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Enhanced electron phase-transfer catalysis due to the formation of substrate–catalyst inclusion complexes

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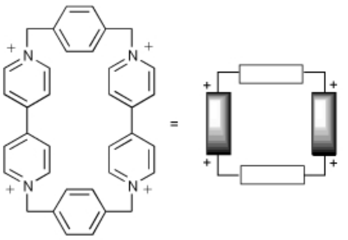
A redox-active macrocyclic ionene oligomer, cyclobis(paraquat-*p*-phenylene), exhibited an enhanced activity as an electron phase-transfer catalyst for the reduction of quinones compared with acyclic benzyl viologen, due to the inclusion of the substrate into the catalyst cavity.

Compounds having one or more viologen units have attracted much attention because of their versatile applications.[1,2] Of particular interest among recent developments are a series of elaborate works on supramolecular chemistry by Stoddart *et al.*[2] which have led to successful construction of a variety of supramolecular architectures such as pseudorotaxanes, rotaxanes and catenanes mainly using a redox-active macrocyclic ionene oligomer,[3] *i.e.* cyclobis(paraquat-*p*-phenylene)[4] **1**. Theirs as well as work by other research groups[5] unambiguously show that **1** and related compounds form inclusion complexes with a variety of guests. However, little is known to date of their applicability in other fields including catalysis.



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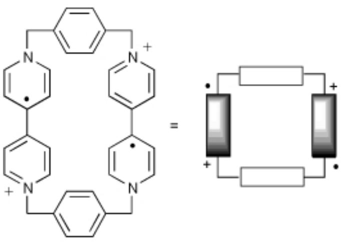

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On the other hand, electron transfer catalysis by viologen compounds, which function as mediators of electron transfer, has continuously been attracting considerable interest.[1,6] Such compounds have been applied to the reduction of various substrates such as aldehydes and ketones,[6a,b] quinones,[6c] azobenzene,[6d] acrylonitrile,[6e] nitroalkenes,[6f] and nitroarenes,[6g] to the reductive desulfonation of α-nitro sulfones,[6h] and to the dehalogenation of diphenylbromomethane,[6i,j] *gem*- and *vic*-dibromides[6k,l] and α-halogeno ketones[6m] with either zinc or sodium dithionite in either a monophase or a two-phase solvent system. The viologen compounds thus far used include alkyl viologens,[6b,f–h,l,m] ionene polymers[7] having viologen units in the main chains,[6d,i–k] vinyl polymers having viologen units in the pendant groups,[6a,c,e] and so forth. However, no cyclic viologen compounds have ever been examined for catalysis.

The present research combining the above two fields of chemistry was motivated by the premise that, if the substrate is included in the cavity of **2**, a reduced species of **1**, the viologen units might be able to mediate the electron transfer more efficiently than acyclic viologens such as benzyl viologen **3** because of the close vicinity of the substrate to the units, and hence **1** would exhibit a higher activity of electron transfer catalysis than **3**. This communication reports that the experimental results using quinones as substrates validated this conjecture. In addition, to the best of our knowledge, this work presents the first example that the fundamental constituent of a cyclophane, *i.e.* the viologen moiety in the case of **1**, directly plays a pivotal catalytic role for the substrate included in the cavity of the host.

Fig. 1 shows the results of reduction of 1,4-benzoquinone with zinc in the presence of **1** in an alkyl acetate–H_2O (1:1) two-phase system at 25 °C.[8] Conversion of the substrate increased in the order: AcOMe < AcOEt < AcOBu. Thus, in general, the extent of reduction in the two-phase solvent systems became increasingly higher with increase in the hydrophobicity of the organic phase.[9] 1,4-Naphthoquinone could also be reduced similarly to 1,4-dihydroxynaphthalene. It should also be noted that, under the present reaction conditions, the reduction of quinones occurred to a considerable extent even in the absence of catalyst, and that **3** exhibits almost no ability to mediate electron transfer. However, it is obvious that **1** is, as expected, a much better mediator of electrons than **3**.

Fig. 2 depicts the results of the inhibition experiments using compounds having a phenyl or *p*-phenylene group, which can be included in the cavity of **1**, for the reduction of benzoquinone with zinc in different two-phase solvent systems, using either **1** or **3** as a catalyst.[8] The reduction of benzoquinone in AcOBu–H_2O (1:1) with use of **1** was retarded by the addition of 1,4-bis[2(2-hydroxyethoxy)ethoxy]benzene **4**.[10] Similarly, the same reduction in methyl benzoate[11] (BzOMe)–H_2O (1:1) or phenyl acetate[11] (AcOPh)–H_2O (1:1) two-phase systems was also retarded in comparison with the reduction in AcOBu–H_2O (1:1), in spite of the hydrophobic nature of these organic solvents (see above). On the other hand, almost no distinct inhibition effect was observed when **3** was used as a catalyst.

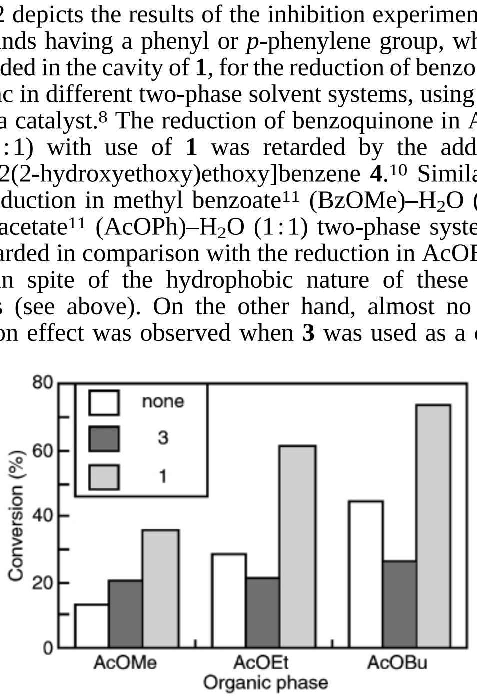

Fig. 1 Reduction of benzoquinone with zinc in alkyl acetate–H_2O (1:1) two-phase systems in the presence of **1** or **3** and in the absence of catalyst. *Conditions*: benzoquinone, 40 mM, 1.0 ml; viologen compound, 20 mM (as viologen unit), 1.0 ml; Zn, 0.20 mmol; 25 °C, 1.0 h.

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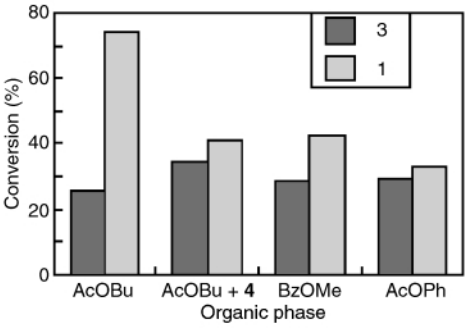
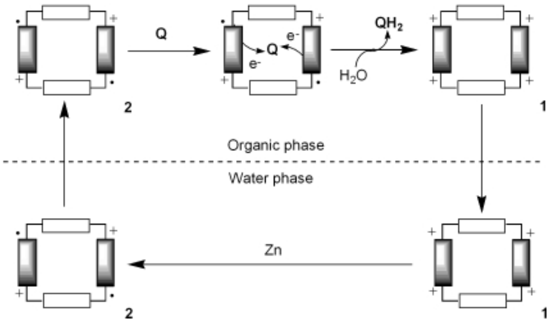


Fig. 2 Reduction of benzoquinone with zinc in the presence of **1** or **3** in different two-phase systems to prove that inclusion of the substrate into the cavity of **1** occurs; AcOBu–H_2O (1 : 1), AcOBu–H_2O containing 1,4-bis[2(2-hydroxyethoxy)ethoxy]benzene **4**, BzOMe–H_2O (1 : 1), and AcOPh–H_2O (1 : 1) (from left to right). *Conditions:* benzoquinone, 40 mM, 1.0 ml; viologen compound, 20 mM (as viologen unit), 1.0 ml; template compound **4**, 0.10 mmol; Zn, 0.20 mmol; 25 °C, 1.0 h.

Thus, it is concluded that inclusion of the substrate in the cavity of **1** does occur, and hence the enhancement of the catalytic activity of **1** compared with that of **3** (*cf.* Figs. 1 and 2) in the two-phase solvent systems can be attributed to the easier electron mediation due to the close proximity of the included substrate to the redox-active viologen units.

Cyclic voltammetry of **1** in acetonitrile exhibits only two reversible reduction processes,[12] suggesting that the two viologen units in **1** are independent of each other in the reduction process. Thus, the species produced by the initial two-electron reduction of **1** with zinc is most likely to be radical cation **2**. From this the fundamental mechanism of the catalysis in a two-phase solvent system can be derived as illustrated in Scheme 1. First, **1** is reduced with zinc in the aqueous phase to **2**, which is then transferred into the organic phase[13] where the substrate (**Q**) is included in the cavity of **2**. The substrate is then reduced to hydroquinone (**QH_2**) with concomitant reoxidation of **2** to **1**. The regenerated **1** is transferred back into the aqueous phase to participate in the next catalytic cycle. The slow reactions in the two-phase solvent systems as compared with that in homogeneous DMSO–H_2O (1 : 1)[14] could possibly be attributed, at least in part, to the slow extraction rate of **2** from the aqueous phase into the organic phase. The mechanism for the reduction in a homogeneous mixed solvent would be essentially the same as above, apart from the absence of the phase transfer processes. However, since chemical shift values of the protons of **1** were changed on mixing it with quinones in DMSO-d_6–D_2O (4 : 1), the possibility cannot be ruled out, irrespective of the reaction modes, that the substrate first included in the cavity of **1** is then reduced after reduction of the host in the inclusion complex.

In summary, when a viologen-containing macrocyclic ionene oligomer was used as catalyst, electron transfer catalysis on quinone reduction could be enhanced due to facilitated electron mediation between the substrate and the viologen units in the inclusion complex. Further investigation of catalysis using **1** and related compounds is in progress to reveal the scope and limitations as well as to gain a deeper insight into the reaction mechanism.



Scheme 1 Fundamental mechanism for the reduction of a quinone compound (**Q**) with zinc in an organic solvent–H_2O (1 : 1) two-phase system in the presence of **1**.

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8 A typical reaction procedure was as follows. In an atmosphere of oxygen-free nitrogen 1.0 ml of a 40 mM quinone solution in an organic solvent and 1.0 ml of a 10 mM solution of **1**·4Cl$^-$ in 50 mM phosphate buffer (pH 7.0), were placed in a Schlenk tube, and the mixture was deaerated three times by the freeze–thaw technique. Then, 0.20 mmol of activated zinc powder, was added in an atmosphere of nitrogen. The mixture was vigorously stirred (> 1200 rpm) with a Teflon-coated magnetic bar for l h at 25 °C. The product was solely hydroquinone and quantified by HPLC. In all the experiments, the concentration of the viologen unit was the same (20 mM) with chloride as counter ion. To ensure the accuracy of the concentration of **1**·4Cl$^-$, special care was taken of the water content in its synthesized sample, which was determiend by elemental analysis.

9 It should be noted that this statement is only superficial, because the solubility of the alkyl acetates in water greatly depends on the alkyl groups, indicating that the reaction conditions can be considerably different from one another.

10 This compound has been used as a template in the template-directed synthesis of **1**,[4] and therefore can be included in the cavity of **1**.

11 Note that the phenyl groups of these organic solvents can be included in the cavity of **1**. See for example: T. T. Goodnow, M. V. Reddington, J. F. Stoddart and A. E. Kaifer, *J. Am. Chem. Soc.*, 1991, **113**, 4335.

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13 Note that **2** is more hydrophobic than **1**, and hence will be transferred into the organic phase more easily than **1**.

14 The reduction of quinones with zinc in a homogeneous mixed solvent such as DMSO–H_2O (1 : 1) was, on the whole, faster than the same reaction in a two-phase solvent system. However, clear comparison of the catalytic activities of viologen compounds **1** and **3** was hampered by the precipitation of radical cation **2**.