from RCl to RBr to RI.[12] This is the order of increasing softness of the leaving group. In conclusion, it should be emphasized that explaining phenomena of organic chemistry by means of the principle of hard and soft acids and bases[8,9] does not necessarily invalidate other, more fundamental explanations. The principle is supposed to be correlative and phenomenological in nature, rather than theoretical.

Experimental Section

Methyl tosylate was made according to the literature[13] and was carefully purified by distillation and crystallization. Titration of the acid formed by complete hydrolysis indicated 100 ± 0.4% purity. Baker Analyzed methanol was refluxed for 5 hr with magnesium methoxide and distilled under nitrogen free from moisture and carbon dioxide. The first 15% of the distillate was discarded and the middle portion was stored under nitrogen for use. The purification of the nucleophiles will be described elsewhere.[7] The rates of reaction with bromide, iodide, and thiocyanate ions were determined by titration of liberated acid due to solvolysis and, simultaneously, following the concentration of these ions by silver nitrate titrations using eosin as indicator. In the case of chloride ions, potassium chromate was used as indicator after neutralizing the sample with $NaHCO_3$. The rate with $SeCN^-$ was determined by potentiometric silver nitrate titration. The rate of solvolysis was followed by titrating the hydrogen ion produced with base. All titrations with base were carried out under nitrogen.

The reaction with triethylamine was studied in a system containing triethylammonium ion as well in order to minimize the reaction with hydroxide ion. The ratio of amine to its conjugate acid was in the range 5:1–10:1. The rate was found by titration of the remaining amine with standard acid. Reactions with triphenylphosphine, thiourea, and thiophenoxide were studied spectrophotometrically at wavelengths of 280, 250, and 290 mμ, respectively, using a Cary spectrophotometer. The optical density at infinite time was found from the spectra of methylisothiuronium tosylate or methyltriphenylphosphonium tosylate for the first two cases. These spectra were the same as those of the kinetic runs after 15–20 half-lives. Since the solvolysis rate for methyl tosylate is quite large, it is necessary to correct for concurrent solvolysis. For equal starting concentrations a and b of ester and nucleophile, we have the following equation[14]

$$k_2 = \frac{k_1[a - (a - x)e^{k_1t}]}{a(a - x)(e^{k_1t} - 1)}$$

where k_2 refers to the nucleophile, k_1 refers to solvolysis, and x is the concentration of ester hydrolyzed.

In each run, six to eight determinations of both the nucleophile and hydrogen ion were made except for thiophenoxide, thiourea, and triphenylphosphine. In the case of the thiophenoxide ion, the starting concentration of the ion and the ester was about 5×10^{-3} M in the presence of 0.05 M sodium perchlorate. The rate constant for the thiophenoxide ion was calculated on the assumption that the reaction between thiophenol and methoxide ion goes to completion (30% excess of thiophenol was usually added). A small error is introduced in this way. This rate constant was further checked by titration with 0.01 M HCl.

Runs with thiourea and triphenylphosphine were performed with starting concentrations in the range from 2×10^{-2} to 4×10^{-2} M. Owing to the high extinction coefficients of these nucleophiles, aliquots had to be diluted for 25 to 50 times before measurements on the spectrophotometer could be performed. For the other ionic reagents, the starting concentrations were in the range 0.04–0.055 M. Ionic strength was made up to 0.05 with sodium perchlorate in solutions in which the concentration of nucleophile was less than 0.04 M. Good agreement with the theoretical rate equation was found for all cases up to 70% reaction except for chloride ion. For this slow reaction, an upward drift of k_2 was noted after some 20% reaction. The drift is small and its is estimated that the rate constant is good to 10% for this case, compared to 2% for the other nucleophiles. All systems were studied at least in duplicate.

Registry No.—Triethylamine, 121-44-8; triphenylphosphine, 603-35-0; thiourea, 62-56-6; thiophenoxide, 13133-62-5.

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The Nucleophilicity of Chloride Ion toward Carbonyl Carbon[1]

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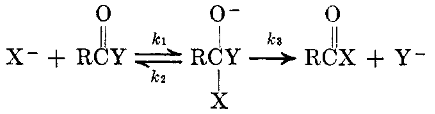
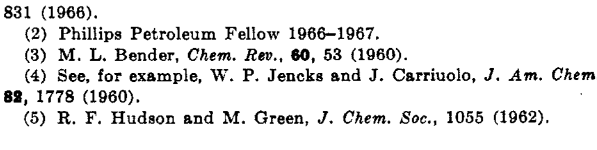
The general problem of assessing quantitatively the nucleophilic reactivity of various species toward unsaturated carbon atoms is complicated by the fact that most displacement reactions on such carbon atoms take place by an addition–elimination mechanism.[3] Thus, under normal conditions the rate is dependent upon the addition step (k_1) as well as the ratio of rate constants for the two possible elimination steps. The observed rate constant for reaction 1 is $k_1/[(k_2/k_3) + 1]$. As a result, most studies involving displacements at unsaturated centers[4] indicate only the gross effects and provide no quantitative measure of the rate of addition k_1 of a nucleophile to an unsaturated carbon.



$$X^- + R\overset{\overset{O}{\|}}{C}Y \underset{k_2}{\overset{k_1}{\rightleftharpoons}} R\underset{\underset{X}{|}}{\overset{\overset{O^-}{|}}{C}}Y \xrightarrow{k_3} R\overset{\overset{O}{\|}}{C}X + Y^- \qquad (1)$$

Hudson and Green[5] have reported that bromide and iodide ions in aqueous solution do not add to carbonyl carbon at a measurable rate. These conclusions were based on the absence of any rate effect of these halide ions on the rate of hydrolysis of ethyl chloroformate in aqueous acetone solution. These observations may, however, be rationalized in one of two ways: (1) the rate of addition (k_1) of halide ion to form the tetrahedral intermediate is too slow to be of any significance; (2) the addition intermediate **1** reverts to starting material faster than it proceeds to products ($k_2/k_3 \gg 1$).



$$CH_3CH_2O\overset{\overset{O}{\|}}{C}Cl + Br^-(I^-) \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \underset{\mathbf{1}}{CH_3CH_2O\underset{\underset{Cl}{|}}{\overset{\overset{O^-}{|}}{C}}Br(I)} \xrightarrow{k_3} CH_3CH_2O\overset{\overset{O}{\|}}{C}Br(I) + Cl^- \qquad (2)$$

We have investigated this problem by studying in aqueous acetonitrile solution the symmetrical ex-

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[1] Part II in the series "Nucleophilic Reactivity at Unsaturated Centers." For part I, see L. B. Jones and T. M. Sloane, *Tetrahedron Letters*, 831 (1966).

[2] Phillips Petroleum Fellow 1966–1967.

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[4] See, for example, W. P. Jencks and J. Carriuolo, *J. Am. Chem. Soc.*, **82**, 1778 (1960).

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

change reaction between an acid chloride, ethyl chloroformate, and tetra-*n*-butylammonium chloride-^{36}Cl, an ionic chloride known to be dissociated in aqueous organic solvents.[6] This type of study has the advantage that the addition intermediate has an equal probability of partitioning between reactant and product ($k_2/k_3 = 1$). As a result, the rate of radiochloride incorporation is twice the rate of chloride addition to the carbonyl carbon (k_1). Similarly, the rate of addition of water to the carbonyl carbon may be approximated by the rate of hydrolysis of the acid chloride since acid chlorides show little or no carbonyl oxygen-18 exchange[7] ($k_2/k_3 \ll 1$). Evidence for the presence of a tetrahedral intermediate in the hydrolysis of ethyl chloroformate has been presented by Hudson and Green[5] and Kivinen.[8] Consistent with this suggestion is our observation that the hydrolysis of this acid chloride shows no electrophilic catalysis when studied in the presence of silver perchlorate. The rates of nucleophilic chloride exchange and solvolysis of ethyl chloroformate at 30° are tabulated in Table I. The ratio $2k_e/k_s$ is a measure of the rate of chloride *vs.* water addition to the carbonyl carbon to give the tetrahedral intermediate.

TABLE I

RATES OF CHLORIDE EXCHANGE AND SOLVOLYSIS FOR ETHYL CHLOROFORMATE IN WATER–ACETONITRILE MIXTURES AT 30.1°[a]

H_2O, %	$k_e \times 10^5$, M^{-1} sec^{-1}	$k_s \times 10^6$, M^{-1} sec^{-1} [b]	$2k_e/k_s$
40	12.1 ± 1.3	5.35 ± 0.12	45
60	6.32 ± 0.22	6.74 ± 0.13	19
85	6.71 ± 0.10	7.31 ± 0.10	18

[a] For these measurements, the n-$BuN_4^+Cl^-$ concentrations were varied from 0.021 to 0.380 *M* and the ethyl chloroformate concentrations were varied from 0.021 to 0.210 *M*. [b] Second-order rate constant for solvolysis were obtained by dividing the observed first-order rate constant by the water concentration.

These data clearly indicate that at least in this one system chloride ion in aqueous solution is a more reactive nucleophile toward the carbonyl carbon atom than is water. Its reactivity, however, appears to be somewhat less than that observed for displacement at saturated carbon.[9] These results also suggest that Hudson and Green[5] failed to observe bromide or iodide ion catalysis for ethyl chloroformate in 85% aqueous acetone because the halide ion concentrations employed in their studies were too low to permit the detection of such displacement reactions by titrimetric methods. This would be true even though bromide is normally a better nucleophile than chloride ion in aqueous solution[9] because the breakdown of the tetrahedral intermediate (eq 2) would be unfavorable ($k_2/k_3 > 1$). Bromide is a more effective leaving group than chloride ion.[10]

Experimental Section

Materials.—Eastman practical grade acetonitrile was purified by preliminary distillation from sodium hydroxide followed by distillation from phosphorus pentoxide to yield material having bp 80–81°. Matheson technical grade *n*-hexane was stirred over concentrated sulfuric acid, washed with water, dried over sodium hydride, and distilled to give material having bp 68–69°. Eastman White Label ethyl chloroformate was filtered to remove the calcium carbonate stabilizer and distilled through a short Vigreaux column to give material having bp 93.5–94.5°. Dioxane and tetrahydrofuran were purified by standard procedures.[11]

Tetra-*n*-butylammonium Chloride-^{36}Cl.—Tri-*n*-butylamine (43 g, 0.23 mole) and *n*-butyl bromide (32 g, 0.23 mole) were refluxed for 2 days in 250 ml of dry acetonitrile. The pale yellow solution was poured into 700 ml of dry ether and the resultant crystalline precipitate was filtered. The tetra-*n*-butylammonium bromide was dissolved in 100 ml of water and the solution was passed through a Dowex 1-X8 anion-exchange resin in the chloride form enriched with chlorine-36. The water was removed under reduced pressure and the viscous solution was dried in a vacuum desiccator over phosphorus pentoxide to yield 38 g of a white powder. This compound was extremely hydroscopic and had to be stored in a dry atmosphere.

Scintillation Solution.—To 750 g of dioxane and 250 g of tetrahydrofuran was added 4 g of 2,5-diphenyloxazole (PPO) and 0.2 g of 1,4-bis(4-methyl-5-phenyloxazolyl)benzene (POPOP). PPO and POPOP were obtained from Packard Instrument Co.

Exchange Measurements.—A reaction flask containing the aqueous acetonitrile solvent and the desired quantity of tetra-*n*-butylammonium chloride-^{36}Cl was allowed to reach thermal equilibrium in a constant-temperature bath maintained at 30.1 ± 0.05°. The required amount of ethyl chloroformate was added and aliquots of the reaction mixture were removed at various time intervals and extracted with *n*-hexane. Experiments indicated that equilibration of the ethyl chloroformate between the aqueous and *n*-hexane layers was rapid and required less than 2 min. The ionic chloride remained in the aqueous layer. A 1-ml sample of the *n*-hexane layer was then placed in a counting vial containing 15 ml of scintillation solution and the radiochloride concentration was determined by counting with a Nuclear Chicago Mark I liquid scintillation counter. High specific activities of tetra-*n*-butylammonium chloride were employed to increase the sensitivity of the measurements. Product studies by Hudson and Green[5] indicate that the radioactivity in the hexane layer must be due to labeled ethyl chloroformate.

Solvolytic Measurements.—For internal consistency a kinetic technique analogous to that employed for the chloride-exchange measurements was followed except unlabeled tetra-*n*-butylammonium chloride was used. Samples taken from the extracted *n*-hexane phase were analyzed for ethyl chloroformate according to the procedure of Kivinen.[8]

Kinetic Treatment.—The kinetic analysis of the solvolytic reactions has been described elsewhere[7] and was used without modification. The kinetic treatment for the chloride-exchange rates was similar to that used by McCleary and Hammett.[12]

Registry No.—Ethyl chloroformate, 541-41-3; tetra-*n*-butylammonium chloride-^{36}Cl, 13096-55-4.

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Single-Pass Zone Refining. Preparation of an Enantiomerically Pure Compound

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Multipass zone melting is now an established technique for the ultrapurification of metals, semiconduc-