MODERN APPROACHES TO THE CONSTRUCTION OF HIGHLY EFFICIENT NUCLEOPHILIC SYSTEMS

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In this review we present a summary and correlation of research results obtained in several different approaches aimed at increasing the efficiency and selectivity of nucleophilic reactions, namely the \( \alpha \)-effect in aqueous media and specific interactions in nontraditional systems such as "melts" of salts, microemulsions, micelles, and liquid/liquid and liquid/solid interfacial systems.

INTRODUCTION

Physical organic chemistry of the 20th century is in an epoch in which classical mechanisms of organic reactions have been developed, and searches have been made for quantitative relationships between the reactivity of organic compounds, on the one hand, and the structure of the compounds and the properties of the medium, on the other hand. Research during this period has been characterized by the deliberate selection of relatively simple chemical systems in homogeneous solutions (primarily dilute solutions) as the objects of investigation. We will call such systems and media "traditional." This approach was justified at a certain stage of development. It advanced the theory of organic chemistry, but at the same time it moved away from the processes that take place in the real living world.

On the threshold of the 21st century, physical organic chemistry is undergoing radical changes. Researchers are no longer working on traditional systems, more and more turning to systems with multiple interactions – specifically, reactions in microorganized and biological media. One obvious indicator of this trend is the theme of at least two recent international forums, one on homogeneous catalysis (Princeton, USA, 1996) [1] and one on physical organic chemistry (Inchon, South Korea, 1996) [2]. For the reaction media that are of the most current interest (which we will call "nontraditional"), the distinctive feature is a high degree of structurization and the presence of an interfacial surface (IFS).

A high degree of structurization of water or alcohols can be achieved in concentrated solutions of quaternary ammonium salts (QAS) that are not surfactants. We will call such media "melts" of salts [3]. They have a number of unusual properties that can be attributed to their high degree of structurization, i.e., the association of liquid molecules with each other [4, 5]. Although there is no IFS in such solutions, their properties can still be considered from the theory of microheterogeneity. Thus, the behavior of "structurized" water has been described on the basis of a model of rapidly appearing and disappearing accumulations ("flickering clusters") [4]. According to another hypothesis [6], there are certain analogies in the behavior of polymolecular associates of alcohols as components of the medium and the behavior of flexible-chain polymers, so that the scaling approach that has been developed in polymer chemistry [7] can be applied to associated liquids.

In aqueous solutions of surfactants, polymolecular spherical associates (micelles) are formed. These micelles are representatives of the general class of extremely small aggregates (nanoparticles) that have an IFS [8, pp. 72-123]. The micelle surface is a monomolecular layer that closes on itself [9, 10]. In the region of the critical micelle concentration (CMC), the micelle diameter is some 2-5 nm. The discovery of these particles led to the creation and development of an entire field of physical organic chemistry – micellar catalysis [11, 12]. Under certain conditions, considerably larger particles known as vesicules are formed in aqueous surfactant solutions [13]. These are "bubbles" with a surface formed by a double monolayer...
(bilayer) of oriented surfactant molecules. Vesicles may be extremely large, up to $2 \times 10^5$ nm in diameter, which qualifies them to be known as giant vesicles [13]. Therefore, they can be observed under an optical microscope.

Thermodynamically stable microemulsions [8, pp. 469-566], [14-16], of either the water/oil or oil/water type, in which the oil may be any nonpolar organic solvent that is immiscible with water, are formed in the presence of a detergent (ionic surfactant) and a codetergent (nonionic surfactant, usually an alcohol with $C > 4$-6). Thus, in contrast to two-component micellar solutions, microemulsions consist of at least four components. Microemulsions and micelles are similar in many respects; however, the microemulsions have a much more highly developed surface and a greater volume of drops. In microemulsions, the submicroscopic aggregates may have diameters as large as 10-250 nm [8]; nevertheless, the liquids remain optically transparent, like micellar or homogeneous solutions. The structure and microstructure of microemulsions may vary widely, depending not only on the type of microemulsion but also on the nature of the detergent and codetergent, the temperature, the salt composition of the aqueous phase, and other factors. The addition of polymers to microemulsions leads to dramatic changes in structure, increasing the microemulsion stability [16]. Under certain conditions, the drops of a microemulsion will aggregate to form new clusters, the lifetime of which may be on the order of microseconds [8, 14, 17]. The cluster formation leads to more bulky structures, all the way up to the formation of giant cavities [18], spongy phases [19], etc. The surface of such formations is in a constant state of flux. Additives will bring about various morphological changes; some "wound" the surface, others "heal" it [18]. In this aspect, the surface of nanoparticles and larger formations (particularly those based on synthetic lipids) are similar to living biological membranes and are widely used to model these membranes (see for example [18, 20-24]. In general, the interest in micelles and microemulsions is extremely high. By way of illustration, we will only mention several recent reviews of research on the structure and dynamics of these systems [16, 17, 25-31], methods of investigation [32-34], certain areas of practical utilization [35-40], and other aspects.

In contrast to microemulsions, emulsions and colloidal solutions (with particle dimensions some 100 times larger) are thermodynamically unstable, optically opaque liquids; and in this respect, they are more similar to two-phase liquid/liquid (L/L) or liquid/solid (L/S) systems, the surface dimension of which is determined largely by external factors such as the degree of milling, stirring rate, etc. Any intensive study of the kinetics and mechanism of organic reactions in these systems has been initiated only quite recently, owing to the discovery of phase-transfer catalysis [41, 42]. Thus, the common property of nontraditional media is their high degree of structurization in disperse systems, while distinctions within this broad group are based on the degree of dispersity.

Research on the kinetics and mechanism of nucleophilic reactions in nontraditional media is today one of the approaches that is being pursued vigorously in attempts to create systems with higher nucleophilicity, characterized at the same time by high specificity and selectivity.

Nucleophilic substitution reactions have played a historic role in the development of theory of organic reaction mechanisms [43], enzyme catalysis [44], and antibody catalysis [45]. The practical aspects of these processes are also very diverse. One approach that has been taken is to search for and construct systems, acting through a nucleophilic mechanism, that are able to break down rapidly and irreversibly certain low-reactivity substrates that are ecological toxicants. This approach is being pushed today mainly in connection with the increasing threat of ecological hazard due to industrial accidents, and also due to the accumulation of large reserves of chemical weapons on our planet. Most ecological toxicants (pesticides, for example), toxic substances that act by neuroparalytic effect and poisons that are cholinesterase inhibitors, are derivatives of phosphorus acids such as compounds I-III [46]. In this same class are low-reactivity, mechanistically similar derivatives of carboxylic acids (IV) and arylsulfonic acids (V), as well as alkyl and aryl halides RX (VI):

\[
\begin{align*}
\text{I} & : \quad R_1 Y \quad P \quad Y \\
\text{II} & : \quad R_1 Y \quad P \quad Y \\
\text{III} & : \quad R_1 Y \quad P \quad Y \\
\text{IV} & : \quad R \quad C \quad Y \\
\text{V} & : \quad O \\
\end{align*}
\]

where $Y$ is usually O, S, or an NRN fragment; $X$ is YR, YAr, Hal, etc. These compounds are being used as the electrophilic component in nucleophilic reactions simulating the decomposition of toxic substances. Rarely do researchers resort to the use of objects of investigation that are so highly toxic and hence the most difficult to