

ON THE COMPETITIVE REACTIVITIES OF HYDROXIDE, METHOXIDE, ETHOXIDE, AND  
ALLYLOXIDE IONS IN  $S_N1$  AND  $S_N2$  DISPLACEMENT REACTIONS

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It is generally accepted that there is a loose correlation between basicity (used here to mean the equilibrium constant for coordination of nucleophiles with a proton) and nucleophilicity (used here to mean the rate constant for coordination of nucleophiles with carbon) within any homologous series of nucleophiles with a common attacking atom, such as the series hydroxide, methoxide, and ethoxide. However, nothing is known about the changes in the relative nucleophilicities of hydroxide, methoxide, and ethoxide ions as one proceeds from the  $S_N2$  reactions of n-butyl bromide through benzyl bromide to the  $S_N1$  reactions of triphenylmethyl bromide; and even the relative nucleophilicities of these nucleophiles in different  $S_N2$  reactions is still in doubt. The best work is that of Murto (1) and of Alet and England (2) who have studied the reaction of hydroxide, methoxide, and ethoxide nucleophiles with methyl iodide. Murto concludes their relative nucleophilicities are 0.08, 0.5, and 1 respectively; Alet and England give similar values of 0.2, 0.6, and 1.0 respectively.

There are difficulties in establishing a scale of relative nucleophilicities based on kinetic studies of the reaction of each nucleophile separately with a given substrate. Every change in the concentration or nature of the reactants causes a change in the characteristics of the solution and consequently the observed differences in the reaction rate constants are often difficult to interpret. We circumvented this problem by allowing two or more nucleophiles in the same reaction mixture to competitively attack a limited amount of substrate. Their competitive reactivities could then be calculated from an analysis of the products of the reaction.

There is a real need for a consistent body of data on competitive reactivities of a series of nucleophiles with a group of alkyl halides so chosen as to provide a continuous spectrum of reactions proceeding by  $S_N1$ ,  $S_N2$ , and border-line mechanisms. We have started to satisfy this need by measuring the competitive reactivities of hydroxide, methoxide, ethoxide, and allyloxide ions in protic solvents with butyl, benzyl, and triphenylmethyl bromides, as well as with ethylene oxide.

In a typical experiment, 0.06 gram atom of sodium metal was added to a mixture of one mole each of the two (or three) alcohols, and to this was added 0.05 mole of the alkyl bromide. Water was treated as though it were an alcohol. The reaction mixture was allowed to stand at 25 - 27° until all of the alkyl bromide had reacted, and the reaction mixture without any prior processing was then analyzed by vpc. In other experiments, the relative concentrations of the two alcohols were varied; this did not change the competitive reactivities observed as long as the appropriate concentration terms were included in calculating the ratio. In the experiments employing triphenylmethyl bromide, the reaction with the alcohols is so rapid that it occurs on the surface of the crystals. To insure that the reaction occurred in solution, a concentrated, anhydrous acetone solution of the triphenylmethyl bromide was added to the alcoholic solution of the nucleophiles being studied. Addition of sodium bicarbonate and evaporation of the solvent gave a mixture of ethers which was then analyzed by nmr. The results with the three bromides and with ethylene oxide are summarized in Table I.

TABLE I  
Competitive Reactivities (and Relative Nucleophilicities) of Ions  
with Alkyl Bromides and Ethylene Oxide

	Substrates				Relative acidities of ROH <sup>2</sup> :
	n-C <sub>4</sub> H <sub>9</sub> Br	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Br	(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> CBr	Ethylene Oxide	
Temp. <sup>1</sup>	25-27°	25-27°	25-27°	0-2°	
Approx. time for 50% of substrate to react	3 days	15 min.	< 1 min.	1 day	
Competitive reactivities of anions (unparenthesized):					
Relative nucleophilicities (in parenthesis):					
<sup>-</sup> OH	0.1 (0.08)	0.09 (0.07)	0.8 (0.6)	0.08 (0.06)	1.2
<sup>-</sup> OMe	3.7 (0.9)	3.4 (0.8)	4.4 (1.0)	2.3 (0.5)	4.0
<sup>-</sup> OEt	1.0 (1.0)	1.0 (1.0)	1.0 (1.0)	1.0 (1.0)	0.95
<sup>-</sup> OC <sub>2</sub> H <sub>5</sub>	4.2 (1.5)	4.0 (1.4)	1.5 (0.5)	ca. 2 (0.8)	2.7

<sup>1</sup> Room temperature and cold-room temperature which varied within the limits indicated.

<sup>2</sup> Ref. 3.

The competitive reactivity values of Table I were obtained not only from comparisons using any two alcohols (including water) as solvent, but from comparisons using two alcohols and water and the three alcohols and water. In general, the data agree with the averaged results in Table I within 10%. The consistent results in aqueous and non-aqueous solvents shows that the influence of ion-pairing is small. The "competitive reactivities" are to be differentiated from "relative nucleophilicities" in that the relative concentrations of the anions present in any of the mixtures depends on the relative acidities of the alcohols. Since the acidities of the alcohols are known (3), the relative concentrations of the anions can be approximated. Thus methanol is 4.2 times as acidic as ethanol, so the methoxide/ethoxide competitive reactivity ratio of 3.7 with n-butyl bromide is divided by 4.2 to give 0.9 as the ratio of their nucleophilicities. Correction for this acidity factor yields the relative nucleophilicity values given in parenthesis in Table I.

Benzyl bromide and triphenylmethyl bromide react rapidly enough with the neutral alcohols so that the relative reactivities of even the alcohols themselves can be measured. The relative nucleophilicities of the neutral alcohols are the same as the competitive reactivities since there are no acidity corrections to be made. The results are in Table II:

TABLE II  
Competitive Reactivities of Neutral Alcohols with Benzyl  
Bromide and with Triphenylmethyl Bromide at 25 - 27°

	Substrates	
	$C_6H_5CH_2Br$	$(C_6H_5)_3CBr$
Approx. time for 50% of substrate to react	10 days	< 1 min
Competitive reactivities:		
Water	0.07	3.3
Methyl alcohol	1.3	2.6
Ethyl alcohol	1.0	1.0
Allyl alcohol	0.6	0.6

The trityl bromide data in Table II pertain to the reaction between trityl cation and the neutral alcohols; in contrast, the data in Table I result from competitive reactions between

trityl cation and both the alcohol and the alkoxide. The relatively constant ratios of the methoxide to ethoxide nucleophilicities in Table I with n-butyl bromide, benzyl bromide and trityl bromide, coupled with the large increase in this ratio in Table II, suggest that the predominant reaction in the first series is between alkoxide and the trityl cation. A similar comparison of the ratios of the nucleophilicities of hydroxide to ethoxide with the three alkyl bromides in Table I shows trityl bromide to have a value eight fold greater than n-butyl or benzyl bromides and this, in conjunction with the high value for water in Table II, suggests that water molecules in this case may be effectively competing with the hydroxide ions.

The conclusions to be drawn from all of the above data are as follows: 1. Hydroxide is a surprisingly weak nucleophile; it has approximately one-tenth the nucleophilicity of ethoxide in  $S_N2$  reactions whereas its basicity relative to ethoxide would lead one to expect it to be nearly equal to ethoxide in nucleophilicity. 2. Taking ethoxide as unity, methoxide and allyloxide in  $S_N2$  displacements are two to five times more nucleophilic than one would expect based on the relative acidities of the alcohols. 3. Relative nucleophilicities for a given pair of nucleophiles are not constant with different substrates if the mechanism changes from  $S_N1$  to  $S_N2$ . Thus water is the best of the neutral nucleophiles studied here in its reaction with trityl bromide and the poorest of the nucleophiles in its reaction with benzyl bromide. 4. In synthetic work in which the nucleophilic anions are in equilibrium with a protic solvent, "competitive reactivities" are more meaningful than "relative nucleophilicities".

#### REFERENCES

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