

Solvent Effects in the Halogen Exchange Reaction of 2,3-Dibromonitrobenzene and Tetrabutylammonium Dichlorocuprate(I)

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The copper(I) catalyzed halogen exchange reaction of 2,3-dibromonitrobenzene with tetrabutylammonium dichlorocuprate(I) has been studied kinetically in dimethyl sulfoxide and in aqueous dimethyl sulfoxide, where reactions are faster than in chlorobenzene or toluene. The enhancement of the reaction rate observed in aqueous dimethyl sulfoxide compared to dry dimethyl sulfoxide is primarily due to stronger solvation of the initial state, mainly of the large CuCl_2^- anion, by DMSO than by water.

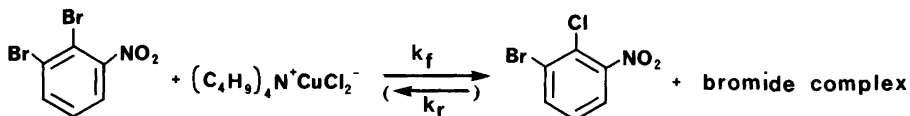
If we could carry out our reaction in the gas phase, we could measure the intrinsic reactivity of the “bare” reactants. Unfortunately, most reactions are not suitable for gas phase study and consequently reactions are generally studied in a solvent medium.

Chemical reactions in solution are strongly influenced by the medium; solvents can bring about large effects on both reaction rates and equilibria. The initial reactants, as well as the activated complex, will be solvated to a different extent depending on the solvating power of the solvent used. Solvation of the reactants will reduce the reactivity, while solvation of the activated complex will bring about an increase in the reaction rate.

In any solution, solutes are constantly “in touch” with solvent molecules and in this sense they are fully solvated. The term “solvation”, however, is reserved for those solutes which interact strongly with neighbouring solvent molecules.^{1a} The solvating power of various solvents depends on their ability to donate electrons to acceptor solutes or to accept electrons from donor solutes in the solvation process.^{1b} The failure of the dielectric permittivities of solvents to provide a rationalisation for solute-solvent interactions has led to the definition of polarity in terms

of empirical parameters,^{2a} one of which, viz. the $E_T(30)$ scale of Dimroth and coworkers,^{2b} has proved to be particularly useful.

In a previous investigation of substituent effects in copper(I) catalyzed halogen exchange reactions of halogenonitrobenzenes with chloride ion, the solvent was aqueous hydrochloric acid-acetic acid. The anion CuCl_2^- was suggested to be the relevant nucleophile³ in the substitution. With the lipophilic tetrabutylammonium dihalogenocuprates(I) available in crystalline form^{4,5a-c} it was possible for us to work in solvents of low polarity. Thus, we hoped to narrow the gap between reactions carried out in the gas phase and in solution. In a preceding work the kinetics of exchange reactions of 2-halogeno-3-bromonitrobenzenes with tetrabutylammonium dihalogenocuprates(I) were determined in chlorobenzene.⁶ An unexpected result was obtained, viz. that the rate constant for the halogen exchange reaction of 2,3-dibromonitrobenzene with the CuCl_2^- anion, studied in aqueous medium, was five times higher than for the corresponding reaction with tetrabutylammonium dichlorocuprate(I) studied in chlorobenzene. The result was interpreted in terms of solute-solvent effects. The chemical shifts of the tetrabutylammonium protons in chlorobenzene solution appeared to be unaf-



Scheme 1.

ected by change of the anion. In fact, tetrabutylammonium dichlorocuprate, dibromocuprate, diiodocuprate and bromochlorocuprate gave the same chemical shift values, as seen from the ^1H NMR studies.⁶ This result indicates that ion pairing or solvation must be relatively unimportant in chlorobenzene for the tetrabutylammonium dihalogenocuprates(I).

In this work, the solvent effects for the reaction in question have been further studied in dimethyl sulfoxide and aqueous dimethyl sulfoxide. The reaction has also been studied in toluene, but only to a limited extent because of the low solubility of the tetrabutylammonium salts in this solvent.

Results and calculations

The exchange reaction of 2,3-dibromonitrobenzene, which seemed to be an appropriate substrate for our purpose,³ with tetrabutylammonium dichlorocuprate(I) (Scheme 1) was studied in dimethyl sulfoxide and aqueous dimethyl sulfoxide by means of GLC and ^1H NMR spectroscopy at 80–100°C. From the results of our earlier study,⁶ performed in chlorobenzene, it became evident that both of the chlorine atoms of the dichlorocuprate(I) anion participate in the substitution reaction, which was of first order in

both haloarene and dichlorocuprate ion (Fig. 1).

No appreciable reversibility of the reaction during the reaction time employed was noticed.⁶

The rate constant, k_f , was calculated from eqn. (2), where k_f stands for the average value of the rate constant for the reaction of the "first and second chloride" of tetrabutylammonium dichlorocuprate(I) with the aromatic compound.

$$-\frac{d[\text{ArBr}]}{dt} = k_f [\text{ArBr}] [\text{Cl}^-] \quad (1)$$

$$\frac{1}{[\text{Cl}^-]_0 - [\text{ArBr}]_0} \ln \frac{[\text{ArBr}]_0 [\text{Cl}^-]}{[\text{Cl}^-]_0 [\text{ArBr}]} = k_f \cdot t \quad (2)$$

Because of the difficulties involved in protecting the copper(I) salt from oxidation in aqueous medium, exhaustive calculations of the rate constant for the exchange reactions in aqueous dimethyl sulfoxide were limited to a water mole fraction of $X_{\text{H}_2\text{O}} < 0.25$. Initial values of the rate constants are, however, given up to $X_{\text{H}_2\text{O}} < 0.8$ in order to illustrate the dependence of the rate constants on the solvent composition. The rate constants increase with increasing water content of the DMSO/H₂O solvent, thus supporting the results of previous investigations in water³ and in chlorobenzene⁶ (Table 1). Within the scope of our

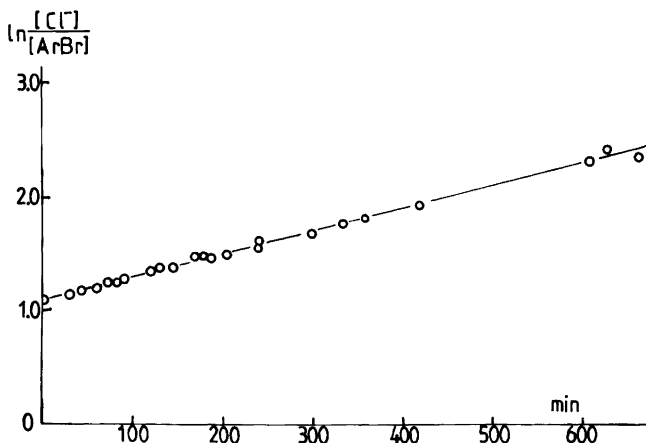


Fig. 1. A representative run for the exchange reaction of 2,3-dibromonitrobenzene with tetrabutylammonium dichlorocuprate(I) in dimethyl sulfoxide at 90°C.

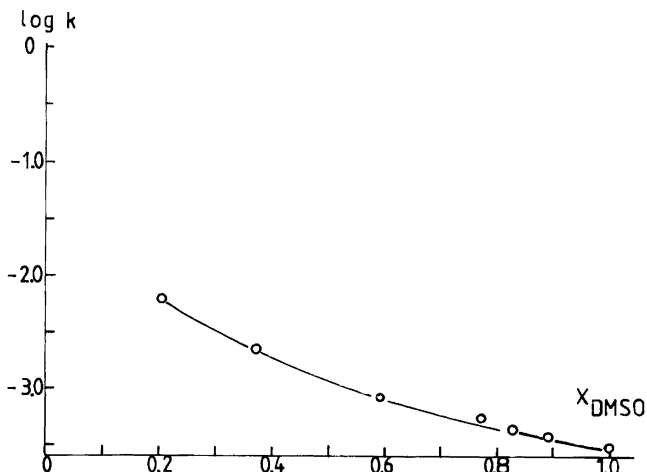


Fig. 2. Log k vs. X_{DMSO} for the exchange reaction of 2,3-dibromonitrobenzene with tetrabutylammonium dichlorocuprate(I) in DMSO/H₂O at 90°C.

measurements, no extreme values in the $\log k - X_{\text{DMSO}}$ curve were observed (Fig. 2).

The values of the rate constants for the exchange reaction of 2,3-dibromonitrobenzene with Cl⁻ in pure organic solvents are very close to each other: 3.04×10^{-4} in DMSO, 2.57×10^{-4} in chlorobenzene and $1.8 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$ in toluene (90°C),

Table 1. Rate parameters for exchange reactions of 2,3-dibromonitrobenzene (0.0546 M) and tetrabutylammonium dichlorocuprate(I) ([Cl] = 0.1638 M) in solvent mixtures.

Solvent mixture	Temp./°C	$k_f/10^{-4} \text{ M}^{-1} \text{ s}^{-1d}$
Org. solvent $X_{\text{H}_2\text{O}}$		
DMSO 0	79.8	1.45(7) ^a
DMSO 0	85.0	2.32(3) ^a
DMSO 0	90.02	3.04(10) ^a
DMSO 0	98.0	5.81(14) ^a
DMSO 0.108	90.02	3.83(13) ^a
DMSO 0.171	79.8	1.82(3) ^a
DMSO 0.171	90.02	4.33(19) ^a
DMSO 0.171	98.0	7.75(11) ^a
DMSO 0.228	90.02	5.81(5) ^a
DMSO 0.409	90.02	8.3 ^b
DMSO 0.627	90.02	22 ^b
DMSO 0.797	90.02	63 ^b
C ₆ H ₅ Cl 0	90.02	2.57(5) ^{a,c}
C ₆ H ₅ CH ₃ 0	90.02	1.8 ^b

^aThe errors are 2 S.E. from the least-squares method calculations. 2–4 runs in every calculation. ^bInitial values. See text. ^cValue from Ref. 6. ^d k_f is average value. See text.

thus showing a decrease of the rate constant with decreasing $E_T(30)$ values of the solvents (188.3 for DMSO, 156.9 for C₆H₅Cl and 141.8 kJ mol⁻¹ for C₆H₅CH₃).

Activation parameters were calculated for the reaction in DMSO and in DMSO/H₂O ($X_{\text{H}_2\text{O}} = 0.17$) using the Eyring equation⁷ and with the assumption that ΔH^\ddagger is constant in the temperature interval 80–100°C (Table 2).

¹H NMR spectra were recorded in DMSO and in DMSO/H₂O ($X_{\text{H}_2\text{O}} = 0.17$) for tetrabutylammonium dibromo- and dichlorocuprates(I) at 25–90°C. The chemical shifts for the tetrabutylammonium protons in these solvents were unaffected by change of the anion, as was the case in chlorobenzene,⁶ and were almost unaltered by variations in temperature from 25 to 90°C.

Discussion

Among protic solvents, water has been studied very extensively; it is unique in being highly structured. Special effects are encountered in hydration that are generally absent when ions are solvated by other solvents. "Hydrophobic interaction" is a concept that is unique to aqueous solutions, and it involves increased intermolecular structure of the water molecules surrounding certain ions, such as the tetrabutylammonium ion.^{8a} Dimethyl sulfoxide, a dipolar aprotic solvent, is considered to be a valuable solvent for studying medium effects in organic chemistry.⁹ Certain nucleophilic substitution reactions, involving small anions in dipolar aprotic solvents such as DMSO, experience rate enhancements of

Table 2. Activation enthalpies and entropies for the substitution reaction of 2,3-dibromonitrobenzene and tetrabutylammonium dichlorocuprate(I).

Solvent	$X_{\text{H}_2\text{O}}$	$\Delta H^\ddagger/\text{kJ mol}^{-1}$	$\Delta S^\ddagger/\text{J K}^{-1} \text{mol}^{-1}$
Org. solvent			
$\text{C}_6\text{H}_5\text{Cl}$	0	71(1) ^{a,b}	-119(2) ^{a,b}
DMSO	0	80(8) ^a	-94(21) ^a
DMSO	0.17	84(5) ^a	-80(13) ^a

^aThe errors are 2 S.E. from the least-squares method calculations. ^bFrom Ref. 6.

the order of 10^{11} compared to corresponding reactions in hydroxylic solvents. In contrast, nucleophilic substitution reactions involving large polarizable anions will usually be retarded in DMSO,⁹ thus indicating also the importance of polarizability on solvation. It has been common practice to attribute the rate enhancement with small anions in DMSO to the formation of a less solvated state than in protic solvents with their ability to form strong hydrogen bonds.

Krumgalz found from ionic limiting equivalent conductance measurements and calculations using the Stokes equation¹⁰ that the radius of the tetrabutylammonium ion in organic solvents was independent of the nature of the solvent. He obtained a constant value for the radius of 3.82 Å (25 °C), which proves that this ion and other large tetraalkylammonium ions are unsolvated in organic solvents. In water, where specific hydrophobic phenomena occur, the radius of the tetrabutylammonium ion is 4.77 Å (25 °C). However, with increasing temperature the hydration radius decreases and approaches the radius of the ion in the unsolvated state (~100 °C), which means that the hydration disappears.¹⁰ Sitaraman and Unni¹¹ have analyzed conductance data for some quaternary ammonium halides in DMSO by the Fuoss equation¹² and they too concluded that the solvation of the tetrabutylammonium ion in DMSO is practically nil.

If a solute is transferred from water, where the solute-solvent interaction is well known, to an organic solvent, S, the free energy of transfer, $\Delta G_{\text{tr H}_2\text{O} \rightarrow \text{S}}^\circ$, and the corresponding values of $\Delta H_{\text{tr}}^\circ$ and $\Delta S_{\text{tr}}^\circ$ will reflect the difference in the solute-solvent interaction of these solvents.^{8b}

In our present investigation of the substitution

reaction of 2,3-dibromonitrobenzene with tetrabutylammonium dichlorocuprate(I) in DMSO and in aqueous DMSO, our attention is focused on the behaviour of the large CuCl_2^- anion in these solvents.

Ahrland *et al.*¹³⁻¹⁴ have determined $\Delta G_{\text{tr H}_2\text{O} \rightarrow \text{DMSO}}^\circ$ for Cu^+ and copper halide complexes [with the Grunwald assumption $\Delta G_{\text{tr}}^\circ(\text{Ph}_4\text{B}^-) = \Delta G_{\text{tr}}^\circ(\text{Ph}_4\text{As}^+)$]. They reported an exceptionally large negative value, viz. $\Delta G_{\text{tr H}_2\text{O} \rightarrow \text{DMSO}}^\circ(\text{Cu}^+) = -40 \text{ kJ mol}^{-1}$ (25 °C), which means that Cu^+ is more easily solvated by DMSO than by water. Copper(I) complexes are also strongly solvated by DMSO: $\Delta H_{\text{tr}}^\circ(\text{Cu}^+)$ is approximately -60 kJ/mol .¹⁴ In contrast, the small anion Cl^- has a positive $\Delta G_{\text{tr H}_2\text{O} \rightarrow \text{DMSO}}^\circ$ value, 38 kJ mol^{-1} .¹⁵ The Cl^- anion is thus clearly better solvated by water than by DMSO.

The observed enhancement of the reaction rate for the exchange reaction of 2,3-dibromonitrobenzene and tetrabutylammonium dichlorocuprate(I) in aqueous DMSO compared to dry DMSO is due to a smaller energy gap between the solvated reactants and the solvated transition state (ΔG^\ddagger) in DMSO/ H_2O . The CuCl_2^- anion is more strongly solvated by DMSO than by water (*vide supra*) and this is likely to be the case for the aromatic compound also.¹⁶ The solvation of the ionic transition state, however, is less favourable in both protic and aprotic solvents.¹⁷ The rate increase is not so dramatic; the rate constant, k , varies from $3.04 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$ in dry DMSO to $63 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$ DMSO/ H_2O ($X_{\text{H}_2\text{O}} = 0.8$) at 90 °C.

A description of solvation of ions in solvent mixtures is always complicated. Besides interaction between solvent and solute there is interaction between unlike solvent molecules^{8c} and competition for solvation. Marcus¹⁸ has investigated preferential solvation of Ag^+ by DMSO in mixed $\text{H}_2\text{O}/\text{DMSO}$ solvents; the behaviour of Cu^+ in these solvents ought to be similar. The plot of $\log k$, for our CuCl_2^- -participating substitution reaction, against X_{DMSO} (Fig. 2) shows the same dependence as Marcus' plot of $\Delta G_{\text{tr H}_2\text{O} \rightarrow \text{DMSO}}^\circ$ against X_{DMSO} for Ag^+ . Kundu and Parker,¹⁹ as well as Wells,²⁰ have also calculated $\Delta G_{\text{tr H}_2\text{O} \rightarrow \text{DMSO}}^\circ$ for Ag^+ in DMSO/ H_2O mixtures; their values agree with those of Marcus.

The conclusion that the solvation of the CuCl_2^- ion is important for the aromatic halogen exchange raises further questions. Solvation of

CuCl_2^- by the polarizable solvents toluene and chlorobenzene should lower the energy of this reagent and would contribute to the lower reaction rates in these solvents.

Soft donor ligands, such as pyridines or phosphines, are important for the cross-coupling of arylcopper compounds with halogenoarenes,²¹ a reaction which bears some formal resemblance to halogen exchange. It seems that the influence of polar solvents and of soft donor ligands has not yet been fully explored for the reactions of organocopper compounds and lithium diorganocuprates with electron-deficient substrates.²²

The values of the activation parameters, ΔH^\ddagger and ΔS^\ddagger , for the reaction of 2,3-dibromonitrobenzene with tetrabutylammonium dichlorocuprate(I) in chlorobenzene, dimethyl sulfoxide and aqueous dimethyl sulfoxide ($X_{\text{H}_2\text{O}} = 0.17$) are very close (Table 2). The differences between the values are within the error limits.

Experimental

The reactions between 2,3-dibromonitrobenzene and tetrabutylammonium dichlorocuprate(I) in DMSO and aqueous DMSO were performed in a nitrogen atmosphere. Nitrogen was carefully dried by first passing it through concentrated H_2SO_4 and then over KOH pellets. The GLC analyses of the halogenoarenes were performed on a Perkin Elmer 3920-B gas chromatograph with a hot-wire detector and coupled to a Hewlett Packard 3380 A integrator. A 3 mm \times 2 m SE-30 (3% on Chromosorb) column was used. The carrier gas was He.

The ^1H NMR spectra were obtained on a Bruker WH 270 spectrometer with TMS as internal standard.

The dimethyl sulfoxide was dried over CaH_2 and distilled in vacuum just before use. 2,3-Dibromonitrobenzene and tetrabutylammonium dichlorocuprate(I) were available from previous investigations.⁴⁻⁶ The exchange reactions were performed with the apparatus described in Ref. 23. Aliquots taken from the reaction mixture were quenched in ice-water, made alkaline, extracted with ether and analysed by GLC.

2,3-Dibromonitrobenzene. ^1H NMR (270 MHz, DMSO): δ 7.97 (H-4, q), 7.57 (H-5, q), 8.07 (H-6, q). $J_{4-5} = 7.95$ Hz, $J_{5-6} = 7.9$ Hz, $J_{4-6} = 1.4$ Hz.

Tetrabutylammonium dichlorocuprate(I). ^1H NMR (270 MHz, DMSO): δ 3.17 (αH , m), 1.58 (βH , m), 1.32 (γH , m), 0.93 (δH , t).

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