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The Reactivity of Atoms and Groups in Organic Compounds. XVIII. The Effect of the Solvent on the Rate of the Reaction between Benzoyl Chloride and Ethyl Alcohol¹

By JAMES F. NORRIS AND EDWARD C. HAINES

Although much experimental work has been devoted to the study of the influence of the solvent on the rates at which chemical reactions take place (the "adjuvance" of the solvent),² no satisfactory general theory of the cause of the effect has been developed.³ It seemed advisable, nevertheless, to study the influence of solvents on the reaction between benzoyl chloride and ethyl alcohol to learn the facts in regard to a reaction that has been studied from many points of view in this Laboratory.⁴ It was thought that the determination of the rates of the reaction in solvents that differed widely in composition and a comparison of the results with the relative rates of different types of reactions in the same solvents might throw some light on the mechanisms of the reactions involved.

When the rates at which benzoyl chloride reacts with methyl alcohol and with ethyl alcohol are determined as reactions of the first order the excess of the alcohols serves as solvent. In the latter capacity the two alcohols have different adjuvances. The increased rate with methyl alcohol is the result of this difference and the difference in chemical reactivity of the two alcohols. Recent work has shown that *p*-nitrobenzoyl chloride reacts with methyl alcohol at 0° 4.4 times as fast as it does with ethyl alcohol when the velocity constants of the first order reactions are compared; in this case there was a change in the solvent. When the relative rates were determined as reactions of the second order at 25° and the solvent was ethyl ether in both cases, methyl alcohol reacted 2.1 times as fast as ethyl alcohol.⁵ It has been shown that in several reactions methyl alcohol has a greater adjuvance than ethyl alcohol,^{2,6} the values varying from about 1.4 to 2.

(1) From a part of the thesis of Edward C. Haines presented in partial fulfillment of the requirements for the degree of Doctor of Philosophy 1924.

(2) Norris and Prentiss, *THIS JOURNAL*, **50**, 3042 (1928).

(3) A recent paper by Arthur W. Chapman, *J. Chem. Soc.*, 1550 (1934), is significant, in which the influence of solvents is correlated with dipole moments.

(4) Norris, Fasce and Staud, *THIS JOURNAL*, **57**, 1415 (1935); Norris and Young, *ibid.*, **57**, 1420 (1935).

(5) Norris and Ashdown, *ibid.*, **47**, 837 (1925).

(6) Menshutkin, *Z. physik. Chem.*, **6**, 41 (1890).

Such facts as the above serve to emphasize the importance of a knowledge of these effects, irrespective of theoretical explanations, in interpreting chemical reactivity from velocity constants of reactions.

The rates at which benzoyl chloride reacted with ethyl alcohol in a variety of solvents are given in Table I. Equal molar weights of the reactants were used and second order velocity constants

TABLE I
SECOND ORDER VELOCITY CONSTANTS

Temp. 25°. Time in hours. $C_6H_5COCl + C_2H_5OH = C_6H_5COOC_2H_5 + HCl$. Concentration expressed in mole fractions

Solvent	K		Average K
Ethyl ether	0.0800	0.0827	0.081
<i>n</i> -Butyl ether	.103	.109	.11
Ethyl acetate	.149	.178	.16
Ethyl benzoate	.231	.238	.23
Acetone	.405	.414	.41
Anisole	.476	.475	.48
Toluene	.496	.492	.49
Nitrobenzene	.511	.498	.51
<i>n</i> -Butyl chloride	.543		.54
Benzene	.614	.624	.601
Chlorobenzene	.626	.620	.62
Iodobenzene	.646	.650	.65
Hexane	.684	.674	.68
Carbon tetrachloride	.728	.729	.73
Dimethylaniline	2.02	2.20	2.1
Ethyl alcohol	2.99		3.0
Equal vols. benzene and ether	0.543		0.543

were calculated. Since these calculations involved the use of concentrations of the solutions, it was necessary to decide how the concentrations should be expressed. On account of the fact that the densities and molecular weights of the solvents differed widely, the calculations of relative rates based on volume concentrations would be different from those calculated on either the weight or molar basis. Since one of the subjects of the work was to discover if there was evidence of any interaction between the solutes and the solvent, it appeared better to express the concentration on the mole fraction basis so that during the reaction the solutes would be under the influence

of the same number of moles of the solvent in each case.

It is seen from Table I that the reaction takes place more slowly in ethers and esters than in hydrocarbons and their halogen derivatives. The presence of oxygen in the solvent decreases reactivity, except in the case of ethyl alcohol. If the mechanism of the reaction between an acyl chloride and an alcohol involves the intermediate formation of an addition product through the oxygen atom in either compound, it is probable that the presence of a solvent containing oxygen would affect the rate at which the reaction takes place. It is of interest to note here that the rates at which benzoic acid and its substitution products react with a diazo compound when dissolved in ethyl acetate are much smaller than those found when the solvent was toluene.⁷ It is known that certain organic acids form addition products with ethyl acetate.

When the relative rates given in the table are compared with the relative rates with which ethyl iodide adds to triethylamine in certain of the solvents listed here, it is found that in the latter case the ratios obtained are not the same.⁶ The reaction of the alkyl halide takes place much more rapidly in esters than in hydrocarbons—the reverse of what happens in the case of the acyl chloride. These facts indicate a difference in mechanism in the two reactions. The relatively high rate of the reaction of benzoyl chloride with ethyl alcohol dissolved in dimethylaniline is in accord with the common use of a tertiary amine to facilitate such reactions.

In order to determine whether or not there was a marked change in physical properties when the solvent and solute were mixed, the indices of refraction and densities of certain mixtures were determined and the results were plotted. In the case of the densities the mixtures of ethyl alcohol with *n*-butyl ether and with benzene gave straight lines. The mixtures of these solvents with benzoyl chloride gave curves which showed in both cases that a small increase in volume had occurred over that calculated on the assumption that no change had taken place. In the case of the mixture containing 50% *n*-butyl ether the calculated density is 0.9849; that taken from the plot 0.975. With the similar mixture which contained benzene, calculated 1.0403, found 1.025. When the indices of refraction were compared in the same

way it was found that the mixtures containing benzoyl chloride yielded values slightly less than those calculated. The differences observed were too small to warrant any definite conclusions.

Experimental Details

The chemicals used were pure and gave satisfactory boiling points. The volumetric apparatus was calibrated. The thermostat held the temperature at $25 \pm 0.01^\circ$.

The mixtures used in determining the rates consisted of 0.1 mole of benzoyl chloride, 0.1 mole of ethyl alcohol and approximately 0.8 mole of solvent. At these concentrations the laws of solutions are only approximations, but it was thought that the results obtained could be compared when the concentrations in the experiment were the same. It was found that the velocity constants calculated by the usual formula for a second order reaction remained constant to about 40% conversion. The values of $x/(1-x)$ plotted against time gave straight lines up to this percentage conversion. The high concentrations were used in order to have the reactions rapid enough to be measured in a reasonable time.

Pipets were calibrated to deliver 0.1 mole of benzoyl chloride and 0.1 mole of ethyl alcohol. Approximately 0.8 mole of the solvent was weighed into a 150-cc. glass-stoppered Erlenmeyer flask which contained the benzoyl chloride. The mixture was placed in the thermostat for fifteen minutes and the alcohol was then added. When the solvents in which hydrogen chloride is very soluble were used—acetone, the esters, butyl ether and dimethylaniline—the flask remained in the thermostat and samples for analysis were withdrawn at intervals by means of a pipet. In the case of the other solvents, excepting ethyl alcohol, equal volumes of the mixtures were measured by means of a pipet into thin glass capsules which were sealed and placed in the thermostat. Each capsule contained a weighed amount sufficient for one analysis. The errors caused by having the mixture removed from the bath during the interval in which samples were being measured were eliminated in the time corrections made in the calculations. The value for the rate in alcohol was determined from the data of Staud.⁸ In making an analysis the sample was mixed in a glass-stoppered bottle with about 10 g. of ice, 15 cc. of water to which was added the amount of standard alkali (0.05 *N*) used in the previous analysis, 10 cc. to 15 cc. of benzene and three drops of methyl orange solution. If the sample was contained in a capsule this was broken under the water. The mixture was shaken for thirty seconds. When the solvent used in the reaction was heavier than water the benzene added was replaced by carbon disulfide. The presence of these substances, which dissolve benzoyl chloride, prevented almost completely the reaction of the latter with water during the time necessary to remove the hydrochloric acid from the solvents. The end-point in the titrations after neutralization of the acid was not changed after shaking for one minute more. Phenolphthalein was used as indicator when dimethylaniline was the solvent.

The second order velocity constants were calculated in the usual way. When the values of

(7) Norris and Strain, *THIS JOURNAL*, **57**, 187 (1935).

(8) Norris, Fasce and Staud, *ibid.*, **57**, 1415 (1935).

$x/(1-x)$ were plotted against time it was found that the values fell on a straight line up to about 40% conversion. The point where the line crossed the axis of time gave the time correction.

A more accurate way of determining the constant and time correction was used in the final calculations. A number of values of t during the first part of the reaction were averaged; the corresponding values of $x/(1-x)$ were also averaged.

TABLE II

SECOND ORDER VELOCITY CONSTANT

$C_6H_5COCl + C_2H_5OH = C_6H_5COOC_2H_5 + HCl$. Solvent, benzene; temp. 25°. Mole fraction of each reactant, 0.1003. Weight of sample for each analysis, 2.813 g.

Time in hours	X (fraction corrected)	K
1.5	0.1221	0.602
2	.1455	.605
2.5	.1726	.629
3.5	.2160	.626
5.5	.2839	.626
6.5	.3192	.638
7.5	.3393	.616
8	.3520	.615
8.5	.3702	.630
9	.3792	.621

Average point 1.5-5.5 hrs., $t = 3.0$, $x/(1-x) = 0.2380$. Average point 6.5-9 hrs., $t = 7.9$, $x/(1-x) = 0.5444$. Time correction, 0.80 hr. Average value of K from values in table, 0.621. Value of K from average points, 0.624.

The results gave one point on the straight line. The values during the latter part of the reaction were treated in the same way. The points obtained in the two cases served to fix the best straight line, the slope of which determined the constant of the reaction. From the coordinates of the two points the time correction could be calculated. In making these calculations the observations were rejected which were made during the first hour and those made after the plotted points fell on a curve rather than a straight line (after about 40% conversion). In Table II are given as an example the results of one measurement.

Summary

1. The rates have been determined at which benzoyl chloride reacts with ethyl alcohol in a variety of solvents.

2. The rates in solvents containing oxygen are less than in hydrocarbons or their halogen derivatives. In this respect the acyl chloride differs from an alkyl chloride.

3. The importance is emphasized of a knowledge of the effects of solvents on rates in the use of reaction velocities in determining the relative reactivities of bonds.

CAMBRIDGE, MASS.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FORDHAM UNIVERSITY]

Quantitative Isotopic Exchange Reactions in the Carbohydrate Group¹

BY W. H. HAMILL AND WERNER FREUDENBERG

The literature accumulated since heavy water has become generally available as a research tool comprises a number of reports on exchange experiments of organic compounds.² In the carbohydrate group Bonhoeffer and Brown³ found for sucrose that approximately one-half of all hydrogen atoms is exchangeable, but no precise value was claimed. In a more recent communication from the same laboratory,⁴ on the mutarotation of *D*-glucose in heavy water, it is reported that this aldohexose exchanges five of its hydrogen atoms,

indicating that all hydroxyhydrogens are easily replaceable with deuterium.

In the course of another investigation,⁵ on the basis of certain assumptions which had to be made at that time, one of us (W. H. H.) observed that glucose, in 30% deuterium oxide, gave a different exchange value, namely, six.

In an effort to clarify this apparent disagreement we set out to determine systematically exchange numbers in the carbohydrate group, emphasizing the structural aspects. We used free hexoses, their methyl glycosides and other partly alkylated derivatives. It was hoped that concurrently such a study would lead to a method for the determination of reactive hydrogen atoms present in the carbohydrate molecule.

(1) Presented in part before the Organic Section at the New York Meeting of the American Chemical Society, 1935.

(2) For bibliographies see Urey and Teal, *Rev. Modern Physics*, **7**, 34 (1934); Ann R. Young, "Deuterium Bibliography," Penn. State College, 1934, Supplement 1935.

(3) Bonhoeffer and Brown, *Z. physik. Chem.*, **B23**, 172, 1933.

(4) Moelwyn-Hughes, Klar and Bonhoeffer, *ibid.*, **A169**, 114 (1934).

(5) Hamill and La Mer, *J. Chem. Phys.*, **2**, 891 (1934); and unpublished work.