Mechanisms in Heterogeneous Liquid-phase Catalytic-transfer Reduction: the Importance of Hydrogen-donor Concentration

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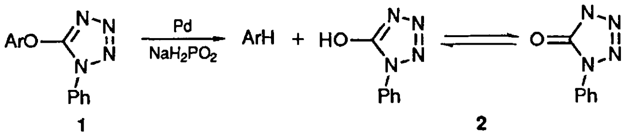
In liquid-phase heterogeneous catalytic-transfer reduction, the concentration of hydrogen donor is of extreme importance, being able to suppress reaction entirely if it is not kept very low relative to the concentration of the reducible substrate; biphasic solvent systems provide a simple means of exercising the required control.

Heterogeneous liquid-phase catalytic-transfer reduction is of increasing importance, particularly in large-scale industrial processes, which might normally require usage of hazardous molecular hygrogen.[1] Mechanisms in these systems are poorly understood but, for the hydrogeneolysis of aryloxytetrazoles (**1**; Scheme 1) to give arenes, we have shown that incorporation of hydrogen is site-specific[2] and that the reaction is characterized by 'burst kinetics' in which a steady-state is controlled by the rate of release of the tetrazolone **2**.[3] Usually, this reaction is carried out in a biphasic solvent system (benzene–water) in which the heterogeneous catalyst resides in the upper organic layer, the substrate is dissolved in the same layer and the hydrogen donor (sodium phosphinate) is mostly contained in the lower, aqueous phase. In considering reaction rates in such heterogeneous systems containing a solid and two partially miscible liquids,[3] it is not obvious just what should be considered as concentrations of substrate and donor with respect to the catalyst surface. In an attempt to overcome this problem, monophasic solvent systems were examined, using hydrogen donors soluble in organic solvents.

The donors mostly used in Scheme 1 are sodium phosphinate (hypophosphite) or sodium formate and, accordingly, tetra-n-butylammonium phosphinate (TBP) and tetra-n-butylammonium formate (TBF) were synthesized and found to be completely soluble in such solvents as benzene, ethanol and water. Transfer hydrogenolysis of 5-(2-naphthoxy)-1-phenyltetrazole (Scheme 1; Ar = 2-naphthyl) with TBP in a monophasic solvent system (benzene saturated with water) was attempted using 10% palladium-on-charcoal as catalyst. In complete contrast to the corresponding biphasic system



Scheme 1

(benzene–water) in which reduction was rapid and high yielding, no hydrogenolysis occurred. A major difference between the two solvent systems lies in the concentration of the hydrogen donor. In the biphasic solvent system, most of the phosphinate anion is dissolved in the lower, aqueous phase with little in the upper phase in contact with the catalyst. In the monophasic solvent system, all of the donor is in the organic layer and is able to approach the catalyst surface. To investigate the effect of the concentration of the phosphinate donor on the rate of reduction in the monophasic system, its steady-state concentration was reduced to a low level and controlled by one of three means: (*a*) by gradual dropwise addition of a solution of TBP to the substrate–catalyst–solvent system; (*b*) by slow transfer of TBP to the substrate–catalyst–solvent system through its continuous liquid–liquid extraction by benzene from an aqueous solution; (*c*) by addition of solid (insoluble) sodium phosphinate to the substrate–catalyst–solvent system, together with a trace quantity of 18-crown-6 ether as a phase-transfer catalyst. Under these conditions of low phosphinate anion concentration in the monophasic system, the hydrogenolysis (Scheme 1) proceeded smoothly, as in the biphasic solvent system. Confirmation of this importance of donor concentration came in two ways. First, use of sodium phosphinate in the monophasic solvent system with a stoichiometric ratio of 18-crown-6 ether to solubilize a substantial proportion of donor led to no reduction, unlike those experiments in which only a trace of crown ether was used. Secondly, direct observation of the effect of the donor was obtained by stirring catalyst with a known concentration of 5-(2-naphthoxy)-1-phenyltetrazole in benzene at 20 °C. After 50 min, the concentration of substrate in solution was measured to give the equilibrium amount adsorbed onto the catalyst. Addition of a stoichiometric ratio of TBP immediately caused all of the tetrazole compound to desorb back into solution.

These results are readily accommodated by considering that the stability constant for adsorption of donor (phosphinate anion) onto the catalyst surface must be much greater than that for adsorption of substrate. Thus, a reasonably large coverage of catalyst sites by the substrate can be attained only by reducing the donor anion concentration in the solvent phase in contact with the catalyst. Knowledge of the relative stability constants for adsorption of substrate and donor onto the catalyst would enable optimum catalyst site occupancy for rapid reaction to be achieved.

Fortuitously, it appears that a biphasic solvent system provides a simple means of controlling adsorption of donor onto the catalyst by keeping most of the donor in the aqueous phase, away from the catalyst and allowing only a small concentration of donor in the upper, organic phase. Similar control of donor to a low level in a monophasic solvent system by methods such as those (*a*–*c*) outlined above, also provide suitable conditions for reduction to proceed.

These results may be applied also to transfer reduction of aromatic nitro compounds to amines[4,5] or hydroxylamines[6] by formates and phosphinates, in which biphasic aqueous organic solvents perform better than does a single phase solvent system. The marked pH dependence of catalytic-transfer reduction of nitro compounds and aryloxytetrazolyl ethers is also explicable in terms of control of the concentration of the free formate or phosphinate anions. For the weak formic and phosphinic acids, at low pH, the concentration of free anion is too low to provide rapid reduction but, at high pH, almost all of the donor is present in the reactive anion form. For optimum rate of transfer reduction using phosphinates or formates, their concentration in the organic phase in contact with the catalyst should be adjusted by pH and/or choice of solvents so as to allow the substrate to have a reasonable competitive opportunity of adsorbing onto catalyst sites. In cases where adsorption of substrate is stronger than that of the donor (as with substrates having aldehyde or ketone groups[7]), it may be necessary to *increase* the relative concentration of donor anion. These results have important consequences for control of rate and selectivity in heterogeneous catalytic transfer reduction.

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