[Contribution from the Polytechnic Institute of Brooklyn]

ELECTRONIC INTERPRETATION OF ORGANIC CHEMISTRY. I. THE ROLE OF SOLVENT IN DETERMINING REACTION RATE

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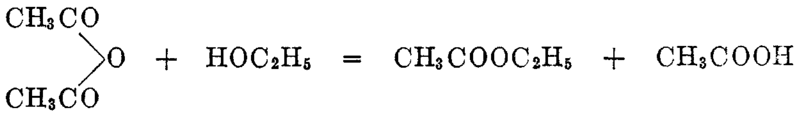
Received August 19, 1946

Solvents are known to affect profoundly the speed of an organic reaction. The main results have been summarized and discussed by Richardson and Soper (15), and the position has been recently reviewed with reference to current theories by Bell (1). The present paper is an attempt to coordinate and synthesize the existing ideas and results from the solvation standpoint alone, in the light of the recent developments in electronic interpretation as applied to organic chemistry, and to suggest a uniformity of treatment based on the current theories of hydrogen bonding and donor-acceptor mechanism.

The viewpoint to be presented herein utilizes only the basic concepts of organic chemists (14, 16) about electronegativity, inductive effect, and mesomeric or resonance effect, and also the idea of hydrogen bonding. The application of our concept can be best made clear with reference to specific cases as follows.

Esterification reactions. Let us consider the reaction, esterification of acetic anhydride according to the equation,



$$(CH_3CO)_2O + HOC_2H_5 = CH_3COOC_2H_5 + CH_3COOH$$

The master step evidently is a reaction between a donor and an acceptor center. We believe that the oxygen of the anhydride is attacked by the hydroxylic hydrogens of the alcohol, since the reaction speed is fastest with primary alcohols. However, to apply our concept, the exact isolation of the active centers is not necessary. Let us now consider how the solvent affects the above reaction. We believe that all solutes are solvated to a greater or lesser degree by the solvent, either by hydrogen bonds or by van der Waals forces. In the above case there will be hydrogen bond formation between the donor centers (oxygen) and the hydrogen of the solvent, the strength of this hydrogen bond depending on the electropositivity of the hydrogen present in the solvent. That hydrogen atoms attached to carbon differ widely among themselves in polarity, depending on the molecule in which they are present, is an admitted fact, and even quantitative data exist for the acidity of quite a few C—H bonds. That hydrogen atoms present in C—H bonds can engage themselves in hydrogen bonding in haloform type compounds has been shown by Copley, Zellhoefer, and Marvel (3) and there is no formal difficulty in assuming that any C—H bond can do so, producing hydrogen bonds of a lesser degree of firmness.

Evidently, the solvents which contain more positive hydrogen and hence form stronger hydrogen bonds with the vulnerable oxygen will more effectively block up these vulnerable points, and hence reduce the speed of the above reaction. Taking an example of benzene and hexane, it is known that benzenoid hydrogens are more positive than aliphatic hydrogens, and hence the former will more effectively block up the vulnerable oxygens from attack than does the hexane or heptane and hence we should expect the reaction to be faster in hexane than in benzene. By the same reasoning the speed will be much less in chloroform than in carbon tetrachloride, because chloroform has a polar hydrogen to block up the reactive oxygen, whereas carbon tetrachloride has none. The values for the speed of the above reaction are given in Table I as determined by Soper and Williams (17) and by Menschutkin (9). It will be observed that the data are in the sense expected from theory.

Evidently, the idea can be applied without any ambiguity to simple solvent pairs like benzene and hexane, or chloroform and carbon tetrachloride, or to those solvents which contain essentially only one type of center, but it becomes sometimes a little ambiguous in application to solvents which contain both donor and acceptor groups. However, it is interesting to note that the results with other solvents are not in violation of the above principle.

TABLE I

ESTERIFICATION OF ACETIC ANHYDRIDE

SOLVENT	BY ETHYL ALCOHOL $K_{50°}$ (17)	BY ISOBUTYL ALCOHOL $K_{100°}$ (9)	BY ISOBUTYL ALCOHOL $K_{100°}$ (9)
Hexane	0.0119	0.0877	0.0307
Heptane	.0126		
Carbon tetrachloride	.0113		
Chlorobenzene	.00533		
Xylene	—	.0510	.0196
Benzene	.00462	.0401	.0148
Anisole	.00293		
Chloroform	.00404		
Nitrobenzene	.00245		

Menschutkin reaction. We now discuss a typical organic reaction of the electron pair sharing type, the reaction of a halide with a base. This type of reaction in its various modifications has received the most attention from the viewpoint of solvent effect. In general, the reaction of, say, ethyl iodide with any base, B, can be represented as

$$C_2H_5 : I + : B = [C_2H_5 : B]^+ + [: I]^-$$

i.e., the net effect of any such nucleophilic substitution on carbon is the gain of the electron pair by the covalent iodine atom to form an iodide ion. Let us consider the effect of solvents on the sharing of this electron pair. Strong donor solvents like nitrobenzene will form weak hydrogen bonds with the alkyl CH groups. This donation will be inductively transmitted to the C → : I bond, making the electron pair shift towards iodine. In other words a donor solvent will help the reaction. This mechanism is necessarily very weak and only partly accounts for why the reaction, $C_2H_5I + (C_2H_5)_3N \rightarrow$ runs over 1000 times faster in nitrobenzene and over 200 times faster in anisole than in hexane. The data for this reaction from Menschutkin's (10) classical work and from recent work of other authors (6) are given in Table II, which clearly establishes the above effect of donor solvents. The agreement between the data of Menschutkin and those of Grimm and co-workers is, however, very poor, the discrepancy being 2 to 4 times in all cases where data exist, and so we shall only put reliance on these figures as far as the order of speed in different solvents goes, and not in their absolute values.

TABLE II

KINETICS OF THE REACTION $(C_2H_5)_3N + C_2H_5I \rightarrow (C_2H_5)_4N^+I^-$ IN VARIOUS SOLVENTS AT 100°

SOLVENT	k_2 (10)	k_2 (6)
Hexane	0.00018	0.0003
Cyclohexane		.0006
Heptane	.00023	
Toluene		.0152
Benzene	.00584	.0239
Xylene	.00287	
Chlorobenzene	.0231	.0827
Bromobenzene	.0270	.0959
Iodobenzene		.1590
o-Dichlorobenzene		.150
m-Dichlorobenzene		.0665
p-Dichlorobenzene		.042
Benzonitrile		.673
Nitrobenzene		.830
Anisole	.0403	
Acetone	.0608	
Acetophenone	.1294	
Methyl alcohol	.0516	
Ethyl alcohol	.0366	
Benzyl alcohol	.133	

We are not in a position to compare two hydrocarbons, such as hexane and benzene, on the above consideration alone, because our present knowledge is not sufficient to tell how the electron pair in question will be affected by van der Waals forces between the alkyl group and the hydrocarbon solvent. Fortunately, however, we can approach the problem in this case in another way, since other forces stronger than van der Waals forces are operative here and have more influence in the matter. Since iodide ion is a base in the Lewis sense, the hydrogen in the solvent will tend to function, though very weakly, as acceptor from iodine at the iodine end as shown below:

$$C_2H_5\ :\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{I}}}:\ \longrightarrow\ \underset{\text{Solvent}}{\mathrm{H{-}C}}\quad \text{(arrow shows donation tendency)}$$

Evidently the more electrophilic or polar is this hydrogen, the stronger will be this disruptive influence on iodine and so higher the speed. Hence, benzene will be more powerful than hexane and similarly for other solvents. This is in complete accord with the data for the above reaction in Table II.

Similarly, we expect chloroform to produce higher speed than carbon tetrachloride; we do not have data to the point from Menschutkin but this is confirmed by the data from Norris and Prentiss (11) (see Table IV) on a similar reaction between pyridine and methyl iodide. This idea of higher speed caused by electrophilic centers for this reaction accounts for the high speed in alcohols whose hydroxylic hydrogen is undoubtedly a better hydrogen bonding or electrophilic center than a hydrogen in a C—H bond. An evident consequence is that the reaction speed will vary in the order primary > secondary > tertiary, since the acidity or polarity of the hydroxylic hydrogen varies in the above order. We have no available data to test this point.

We might point out that of the above two mechanisms suggested for the enhancement of speed, *viz.*, (a) by the donor property of oxygen acting on the weakly electrophilic alkyl hydrogen, and (b) by the acceptor or electrophilic property of the solvent hydrogens acting on the iodine, we do not know for certain which one has a stronger effect. The fact, that all the donor solvents which can also act as acceptors produce much higher speed than that in ether, which can function only as a donor, suggests that mechanism b is much more important than mechanism a in enhancing the reaction speed. It should also be pointed out here that these solvent effects will also act on the base used in the above reaction, but that they will have negligible effect on the reaction speed in this case, because these bases are strong enough (primary base in the Lewis sense) to require no energy of activation in any solvent to react with an acid, particularly a strong acid of the carbonium type.

DISCUSSION

Basic principle. We might now attempt to express the above concept in a more formal and succinct way, but before doing so it might be well to review the basic ideas which we have built upon. We have made free use of three different current ideas. First, we have accepted the electronic mechanisms as envisaged by organic chemists following the cue from the Lewis theory. Second, we have accepted the idea of hydrogen bonding taking place between any positive hydrogen and any negative element present in the system. Third, we have extended the latter idea so that all hydrogens, including even those in the alkanes, can take part in hydrogen bonding process; the strength of the hydrogen bond will depend on the polarity of the C—H bond, and hence these bonds will certainly be extremely weak with hydrocarbons but will differ greatly among themselves.

We can now formulate the basic principle we have utilized, thus: *The more a solvent blocks up by hydrogen bond or otherwise the active centers which take part in a chemical reaction, the less will be the speed in it; the more a solvent, by suitable hydrogen bond or otherwise, helps electron shift necessary to the reaction, the higher will be the speed in the solvent.*

An interesting consequence of the above principle is that if a reaction consists of a direct attack of an electrophilic center by a nucleophilic center, say a hydrogen atom in a molecule by an oxygen, the speed will be maximum in an inactive solvent, and the introduction of any electrophilic or electrodotic group in the solvent will retard the reaction. Besides our first case which illustrates this type of behavior, another very apt illustration of this mechanism is the photochemical oxidation of chloroform by oxygen investigated by Plotnikov (13). It will be observed from his data (Table III) that the speed is the highest in CCl_4, hexane, etc., and any increase of acidic or basic tendency in the solvent molecule reduces the speed by blocking off the active centers of reaction.

In attempting to apply the above concepts to some more known cases, it is surprising and regrettable that reliable and systematic data exist for very few uncatalyzed reactions of any other type. Most organic reactions studied with regard to solvent effect are either of the Menschutkin type or esterification type and the same kind of solvent effect persists in practically all of them, as was noticed in as early as 1912 by Patterson and Montgomerie (12) who remarked, "it appears that solvents influence quite different reactions in a uniform manner; although the manifestation of this effect may be of an opposite character, a given set of solvents may hasten a particular reaction in a certain sequence, whilst in the same or very nearly the same sequence they retard another reaction." That this is true on the Menschutkin type reaction is shown by the data in Table IV, collected from various authors. There is one interesting point to note from Table IV.

TABLE III

RELATIVE REACTION VELOCITY OF THE PHOTOCHEMICAL OXIDATION OF IODOFORM IN VARIOUS SOLVENTS

SOLVENT	RELATIVE RATE
Carbon tetrachloride	39.4
Benzene	34.6
Carbon disulfide	24.1
Ether	17.0
Ethyl acetate	8.1
Methyl alcohol	3.2
Ethyl alcohol	2.3
Acetone	0.7

Data from Plotnikov (13).

$$\text{(a) } RCOCH_2{:}Br + \text{Base} = Br^- + [RCOCH_2{:}\ \text{Base}]^+$$
$$\text{(b) } RCH_2CH_2{:}Br + \text{Base} = Br^- + [RCH_2CH_2{:}\ \text{Base}]^+$$

It follows from our theory that if we have two reactions, (a) and (b), in two solvents, say hexane and benzene, the increment in speed for reaction (a) will be much less than that for reaction (b) because the increased polarity of benzene will no doubt enhance the speed by acting through mechanism II at the bromide end, but will also retard the speed by attaching itself more firmly on the keto oxygen and hence tend to oppose the electron shift necessary for the reaction. Therefore the rate of increase of speed with increasing electrophilic nature of the solvent will be less for (a) than for (b). In other words, we deduce the relation

$$\frac{(K_a)\ \text{active solvent}}{(K_a)\ \text{hexane}} < \frac{(K_b)\ \text{active solvent}}{(K_b)\ \text{hexane}}$$

where K_a and K_b are the speeds of the reaction (a) and (b) respectively and active solvent means any solvent which has more electrophilic hydrogen than hexane.

TABLE IV

Solvent Effect on Reaction Speed

SOLVENT	1	2	3	4	5	6	7
Hexane	0.0018			0.00014			
Ethyl ether	.00063	0.000607		.00025			
Isopropyl ether						1.195	
Ethyl acetate	.0223			.0108			
Carbon tetrachloride						1.65	0.00002
Toluene			.000231		0.00126	2.07	
Benzene	.00584	.000644	.000305	.0024	.00223	2.15	
Chloroform		.000970				2.525	.000434
Chlorobenzene	.0231					2.60	
Anisole	.0403			.0160		2.83	.000886
Nitrobenzene		.00617	.0129	.150	.0848	3.57	.0048
Acetone	.0608	.0139	.00505	.071	.0338		
Benzyl alcohol	.133	.0208		.042			

1$K_{100°}$ for $C_2H_5I + (C_2H_5)_3N \rightarrow$; Menschutkin (10).

2$K_{27.8°}$ for $C_6H_5COCH_2Br + C_6H_5NH_2 \rightarrow$; Cox (4).

3$K_{28.3°}$ for $CH_2 = CHCH_2Br + C_5H_5N$(pyridine) →; Hawkins, *J. Chem. Soc.*, **123,** 1170 (1922)

4$K_{30°}$ for $NO_2C_6H_4CH_2Cl\ (CH_3)_3N \rightarrow$; McCombie, Scarborough and Smith, *J. Chem. Soc.*, 802 (1927).

5$K_{25°}$ for $C_2H_5I + C_5H_5N$(pyridine) →; Norris and Prentiss (11).

6$K_{100°}$ (calculated) for $CH_3I + C_5H_5N$(pyridine) →; Pickles and Hinschelwood, *J. Chem. Soc.*, 1353 (1936).

7$K_{60°}$ for $CH_3I + C_5H_5N \rightarrow$; Thompson and Blandon, *J. Chem. Soc.*, 1237 (1933).

We do not have data in the literature to test this with aliphatic compounds, but the data of Cox (4) in column 2, using ω-bromoacetophenone ($C_6H_5COCH_2Br$), show this trend very strikingly when compared to Menschutkin's data using ethyl iodide (C_2H_5I) in column 1. In every case as we go down the column (Table V) the increase of speed with reference to ether is much less in column 1 than in column 2. As reference speed, hexane would have been much better but unfortunately Cox has given no data for hexane and hence we are forced to take the data for ether as reference, since it is known to have speed in the same range as hexane.

There is, however, one basic difficulty in applying our knowledge of solvent acidity or basicity derived from the study of any particular source towards quantitative deduction. Lewis (8) has clearly pointed out that the order of basic strengths for different bases will differ with the acid used for comparison, and there is no fundamental reason to attach any absolute significance to the order of basicities obtained with the proton as the acid. Now, since many organic reactions occur through the intervention of the carbonium ion, which is an acid in the Lewis sense, strictly comparable results can hardly be expected, though the general trend cannot be masked owing to this factor. Furthermore, it is impossible to classify a solvent as purely acidic or purely basic in the Lewis sense, or pure donor or pure acceptor as Sidgwick would prefer to call it, for they not only differ widely among themselves in degree, but most solvents are capable of exercising both functions. This has been pointed out by many authors, for example, by Bell (2) and by Ewell and co-workers (5), and hence it is impossible to generalize the effect of a solvent with respect to its acidity or basicity, and every case requires consideration on its own merit along the lines indicated.

TABLE V

THE RELATIVE SOLVENT EFFECT IN MENSCHUTKIN REACTION OF A HALOGENATED KETONE AND AN ALKYL HALIDE

(a) $C_6H_5COCH_2Br + C_6H_5NH_2 \rightarrow (C_6H_5COCH_2)(C_6H_5)H_2N^+ Br^-$

(b) $CH_3CH_2I + (C_2H_5)_3N \rightarrow (C_2H_5)_4N^+I^-$

SOLVENT	$\frac{(K_a)\text{ solvent}}{(K_a)\text{ ether}}$	$\frac{(K_b)\text{ solvent}}{(K_b)\text{ ether}}$
Ether	1.0	1.0
Benzene	1.06	9.28
Acetone	24.9	96.6
Benzyl alcohol	46.1	211.

be difficult to predict. However, as we have clearly illustrated our concept by the above typical examples, we shall not extend the same to the other rather limited data available.

The difficulty of any generalized treatment can further be appreciated if we remember that most reactions are essentially, as pointed out by Ingold (7), an interaction between an electrophilic center of one molecule and a nucleophilic center of another molecule, and any solvent which will block up one of these centers will tend to activate the other. Therefore, unless one of the centers is strong enough to overrule this intervention by the solvent molecule or weak enough to be unaffected by such influence, small differences between similar solvents might

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