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Abstract

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ON THE QUESTION OF A DIRECTED SEARCH FOR NEW BIFUNCTIONAL CATALYSTS

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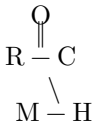
A chemical reaction proceeding under the influence of a bifunctional catalyst may be regarded as the simplest model of an enzymatic process ([1]). Therefore, attempts to elucidate the features of the mechanism of such model reactions open up prospects for finding new effective catalysts possessing the high merits characteristic of biological catalysts.

As was shown previously ([2–4]), the catalytic efficiency of carboxylic acids in the acylation reactions of aromatic amines by anhydrides and acid chlorides of carboxylic acids is determined by the presence in their molecule of two functional groups: a nucleophilic one (the oxygen atom in the carbonyl) and an electrophilic one (the hydrogen atom in the hydroxyl). On the basis of the proposed mechanism of catalysis by carboxylic acids in the acylation of amines ([2–6]), in order to clarify further the nature of bifunctional catalysis, it seemed of interest to study, as potential catalysts, compounds of the type:



(I)

where M is some atom other than an oxygen atom. We studied the catalytic properties of compounds in which, as M, the neighbors of oxygen in D. I. Mendeleev' s periodic system were represented, namely nitrogen and sulfur. Thioacetic acid, diacylamides (dibenzoyl- and diacetylamides), and arylamides of carboxylic acids were taken as such compounds.

The catalytic action of the substances under investigation was studied using the reactions of acylation of aromatic amines with benzoyl chloride in benzene. In studying the catalytic action of diacylamides and amides of carboxylic acids, the rate was measured as indicated previously ([2]), while in the case of thioacetic acid the following procedure was used. The process was stopped by binding the aminoderivative that had not entered into the reaction with a solution of

Fig. 1. Dependence of the rate constants k for the reaction of m-chloroaniline with benzoyl chloride on the analytical concentrations m of thioacetic acid (I) (lower scale along the abscissa), dibenzamide (II), and diacetamide (III) (upper scale along the abscissa).

Figure 1: Fig. 1. Dependence of the rate constants k for the reaction of m-chloroaniline with benzoyl chloride on the analytical concentrations m of thioacetic acid (I) (lower scale along the abscissa), dibenzamide (II), and diacetamide (III) (upper scale along the abscissa).

hydrogen chloride in benzene; the precipitate of the amine salt was filtered off on a glass filter, washed with benzene from thioacetic acid, dissolved in water, and the amine was determined by potentiometric nitrite titration ([2]).

Control experiments ([2,7,8]) showed that under the experimental conditions thioacetic acid, imides, and amides of carboxylic acids do not enter into side processes, and the reaction proceeds quantitatively and irreversibly according to the equation:

$$C_6H_5COCl + 2ArNH_2 \rightarrow C_6H_5CONHAr + ArNH_3^+Cl^-. \quad (1)$$

The observed rate constants k were calculated as indicated previously ([2,6]).

As is seen from Fig. 1, the constants k are in a linear dependence on the analytical concentration m of thioacetic acid, diacetamide, and dibenzamide. These constants are determined by the equation

$$k = k_0 + k_A m, \quad (2)$$

where k_0 and k_A are, respectively, the rate constants of the noncatalytic and catalytic reactions. The linear dependence of k on m apparently indicates that in benzene solution the substances under study are present in monomeric form, in contrast to carboxylic acids, which under analogous conditions occur as a mixture of dimers and monomers, of which only the latter form exhibits catalytic activity ([2,8]). The result obtained for thioacetic acid is consistent with spectral data ([9]), from which it follows that this acid does not form hydrogen bonds and, consequently, exists in monomeric form not only in benzene solutions but also in the free state. Unfortunately, we do not have literature data on the analogous question for solutions of imides of carboxylic acids.

Fig. 1. Dependence of the rate constants k for the reaction of m-chloroaniline with benzoyl chloride on the analytical concentrations m of thioacetic acid (I) (lower scale along the abscissa), dibenzamide (II), and diacetamide (III) (upper scale along the abscissa).

The catalytic rate constants calculated from Eq. (2) are given in Table 1. From these data it is seen that amides of carboxylic acids do not possess catalytic

activity, which is most likely connected with the weakly expressed acidity of the amide hydrogen. As is known ([12]), the presence of two acyl groups in diacylamides so increases the mobility of the hydrogen atom attached to nitrogen that such substances already exhibit appreciable acidic properties. This accounts for their considerable catalytic effect, comparable with that observed for carboxylic acids.

If it is taken into account that the catalytic effectiveness of carboxylic acids is proportional to their strength, then one should expect that thioacetic acid, being appreciably stronger than acetic acid (see Table 1), will also prove to be a more active catalyst. However, thioacetic acid has a catalytic activity approximately 30 times less than acetic acid. Such an unexpectedly small effectiveness of thioacetic acid as a catalyst can be explained in the following way. It is known that, according to spectroscopic studies ([13]), thioacetic acid exists only in the form of

Table 1

Catalytic constants k_A ($l^2/mol^2 \cdot s$) for compounds R—COMH in the reactions of benzoyl chloride with aromatic amines in benzene solution at 25°

Catalyst	k_A, aniline	k_A, *m*-chloroaniline	k_a
C_6H_5COOH	22.3	3.88	$6.5 \cdot 10^{-5}$ ([10])
CH_3COOH	13.5	1.01	$1.8 \cdot 10^{-5}$ ([10])
$CH_3CO\backslash NH/CH_3CO$	—	0.646 ± 0.009	—
$C_6H_5CO\backslash NH/C_6H_5CO$	—	0.542 ± 0.030	—
$CH_3—C(=O)—S—H$	0.41 ± 0.14	0.0300 ± 0.0029	$4.7 \cdot 10^{-4}$ ([11])
$C_6H_5CONHAr$	0	0	—

thiol form

$$CH_3—C(=O)—S—H.$$

If it is taken into account that the ability of thiocarboxylic acids to form hydrogen bonds is very weak ([9]), then from the experimental results presented it follows that, for the acylation process to proceed through a cyclic transition complex ([6]) of the aminacylating agent-catalyst composition (see structures (II) or (III)), the clearly expressed ability of the bifunctional catalyst to form a hydrogen bond is of essential importance. It is well known that such an ability is possessed by hydrogen atoms

Scheme 1*

joined to oxygen or nitrogen ([14]).

Scheme 1: cyclic transition complexes (II) and (III)

Figure 2: Scheme 1: cyclic transition complexes (II) and (III)

It could also be thought that the loss of catalytic activity in going from acetic acid to thioacetic acid is connected with a weakening of the nucleophilic properties of the oxygen atom in the carbonyl of thioacetic acid. But this assumption must be rejected if one recalls that, when halogen atoms are introduced into the methyl group of acetic acid, there is a sharp increase in the catalytic properties ([7]), although this is also accompanied by a weakening of the nucleophilic ability of the oxygen in the carbonyl. One should also reject the assumption that thioacetic acid, being stronger than acetic acid, converts the amine into an unreactive cationic state. Still stronger monochloroacetic acid does not form appreciable amounts of ionic salt with aromatic amines not only in benzene ([15]), but even in nitrobenzene ([6]), and therefore has high catalytic activity ([7]).

Thus, the catalytic activity of compounds of type (I) depends not only on their acid strength, but probably is determined primarily by their ability to enter into hydrogen bonds. From the latter circumstance arise new possibilities for a scientifically grounded search for effective bifunctional catalysts in reactions of nucleophilic substitution at a carbonyl carbon atom.

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* X is a halogen. Bonds being broken are indicated by a crossed line; bonds being formed, by a dotted line.

Note: Figure translations are in progress. See original paper for figures.