at low frequencies show, at least two water molecules incorporated in the hydration shell retain their rotational mobility, as has been observed for hydration of compound **3** (see Ref. 4). The decrease in absorption indicates hydrophobic immobilization of two or three water molecules, most likely, around the bridging HC—CH group and the four methyl groups. Up to four water molecules are bound according to a mechanism of positive polar hydration through the formation of H-bonds with the carbonyl O atoms.

The rate of enzymatic hydrolysis of *N*-acetyl-L-tyrosine ethyl ester catalyzed by α-chymotrypsin was also studied. The rate noticeably increases in the presence of **1** ($[\mathbf{1}] \le 0.15$ mol L^{-1}): the rate constant of hydrolysis of the acyl-enzyme intermediate is $k = k_{c,1} + k_{c,2}\,[\mathbf{1}]$, where $k_{c,1} = 2.5\ s^{-1}$ is the rate constant of the hydrolysis in the absence of **1**, and $k_{c,2}$ is the second-order rate constant taking into account the effect of **1** on the rate of the enzymatic reaction. When $[\mathbf{1}] \le 0.15$ mol L^{-1}, no structural changes of α-chymotrypsin or its ability to bind **1** were detected; therefore, the accelerating effect of **1** can be attributed mostly to the activation of water as a nucleophilic reagent (generation of additional reactive H_2O molecules with high mobilities[4]).

The denaturing activity of **1** was studied by differential UV spectrophotometry.[5] Up to the concentration $[\mathbf{1}]_{cr} = 0.7$ mol L^{-1} the globular protein (chymotrypsinogen A) is conformationally stable. At higher concentrations of compound **1** denaturation of the protein is observed. Previously[5] it was shown that denaturation of proteins in aqueous solutions of organic nonelectrolytes occurs in those cases where they are able to break the structure of water and also in the case of exhaustion of the bulk water. Denaturation of chymotrypsinogen A was observed at $[H_2O]_{cr} = 49$ mol L^{-1}, which practically coincides with the value $[H_2O]_{cr} = 48$ mol L^{-1} obtained for compound **3** and guanidine chloride.[5] Hence, compound **1** activates the aqueous component and can thus affect the static and dynamic structures of physiologically active proteins as well as their biological activity.

The results obtained and also the suggestion concerning the activation of biological membranes[2] may be favorable for understanding the contributions of solvent effects to the mechanisms of pharmacological activity of **1** and similar materials.

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Palladium-catalyzed homocoupling of aryl halides in a aqueous-organic microemulsion through the action of hydrogen

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Previously[1,2] we studied hydrogenolysis of water-soluble aryl halides in aqueous alkaline solutions through the action of $NaBH_4$ in the presence of $PdCl_2$ as catalyst and showed that the process occurs chemoselectively to give the corresponding arenes. However, aryl halides insoluble in water virtually did not undergo hydrogenolysis under the same conditions even in the presence of a phase-transfer catalyst. A number of techniques for the reduction of water-insoluble aryl halides in aqueous-organic media in the presence of catalysts

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have been reported. Depending on the conditions, a substrate is selectively reduced to give the corresponding arene,[3] couples to give biaryl,[4] or affords both products.[5]

Currently we are studying chemical processes occurring in aqueous or aqueous-organic media in the presence of metal complex catalysts.[1,2] The purpose of the present work is to study reduction of aryl halides insoluble in water in classical microemulsions,[6] which make it possible to provide a homogeneous reaction medium.

Preliminary experiments on the optimization of the reaction conditions showed that the conditions of hydrogenolysis of water-soluble aryl halides in aqueous media cannot be extended to the reactions in microemulsions. $NaBH_4$ causes rapid separation of the microemulsion into layers with coagulation of colloidal Pd. Consequently, the degree of conversion of an aryl halide into the corresponding arene does not exceed several percent. Therefore, we used another reducing agent—catalyst pair: H_2 and $PdCl_2(dmp)_2$, containing water-soluble monosulfurized triphenylphosphine in the coordination sphere of the palladium complex.

Conducting the reaction under these conditions unexpectedly resulted in the direction of the process being entirely changed toward the formation of the products of coupling of the starting aryl halides; the overall degrees of conversion of aryl halides were low (30—50 %):

$$\mathrm{ArX} \xrightarrow[\mathrm{H_2O,\ BuOH,\ SDS,}\ T]{\mathrm{H_2,\ PdCl_2(dmp)_2,\ K_2CO_3}} \mathrm{Ar_2}$$

Ar = RC_6H_4; R = H, *p*-Me, *p*-MeO, *p*-Cl, *m*-CF_3;
X = I, Br

Only traces of the hydrogenolysis products were detected in the reaction mixtures. Previously we observed virtually complete suppression of hydrogenolysis of aryl halides in water, when phosphine complexes of Pd were used as catalysts.[1]

The yield of the product of hydrogenolysis virtually does not depend on the nature of the leaving group, although the rates of oxidative addition of Pd to aryl halides decrease in the order ArI > ArBr (see Refs. 1 and 2). In our opinion, the leveling of the yields of biaryls is determined by two oppositely directed factors. First, in terms of the reactivity of ArX, the yields of the products increase in the case of aryl iodides. Second, stratification of the microemulsion by the action of a halide ion and, as a consequence, dramatic retardation of the process act in the opposite direction, since the stability of an emulsion decreases in the series Br > I. Since aryl chlorides do not react under these conditions, aryl bromides are the optimal substrates for this reaction.

Thus, variation of the nature of the solvent, the type of reducing agent, and the catalyst in the reduction of aryl halides lead to change in the reaction course toward the formation of biaryls.

Typical procedure. Water (4.5 mL), *n*-butanol (0.5 mL), sodium dodecylsulfate (0.25 g), a substrate (1 mmol), $PdCl_2(dmp)_2$ (0.1 mmol), and potassium carbonate (2 mmol) were placed in a reaction vessel equipped with a magnetic stirrer and filled with purified argon. The mixture was heated to 30—50 °C with stirring until a transparent microemulsion formed. The resulting microemulsion was stirred for 24 h in an H_2 atmosphere (p = 1 atm). The reaction mixture was neutralized with dilute HCl and extracted with ether. The ethereal extracts were dried with Na_2SO_4 and passed through a layer of silica gel. The resulting solution was concentrated and analyzed by GLC. The melting points of the compounds isolated coincide with the literature data.[7]

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