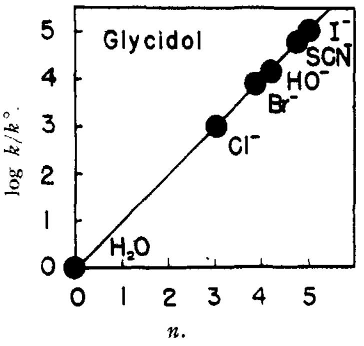

Fig. 3.

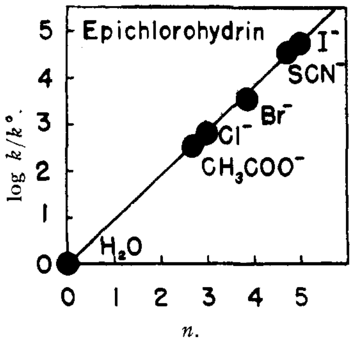

Fig. 4.

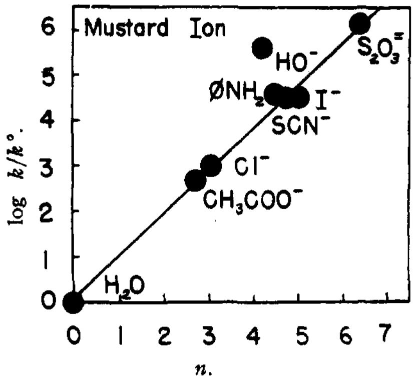

Fig. 5.

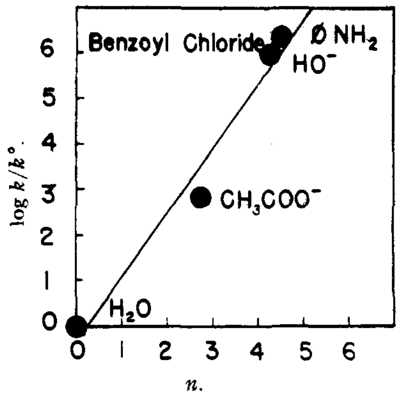

Fig. 6.

These values of n were plotted against log k/k^0 for epichlorohydrin (2,3-epoxypropyl chloride) and a line, of slope s, fitted to the points by the method of least squares. The slope of the line defined a value of s for epichlorohydrin. Using epichlorohydrin, as a secondary standard, a value of n for acetate ion was determined by equation 3. A similar procedure was used with glycidol (2,3-epoxypropanol) to obtain values of n for chloride ion, bromide ion and thiocyanate ion, these data not being available from methyl bromide. The nucleophilic constants, n, are shown in Table II.

TABLE II

NUCLEOPHILIC CONSTANTS[a]

N	n	Number of substrates	Median deviation
H_2O	0.00	9	0.03
CH_3COO^-	2.72[b]	5	.14
Cl^-	3.04[c]	5	.09
Br^-	3.89[c]	4	.09
N_3^-	4.00	1	
HO^-	4.20	6	.15
$C_6H_5NH_2$	4.49	4	.27
SCN^-	4.77[c]	4	.09
I^-	5.04	6	.21
$S_2O_3^=$	6.36	3	.04
		47	Mean 0.12

[a] The n values are based on methyl bromide except where noted. Experimental conditions given in Table I. [b] Calculated from epichlorohydrin. [c] Calculated from glycidol.

A substrate constant, s, was determined for each substrate by plotting the observed values of log k/k^0 against the corresponding n values and fitting the points with a straight line by the method of least squares. The slope of the line is s, and the values of s obtained are listed in Table III. Figures 1–6 show plots of log k/k^0 *vs.* n for six of the substrates.

TABLE III

SUBSTRATE CONSTANTS[a,b]

Substrate[b]	s	Number of N	Median deviation	log k_1	Water, M
Ethyl tosylate	0.66	5	0.28	−5.22	21.6
Benzyl chloride	.87	3	.10	−5.94	21.6
β-Propiolactone	.77	7	.30	−4.25	55.5
Epichlorohydrin	.93	6	.03	−6.01	55.5
Glycidol	1.00	6	.01	−6.55	55.5
Mustard cation	0.95	7	.07	−2.54	52.7
Methyl bromide	1.00	6	(.00)	−5.04[c]	55.5
Benzenesulfonyl chloride	1.25	3	.42	−4.57	27.8
Benzoyl chloride	1.43	4	.20	−3.28	27.8
		47	Mean 0.18[d]		

[a] Calculated by the method of least squares from all data in Table I except for two reactions specifically noted in Table I. [b] Experimental conditions and references given in Table I. [c] In 99% water–1% acetone at 49.8°. [d] Excluding methyl bromide.

The deviations between the experimental points and the best straight line reported in Tables II and III are measured along the n scale. The only serious deviations are +3.74 for β-propiolactone and +1.64 for the mustard cation with hydroxide ion. These are discussed below in the section on the reactivity of hydroxide ion. All the other deviations from equation 3 are less than 0.60, which is remarkably small considering that the structural variations are made at the reacting center rather than at a distance from it (as in *m*- or *p*-substituted benzene derivatives). Some of the minor deviations observed are no doubt due to the unfortunate inconstancy of solvent and temperature of the points determining some of the lines.

The deviations are a measure of the probable precision of the prediction of rate that may be made from the values of *n* and *s*. The mean value of the probable error for the whole table (47 reactions) is only 0.18 in a range of 6.36 in *n* values (2.5% of the range). This means that k/k^0 or k may be estimated with a probable error of a factor of 1.5. Considering the magnitude of the variations correlated (more than 10^5 for the *average* substrate), this is an acceptable fit.

Scope.—Table V further extends the list of nucleophilic constants by the use of the mustard cation as another secondary standard, similar to epichlorohydrin and glycidol. However, as yet there are no data on other substrates to test the accuracy of predictions made with the values in Table IV.

TABLE IV

OTHER NUCLEOPHILIC CONSTANTS[a]

N	*n*
2,4.6-$(NO_2)_3C_6H_3O^-$	1.9[b]
$SO_4^{=}$	2.5
C_5H_5N	3.6
HCO_3^- or $HPO_4^{=}$	3.8[c]
$(NH_2)_2CS$	4.1
HS^- or $SO_3^{=}$	5.1
$HPSO_3^{=}$	6.6[c]

[a] These may be used in the same way as the *n* values in Table II. They are calculated from data[9a] on mustard ion using $s = 1.00$ for methyl bromide, $s = 0.95$ for mustard ion. [b] Glucose and *p*-toluenesulfonate are both < 1.0. [c] At *p*H 8.0. These species liberate acid on reaction with mustard ion or alkyl halides at *p*H 8.0.

TABLE V

CORRELATION BASED ON MUTAROTATION OF GLUCOSE

Substrate	*s*	*s'*	Deviations for N H_2O	CH_3COO^-	HO^-	Deviations for E H_2O	CH_3COOH	H_3O^+
Glucose[a]	1.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00
Acetone[b]	1.32	2.04	− .30	+ .42	− .16	+ .16	− .26	+ .11
Water[c]	1.77	4.33	− .22	+ .32	− .10	− .27	+ .48	− .21
Methyl bromide and epichlorohydrin[d]	0.50	..	−1.24	+1.80	− .56	....	....	....

[a] Mutarotation in water at 18°; log k/k^0 values from equation 5, C. G. Swain, THIS JOURNAL, 72, 4580 (1950). [b] Enolization in water at 25°; log k/k^0 values from equation 7, C. G. Swain, *ibid.*, 72, 4581 (1950). [c] From relative equilibrium constants for ionic dissociation in water at 25°. [d] From Table II; conditions given in Table I.

The high nucleophilic reactivity of feebly basic anions containing elements below the first row of the periodic table (Br^-, I^-, SCN^-, $S_2O_3^{=}$, $HPSO_3^{=}$) is striking. It is probably correlated with the high polarizability of the valence electrons of these elements.

Nucleophilic displacements on hydrogen instead of carbon, exemplified by the rates of mutarotation of glucose or enolization of acetone or the equilibrium basic ionization constants in water, show deviations more than twice those for the nucleophilic displacements on sulfur (benzenesulfonyl chloride). Accordingly it is perhaps better to set up a new n_h scale based on one of these reactions to be applied only to displacements on hydrogen. If the rate of mutarotation of glucose is chosen as a standard, n_h is 2.45 (*vs.* $n = 2.72$) for acetate ion and 7.80 (*vs.* $n = 4.20$) for hydroxide ion, *e* is 1.40 for acetic acid and 3.18 for hydronium ion. The much higher $n_{OH^-}/n_{CH_3COO^-}$ ratio needed to correlate these displacements on hydrogen is noteworthy. Table V shows that this correlation is satisfactory except for the displacements on carbon.

There is no reason why equations 1, 2 and 3 should not be applied to an entirely different medium, *e.g.*, dry benzene solutions. However, with this large a change in conditions, it is reasonable to expect that still other *n* and *e* scales will have to be defined to obtain satisfactory correlation, since the solvation of nucleophilic reagents is quite different in benzene and water. One could set $s = 1$ and $s' = 1$ for methyl bromide at 25° to define scales for the new medium.

Limitations.—None of the deviations for the 47 reactions seem to be clearly attributable to abnormal steric hindrance in the attack of N on S. However, further work will undoubtedly reveal that with more hindered nucleophilic reagents or more hindered substrates serious deviations due to steric differences can occur.[14]

When a major change in reaction type is made, for example from displacements on carbon to displacements on hydrogen, it is necessary to set up a new *n* scale (see previous section).

The reactions of hydroxide ion with β-propiolactone, the mustard cation and the trityl ion are out-of-line (see next section). It may prove desirable to assign special values of *n* to hydroxide ion when it is attacking these special types of carbon atoms.

The Reactivity of Hydroxide Ion.—Hydroxide ion is evidently not abnormally unreactive toward ethylene oxides and acyl halides, relative to water, other anions or aniline, as previously supposed (*cf.* Fig. 1). This conclusion is in agreement with recent comparisons of hydroxide ion and water toward ethylene oxide[15] and benzoyl chloride.[16]

The most striking deviation from equation 3 is the abnormally fast reaction of hydroxide ion with β-propiolactone. Hydroxide ion appears to attack the carbonyl carbon even though other N species with both higher and lower *n* values are attached

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[14] An inversion has been demonstrated in benzene solution: triethylamine is more nucleophilic than pyridine by a factor of 26 toward methyl iodide at 100°, but less nucleophilic by a factor of 6 toward isopropyl iodide. The inversion also occurs in nitrobenzene solution, where the corresponding factors are 28 and 1.5. K. J. Laidler and C. N. Hinshelwood, *J. Chem. Soc.*, 861 (1938).

[15] H. Lichtenstein and G. Twigg, *Trans. Faraday Soc.*, 44, 905 (1948).

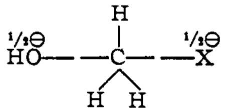
[16] R. F. Hudson and J. E. Wardill, *J. Chem. Soc.*, 1729 (1950).

to the alkyl carbon in the products. This preference of hydroxide ion for the carbonyl carbon suggests that the line for benzoyl chloride based on limited data on water, hydroxide ion and aniline may also be too steep, *i.e.*, that iodide ion and the sulfur anions may lie on a line of lower slope instead. Another serious deviation is in the abnormally fast reaction of hydroxide ion with the mustard cation.

With carbonium ions, relative rates are only poorly correlated by equation 3. For example, trityl ion has $s = 0.61$ for 8 N, median deviation = 0.75 out of a total range of 6.36 in n. The data used were those from trityl chloride in 6% water–2% dioxane–92% acetone at 25°, except for chloride ion, which was studied in 15% water–85% acetone at −34°.[10] The relative rates of thiosulfate, thiocyanate and hydroxide ions and aniline are all low if one regards water, acetate, chloride and azide ions as normal. The unusually low water concentration is not the principal cause of scatter because less complete data from trityl fluoride in 50% water–50% acetone at 25° show that thiosulfate and hydroxide ions are still low.

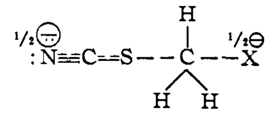
The following paragraphs propose an explanation for the slightly higher reactivity of hydroxide ion toward carbonyl carbons and the mustard cation and its slightly lower reactivity toward the trityl cation than is calculated from equation 3 using methyl bromide as a standard.

The transition state for attack of hydroxide ion on a methyl carbon is close to



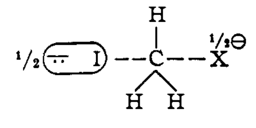
$$\overset{1/2\ominus}{HO}\cdots\overset{H}{\underset{H\ \ H}{C}}\cdots\overset{1/2\ominus}{X}$$

The repulsion between partial negative charges is greater than for attack by AcO^-, N_3^-, SCN^-, $S_2O_3^=$, Cl^-, Br^- or I^-, because in all these other cases the negative charge on N (the entering group) can be moved farther out, *e.g.*



$$\overset{1/2\ominus}{:N}{\equiv}C{=}S\cdots\overset{H}{\underset{H\ \ H}{C}}\cdots\overset{1/2\ominus}{X}$$

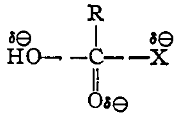
Halide ions (other than fluoride) are so polarizable that they resemble the four polyatomic anions more than hydroxide ion.



$$1/2(\ominus\ I)\cdots\overset{H}{\underset{H\ \ H}{C}}\cdots\overset{1/2\ominus}{X}$$

This polarizability also explains the large dipole moment (about 1.5 debye units) of methyl iodide, which exists in spite of the negligible difference in electronegativity between carbon (2.5) and iodine (2.4).[17]

The transition state for attack of hydroxide ion on a carbonyl carbon is stabilized by greater distribution of the negative charge on the substrate portion.

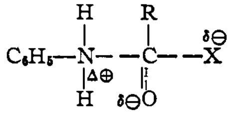


$$\overset{\delta\ominus}{HO}\cdots\overset{R}{\underset{\overset{\|}{O^{\delta\ominus}}}{C}}\cdots\overset{\delta\ominus}{X}$$

The added distribution represents less of an improvement for the other anions because they already had sufficient distribution without it. The result is abnormally high reactivity for hydroxide ion, relative to other anions, when it is attacking a carbonyl carbon.

Similarly hydroxide ion can be expected to be relatively better whenever it attacks a more positive center than that in methyl bromide because this means a less difficult transition state. Thus it should be abnormally reactive toward the mustard ion (because of adjacent positive sulfur) and should show more of a preference for attacking hydrogen instead of carbon than is shown by iodide or acetate ions. This also provides a *natural basis for the Hofmann rule, i.e.*, the exceptional behavior of hydroxide ion in attacking the most positive hydrogen in "onium" ions even though this gives a less stable olefin. On the other hand, triphenylcarbonium ion does not have a concentrated charge on the central carbon, even though it does have a unit charge over-all. The charge is so well delocalized (distributed into the rings) that the charge gradient near the central carbon (which directs the approach of hydroxide ion) is less than in the mustard ion or even in uncharged methyl bromide. Thus if one uses methyl bromide to measure the "normal" relative reactivity of hydroxide ion, hydroxide ion must inevitably appear abnormally good with mustard ion and abnormally poor with triphenylcarbonium ion by comparison.

Aniline generates a positive charge when it reacts. This cannot be well distributed, but may be stabilized by the proximity of an adjacent carbonyl oxygen atom.



$$C_6H_5{-}\overset{H}{\underset{H}{N}}{}^{\delta\oplus}\cdots\overset{R}{\underset{\overset{\|}{{}^{\delta\ominus}O}}{C}}\cdots\overset{\delta\ominus}{X}$$

The result is relatively high reactivity for amines when attacking a carbonyl carbon. However, there should be no such enhancement when amines attack the mustard cation, and within the experimental error none is observed.

Experimental

Reagents.—Benzoyl chloride from Eastman Kodak Co. was redistilled, b.p. 39° (3 mm.), $n^{20}D$ 1.5528.

Benzenesulfonyl chloride from Eastman Kodak Co. was redistilled, b.p. 100° (1 mm.).

Methyl bromide from the Westvaco Co., 99.5% pure, was used without further purification.

Glycidol from Eastman Kodak Co. was redistilled, b.p. 53–55° (12 mm.), $n^{25}D$ 1.4288.

Other reagents were either analytical reagent grade or previously described.[10]

Buffer Solutions.—Due to the great reactivity of acid halides with hydroxide ion and aniline, it was necessary to use buffers which would provide very low concentrations of these reactants. Since the reactivity experiments were conducted in 50% water–50% acetone solution, the equilibrium constants for these buffer solutions in water were not applicable. Hence aniline was titrated in 50% water–50% acetone with 0.985 M nitric acid at 0° using a Beckman model G pH meter. The pH reading at the half-neutraliza-

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[17] L. Pauling, "Nature of the Chemical Bond," Cornell Univ. Press, Ithaca, N. Y., 1945, p. 64.

TABLE VI

SAMPLE KINETIC DATA IN AQUEOUS ACETONE SOLUTIONS

Substrate	Concn. $M \times 10^3$	Water, % by volume	Temp., °C.	Added reagent	Concn., $M \times 10^3$	k_1, sec.$^{-1}$	Run no.
Glycidol	102	100	20	NaOH	178.3	1.2×10^{-5}	229
Methyl bromide	9.4	99	49.8	....	...	9.2×10^{-6}	158
	9.5	99	49.8	$LiClO_4$	100	9.2×10^{-6}	160
	10.5	99	49.8	NaOH	97.3	3.0×10^{-4}	162
	11.2	99	49.8	NaOH	97.3	2.6×10^{-4}	163
	11.8	99	49.8	NaOH	97.3	2.4×10^{-4}	164
	10.0	99	49.8	NaN_3	100	1.9×10^{-4}	165
	10.2	99	49.8	NaN_3	100	1.7×10^{-4}	166
	9.7	99	49.8	NaN_3	200	3.6×10^{-4}	167
	12.3	50	49.8	....	...	3.6×10^{-6}	182
	12.4	50	49.8	....	...	3.7×10^{-6}	183
	11.4	50	49.8	$LiClO_4$	100	3.6×10^{-6}	184
	11.1	50	49.8	$LiClO_4$	100	3.7×10^{-6}	185
	13.4	50	49.8	NaOH	101.7	5.2×10^{-4}	186
	13.0	50	49.8	NaOH	101.7	5.0×10^{-4}	187
	11.4	50	49.8	NaN_3	100	4.8×10^{-4}	170
	7.0	50	49.8	$C_6H_5NH_2$	100	4.1×10^{-4}	269
Benzenesulfonyl chloride	5.7	50	24.8	....	...	2.5×10^{-4}	221
	4.7	50	24.8	$HClO_4$	100	2.4×10^{-4}	232
	4.6	50	24.8	$LiClO_4$	100	2.3×10^{-4}	233
	3.9	50	0.5	$LiClO_4$	40	2.7×10^{-5}	227
	2.1	50	0.5	$H_3BO_3{}^a$	20	1.4×10^{-4}	223
				NaH_2BO_3	20		
	2.1	50	0.5	$H_3BO_3{}^a$	10	1.3×10^{-4}	225
				NaH_2BO_3	10		
	4.4	50	0.5	$HNO_3{}^c$	80	4.0×10^{-5}	234
				$C_6H_5NH_2$	50		
	4.1	50	0.5	$HNO_3{}^b$	40	1.0×10^{-3}	236
				$C_6H_5NH_2$	50		
Benzoyl chloride	4.7	50	0.5	CH_3COOH	80	5.3×10^{-4}	214
	4.5	50	0.5	HNO_3	30	5.2×10^{-4}	219
	2.4	50	0.5	$H_3BO_3{}^a$	20	2.9×10^{-3}	153
				NaH_2BO_3	20		
	2.2	50	0.5	$H_3BO_3{}^a$	10	2.8×10^{-3}	155
				NaH_2BO_3	10		
	4.8	50	0.5	CH_3COONa	40	1.1×10^{-3}	213
				CH_3COOH	40		
	4.7	50	0.5	$HNO_3{}^c$	80	5.3×10^{-3}	216
				$C_6H_5NH_2$	50		

[a] Hydroxide ion concentration = 1.6×10^{-4} *N*. [b] Aniline concentration = 1.1×10^{-2} *M*. [c] Aniline concentration = 1.1×10^{-4} *M*.

tion point, converted to hydronium ion concentration, gave an apparent acid ionization constant for anilinium ion[18] of 3.6×10^{-5} valid only for these conditions. The ratio of aniline to anilinium ion was determined for the reactivity experiments by observing the *p*H reading of the reaction mixture prior to the addition of the acid halide and applying the equilibrium constant obtained above. The validity of this method was checked by allowing benzenesulfonyl chloride to react in two 50% acetone solutions which had aniline concentrations differing by a factor of 100. The rate constants for the reactions of aniline with benzenesulfonyl chloride differed by less than a factor of 1.5.

Since the above method was not applicable for determining hydroxide ion concentration, a correction factor for the *p*H meter was obtained by preparing standard solutions of sodium hydroxide in water and 50% water–50% acetone and observing the *p*H reading of these solutions. The meter averaged 1.2 *p*H units higher in the acetone solutions than in the water solutions for four concentrations between *p*H 10.1 and 11.1. Since the meter read 11.4 in the boric acid buffer which was used for all the kinetic runs, prior to the addition of acid halide, a hydroxide ion concentration of 1.6×10^{-4} *N* was assumed to exist.[19]

Procedure.—Temperature control and analytical methods were discussed previously.[10]

The value of $k°$ in the equation $k/k° = sn$ was obtained from the equation $k_1 = k°(H_2O)$ and calculated as a second-order rate constant using the actual concentration of water present, neglecting contractions of water–acetone mixtures.

The rate of hydrolysis of methyl bromide in 99% water–1% acetone was determined by adding 1.5 ml. of approximately 1 *M* methyl bromide in acetone to 148.5 ml. of water at 0°. Aliquots (10 ml.) were sealed in soft-glass test-tubes with a minimum of vapor space and placed in the thermostat bath simultaneously. Time was noted when the tubes were placed in the thermostat or when the first tube was removed, which was usually after 5 min. immersion. After cooling the tubes under the tap, the contents were shaken with 20 ml. of chloroform or benzene and the aqueous portions titrated for bromide ion with mercuric nitrate. Benzene was used to extract the solutions containing per-

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(18) In pure water, $K = 2.6 \times 10^{-5}$.

(19) In pure water this buffer gives a hydroxide ion concentration of 5.8×10^{-4} *M*.

chlorate ion since chloroform forms an emulsion under these conditions. The infinity point (100% reaction) for the very slow runs was obtained from tubes placed in a 100° thermostat for at least 20 half-lives. For runs in the presence of 0.1 *M* salt, 2.4 g. of lithium perchlorate trihydrate was added to the reaction mixture.

The hydrolysis of methyl bromide in the presence of hydroxide ion was accomplished in a similar manner except that the reaction mixture consisted of 108.9 ml. of 0.973 *N* sodium hydroxide and 1.1 ml. of the stock solution of methyl bromide in acetone.

The reaction of methyl bromide in the presence of azide ion was conducted in a similar fashion. The reaction mixture consisted of 715 mg. (0.011 mole) of sodium azide, 108.9 ml. of water and 1.1 ml. of the stock solution of methyl bromide. The contents of the tubes, after shaking with chloroform, were treated with 5.0 ml. of 0.04 *N* silver nitrate, 10 drops of ferric alum indicator, 4 ml. of concentrated nitric acid to dissolve the silver azide and titrated for excess silver ion with 0.114 *N* potassium thiocyanate. The tubes for 100% reaction were allowed to stand for at least 10 half-lives at 49.8° or placed in a steam-bath to hasten the reaction. Identical results were obtained in either case.

The reactions of methyl bromide in 50% water–50% acetone were conducted similarly.

The same procedure was used for the reaction of methyl bromide with aniline except that the reaction mixture consisted of 1.394 g. (0.015 mole) of aniline, 74 ml. of acetone, 75 ml. of water and 1 ml. of the stock solution of methyl bromide.

The reaction mixture for the hydration of glycidol consisted of 100 ml. of 0.1783 *N* sodium hydroxide and 755 mg. (0.0102 mole) of glycidol. Aliquots (5 ml.) were brought to a brom thymol blue end-point with 0.05 *N* nitric acid and mixed with 5.0 ml. of a solution of 2.1 *M* magnesium bromide and 0.172 *N* sulfuric acid.[20] After at least 10 hr. this new solution was titrated for remaining acid with 0.1783 *N* sodium hydroxide.

Acetyl chloride was hydrolyzed in a 100-ml. round-bottomed flask equipped with sealed stirrer and glass-stoppered side-arm. The reaction solvent, 75 ml. of acetone and 25 ml. of water, was mixed in the cell and the acetyl chloride blown in directly from a pipet. Aliquots (10 ml.) were shaken with 20 ml. of chloroform and the aqueous portion titrated for chloride ion with mercuric nitrate. It was necessary to maintain the pipet and chloroform at or below the temperature of the reaction to prevent warming of the aliquots.

Benzoyl chloride and bromide and benzenesulfonyl chloride were hydrolyzed in the 100-ml. round-bottomed cell. When benzoyl chloride was hydrolyzed in the presence of acetic acid, the reaction mixture consisted of 0.457 ml. of 17.5 *N* acetic acid, 49.6 ml. of water and 45 ml. of acetone. The benzoyl chloride was added in 5 ml. of pre-cooled acetone. Aliquots (10 ml.) were shaken with 20 ml. of chloroform and the aqueous portions titrated for chloride ion with mercuric nitrate. When nitric acid was present, the solvent consisted of 3 ml. of 1 *N* nitric acid, 47 ml. of water, 45 ml. of acetone and 5 ml. of acetone containing the benzoyl chloride. With acetate ion present, the reaction mixture contained 8 ml. of a 0.5 *M* sodium acetate–0.5 *M* acetic acid buffer, 42 ml. of water, 45 ml. of acetone and 5 ml. of acetone with the benzoyl chloride. The hydrolysis of benzenesulfonyl chloride was conducted in 50 ml. of water and 50 ml. of acetone. When 0.1 *M* salt or acid was present, 5 ml. of 2 *N* lithium perchlorate or perchloric acid replaced 5 ml. of the water in the solvent. When 0.04 *M* lithium perchlorate was present, a larger cell was used and the solvent consisted of 4 ml. of 2 *N* lithium perchlorate, 96 ml. of water, 90 ml. of acetone and 10 ml. of acetone containing the acid chloride.

Hydrolyses of all the acid halides in the presence of base were conducted in a 200-ml. round-bottomed flask equipped with mechanical stirrer and side-arm. The reaction mixture used for all runs consisted of 40 ml. of 0.2 *M* boric acid, 22.4 ml. of 0.1783 *N* sodium hydroxide, 37.6 ml. of water and 100 ml. of acetone. Aliquots (20 ml.) were shaken with 20 ml. of chloroform and titrated for halide ion. When the buffer concentration was halved to investigate the effect of boric acid and monobasic sodium borate, the reaction mixture consisted of 20 ml. of 0.2 *M* boric acid, 11.2 ml. of 0.1783 *N* sodium hydroxide, 68.8 ml. of water and 100 ml. of acetone.

The reactions of acid halides with aniline were conducted in the 100-ml. round-bottomed cell described previously. Solutions containing a constant concentration of 1.1 × 10^{-4} *M* aniline were prepared from 8 ml. of 1 *N* nitric acid, 42 ml. of water, 50 ml. of acetone and 464 mg. (0.005 mole) of aniline. Solutions containing 1.1 × 10^{-2} *M* aniline were prepared from 4 ml. of 1 *N* nitric acid, 46 ml. of water, 50 ml. of acetone and 464 mg. (0.005 mole) of aniline.

Table VI gives sample kinetic data.

CAMBRIDGE 39, MASS.

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(20) O. F. Lubatti, *J. Soc. Chem. Ind.*, **54**, 424T (1935).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Neighboring Carbon and Hydrogen. XIV. Participation in Solvolysis of Some Primary Benzenesulfonates[1]

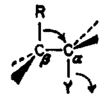
BY S. WINSTEIN, C. R. LINDEGREN, H. MARSHALL AND L. L. INGRAHAM

RECEIVED MAY 15, 1952

The study of the solvolysis of a series of primary benzenesulfonates has supplied evidence on: (a) the magnitude of anchimeric assistance to ionization in the pinacol rearrangement; (b) the participation of β-aryl in solvolysis of $P_\beta P_\alpha$ systems in the common solvents. The data show that the magnitude of anchimeric assistance in the pinacol rearrangement may be large and can compare with that in the Wagner–Meerwein rearrangement. A β-methoxy group has an effect on the driving force due to participation approximately equivalent to that of a phenyl group or two methyl groups. Solvolysis of 2-*p*-anisylethyl *p*-toluenesulfonate is relatively rapid and the data indicate that *p*-anisyl participation in solvolysis of the toluenesulfonate is well developed in acetic and formic acid solvents. The present data together with previous data indicate that the effects of α- and β-methyl groups on free energy of activation of anchimerically assisted ionization are additive with neighboring *p*-anisyl and phenyl. The parameters for the effect per α- or β-methyl group are compared for neighboring *p*-anisyl, phenyl and the neighboring functional groups, I, Br, OH, OCH_3, O^-.

In the present article are reported the results of a study of the solvolysis of several primary benzenesulfonates of interest in connection with participation by neighboring carbon.[2]

In connection with the Wagner–Meerwein rearrangement, it is clear that rate may be very substantially enhanced by participation of carbon in the rate-determining ionization[2] (I). This anchi-



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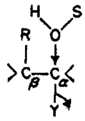

II

III

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[1] Much of the material in this paper was presented in summary at Montpellier, April 26, 1950 [*Bull. soc. chim.*, **18**, 55 (1951)]. Taken from Ph.D. theses of C. R. Lindegren, U. C. L. A., 1950, and H. Marshall, U. C. L. A., 1952.

[2] S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber and J. Corse, THIS JOURNAL, **74**, 1113 (1952).