First Examples of Phase Transfer Catalysis in Electrophilic Substitution Reactions. Acceleration of the Azo Coupling Reaction

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Summary Coupling reactions between 4-nitrobenzenediazonium chloride and *N*-ethylcarbazole or *NN*-diphenylamine in aqueous media are accelerated by using a two-phase water–dichloromethane system containing sodium 4-dodecylbenzenesulphonate as a transfer catalyst for the diazonium ion.

PHASE transfer catalysis is a well established technique in preparative chemistry, but has been confined almost exclusively to nucleophilic reactions.[1,2] We have examined the possibility of accelerating the azo coupling reaction by using an arylsulphonate anion as a phase transfer catalyst for the diazonium ion. Bredereck and Karaca have noted that such anions are capable of transporting diazonium ions from aqueous to aprotic media.[3] Phase transfer catalysis of the coupling reaction between 4-nitrobenzenediazonium chloride and *N*-ethylcarbazole (**1**) or *NN*-diphenylamine has been observed. Catalysis was not evident, however, when substituted *NN*-dimethylanilines of varying degrees of reactivity were used as coupling components. The former reactions appear to be the first examples of phase transfer catalysis in electrophilic reactions.[2]

N-Ethylcarbazole (**1**) is a particularly unreactive coupling component, and attempts to couple it with 4-nitrobenzenediazonium chloride in water, water–acetic acid and water–dimethylformamide (DMF) were unsuccessful. Only trace amounts of the azo dye (**2**) formed by coupling *para* to the *N*-ethyl group were detectable after 48 h at *ca.* 15 °C and decomposition of the diazonium ion was the major reaction. In contrast, when a mixture of the diazonium salt (1 equiv.) in water, *N*-ethylcarbazole (2 equiv.) in dichloromethane, and sodium 4-dodecylbenzenesulphonate (NaDBS) (0·2 equiv.) was agitated vigorously, colour development was rapid and after 48 h the azo dye (**2**) was isolated in 44% yield.†

As the NaDBS was found to be essential for the reaction, it may be assumed that the DBS anion associates with the diazonium ion and transports it into the dichloromethane layer. The reactivity of the diazonium ion is thereby increased by minimisation of solvent interactions, and coupling takes place. The liberated DBS anion can transport more diazonium ion into the organic phase and thus may be regarded as a phase transfer catalyst within the normal meaning of the term. It should be noted that Rufer has shown recently that the azo coupling reaction can be accelerated in water by micelle catalysis, using an anionic surfactant.[4] The mechanism of the reaction is clearly different to that operating in the present case, and acceleration is due to an enhanced local concentration effect within micelles.

The coupling reactions were examined in more detail by measuring the rate of formation of the azo dye (**2**) in various solvent systems, with and without catalyst, under controlled conditions. The results are summarised in Table 1. It can be seen that the NaDBS (0·05 molar proportions) increases the rate of coupling in dichloromethane–water by a factor of at least 20 relative to the reaction in water–acetic acid. Whilst part of this increase can be attributed to incomplete solubility of *N*-ethylcarbazole in the latter solvent, calculations based on the homogenous dioxan–water system (Table 1), and allowing for the actual concentration of diazonium ion in the dichloromethane layer, show that the rate of coupling in the latter solvent is in fact at least 50 times greater than in water-based solvents. It can also be seen from Table 1 that the polarity of the organic phase is important (*cf.* dichloromethane and nitrobenzene which have much higher dielectric constants than toluene and ethyl acetate). This may be attributed to the covalent character of diazonium arylsulphonates,[5] ionisation being greater in the former solvents. Crown ethers will act as transfer agents for the diazonium ion,[6] but, as noted by others,[7] the resultant complexes have low coupling reactivity. The rate retarding effect of the polyethyleneoxide nonionic detergent (Lissapol NX, Table 1) can be attributed to a similar effect.[8]

The generality of phase transfer catalysis by NaDBS in azo coupling was examined using other arylamines as the coupling component. Thus *NN*-diphenylamine (a weak coupler of low basicity) *NN*-dimethylamine (a reactive coupler) *NN*,2,5-tetramethylaniline (a weak *C*-coupler because of steric crowding), and *m*-nitro-*NN*-dimethylaniline (a weak *C*-coupler because of the deactivating

TABLE 1. Initial rates of coupling between 4-nitrobenzene diazonium chloride and (**1**) at 0 °C in various solvent mixtures in the presence and absence of additives

Solvent[a]	Additive[b]	Rate[c] × 10^9/mol s^{-1} dm^{-3}
CH_2Cl_2–H_2O	none	1·25
CH_2Cl_2–H_2O	NaDBS	11·1
CH_2Cl_2–H_2O	18-crown-6	0·28
CH_2Cl_2–H_2O	Lissapol NX[d]	0·56
Toluene–H_2O	none	<0·1
Toluene–H_2O	NaDBS	<0·1
EtOAc–H_2O	none	0·89
EtOAc–H_2O	NaDBS	1·03
$PhNO_2$–H_2O	none	1·39
$PhNO_2$–H_2O	NaDBS	10·5
AcOH–H_2O[e]	none	0·47[f]
DMF–H_2O[g]	none	0·53[f]
Dioxan–H_2O[h]	none	1·33

[a] 1:1 v/v except where stated. [b] 0·05 mmol except where stated. [c] Initial rate of formation of (**2**) for reaction mixture containing 1·0 mmol of diazonium ion and 2·0 mmol of (**1**) in 100 ml solvent. [d] Commercial (I.C.I.) non ionic detergent, mol. wt. *ca.* 600, 0·05 mmol. [e] 95% H_2O v/v containing NaOAc $3H_2O$ (10 g in 100 ml). [f] Suspension of (**1**). [g] 60% H_2O v/v. [h] 60% H_2O v/v homogenous solution containing 1·0 mmol diazonium ion and 1·0 mmol (**1**) in 100 ml solvent.

TABLE 2. Initial rates of coupling between 4-nitrobenzenediazonium chloride and various arylamines under catalysed and non-catalysed conditions at 0 °C

	Rate × 10^9/mol s^{-1} dm^{-3}		
	CH_2Cl_2–H_2O[a]		H_2O–AcOH[b]
Arylamine	Uncatalysed	Catalysed[c]	
N-Ethylcarbazole	1·25	11·1	0·47
NN-Diphenylamine	7·5	1 830	1 330
NN-Dimethylaniline	830	830	11 700
NN-2,5-Tetramethylaniline	28	28	4 700
3-Nitro-*NN*-dimethylaniline	0·44	0·58	12·5

[a] Diazonium chloride (1·0 mmol) and amine (2·0 mmol) in water (50 ml) and CH_2Cl_2 (50 ml). [b] Diazonium chloride (1·0 mmol) and amine (2·0 mmol) in a mixture of water (95 ml) and acetic acid (5 ml) containing NaOAc $3H_2O$ (10 g). [c] Sodium 4-dodecylbenzenesulphonate (0·05 mmol).

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† Spectroscopic and microanalytical data were consistent with the assigned structure.

effect of the nitro group) were examined, and their rates of *C*-coupling with the 4-nitrobenzenediazonium ion determined under phase-transfer conditions (CH_2Cl_2–H_2O) and in homogeneous water–acetic acid solution The results are summarised in Table 2

It is evident that phase transfer catalysis of the azo coupling reaction is not a general phenomenon, and in particular does not occur necessarily with all unreactive amines This is presumably because the *NN*-dimethylanilines readily undergo *N*-coupling prior to *C*-coupling,[9] whereas *NN*-diphenylamine and *N*-ethylcarbazole are less likely to do this because of the low nucleophilicity of the nitrogen atoms Thus phase transfer catalysis may only be observable with amines that have a low rate of *N*-coupling *and* a low rate of *C*-coupling

In practical terms, it has been found that the two-phase catalysed coupling reaction provides a convenient and efficient route to substituted diphenylamine dyes, and in some cases is the only means of preparing the required *C*-coupled product

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