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Interfacial Activity of Quaternary Salts as a Guide to Catalytic Performance in Phase-Transfer Catalysis

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The phase transfer catalyzed ethylation of deoxybenzoin has been studied in several solvents, using symmetrical quaternary ammonium bromides as catalysts. In all cases the reactivity passed through a maximum as the size of the catalyst increased. The catalysts were also found to reduce the interfacial tension between the phases—this effect also passing through a maximum as a function of catalyst size. A correlation was observed between the two parameters, such that those catalysts reducing interfacial tension most markedly were also the best catalysts. Therefore, interfacial tension can be a guide to catalytic activity in certain PTC systems.

Introduction

Numerous phase transfer catalyzed (PTC) reactions, such as alkylations and carbene formation, are considered to proceed by the "interfacial" mechanism proposed by Makosza[1] (eq 1–3, Q represents a quaternary ammonium cation ("quat")), in which a concentrated base, usually aqueous alkali, deprotonates a substrate at the interface. The anion formed is subsequently paired and removed into the bulk phase by a quaternary ammonium or a phosphonium catalyst, where it reacts with an alkylating agent.

$$RH_{(org)} + OH^-_{(aq)} \rightleftarrows R^-_{(interface)} + H_2O \qquad (1)$$

$$R^-_{(interface)} + QX_{(org)} \rightarrow RQ_{(org)} + X^-_{(aq)} \qquad (2)$$

$$RQ_{(org)} + R'X_{(org)} \rightarrow RR'_{(org)} + QX_{(org)} \qquad (3)$$

Although both Makosza[2] and Solaro et al.[3] have used tetrabutyl salts in reactions of this kind, they are generally held to be best catalyzed by small, hydrophilic quats. Makosza[1] generally favored triethylbenzylammonium chloride, and Halpern, Sasson, and Rabinovitz[4] showed tetraethylammonium bromide to be effective in the methylation of deoxybenzoin. The latter explained the preferential activity of small quats in terms of the "accessibility" of their charged nitrogen centre, enabling them to effectively bind the substrate anion in step 2 of the above mechanism. Extreme hydrophilicity, to the extent of inability to enter the organic phase, is of course detrimental, and thus tetramethylammonium bromide was a poor catalyst. In short they considered an ethyl chain to provide the optimum balance between hydrophobicity and "accessibility".[5]

In the literature so far surprisingly little attention has been paid to the interfacial nature of step 2, in which the quat is required to reach the interface in order to bind the substrate anion. How does the nature of a quat affect its ability to be present at the interface? Does the concentration of quat at the interface differ from that in the bulk?

Tetrabutylammonium salts have been shown to be surface-active at various water-organic interfaces,[6] concentrating there as indicated by a lowering of the interfacial tension. It might be postulated that quats in general could similarly concentrate at the solvent–50% NaOH solution interface in PTC alkylation systems. It might further be argued that step 2, which is probably the slowest,[3] should show a dependence upon the local concentration of catalyst *at the interface* and that those quats that concentrate at the interface should be good catalysts.

The present work seeks to examine the hypothesis that the interfacial activity of the catalyst, as measured by interfacial tension reduction (Π, dynes/cm), will correlate with its catalytic activity in PTC alkylation systems.

We chose the substrate deoxybenzoin (previously studied by Halpern, Sasson, and Rabinowitz[4]), using ethyl bromide as an alkylator and 50% aqueous sodium hydroxide solution as a base. A series of symmetrical quaternary ammonium bromides were scanned as catalysts. A mixture of C- and O-alkylation occurs as described in eq 4.

$$PhCH_2COPh + EtBr \xrightarrow{50\%\ NaOH,\ 5\%\ QBr} PhCH(Et)COPh + PhCH{=}C(OEt)Ph \qquad (4)$$

Results and Discussion

The reactions were performed at room temperature as described in the Experimental Section, and full conversion was attained in nearly all cases, with C:O product ratio typically about 6:1 in methylene chloride, 5:1 in benzene, and 4:1 in *p*-xylene. Some of the lower quats showed induction times of up to 2 h prior to reaction. For this reason maximum rate (rather than initial rate) was taken as the measure for catalytic activity. The best catalysts gave rates of about 4×10^{-5} M s^{-1}, reaction being virtually complete in 2 h. Blank reaction was negligible. The reproducibility of the rate values was ±5%.

Interfacial tension was measured for the three-component system consisting of solvent, 50% NaOH, and quat. The quat was initially equilibrated with solvent at the same concentration as in the reactions; however, any undissolved solid was filtered off. It was observed that some 20 min of stirring was required to interequilibrate the bulk aqueous and organic phases and obtain a stable reading, even in the absence of quat, and this precaution was taken before all measurements. Using suitably pure solvent (see the Experimental Section), interfacial tension was found to be in the range 52–54 dynes/cm for all three solvents. The quats were indeed found to be surface active, the best ones reducing interfacial tension to about 35 dynes/cm, giving an interfacial tension reduction (or "surface pressure") of about 20 dynes/cm. The reproducibility of these values was ±1 dyne/cm in most cases.

Several solvents—methylene chloride, benzene, and *p*-xylene—were investigated as reaction medium. This is because factors such as polarity and hydrophobicity of the organic phase can be expected to influence the surface activity of the quaternary salts, much as the choice of

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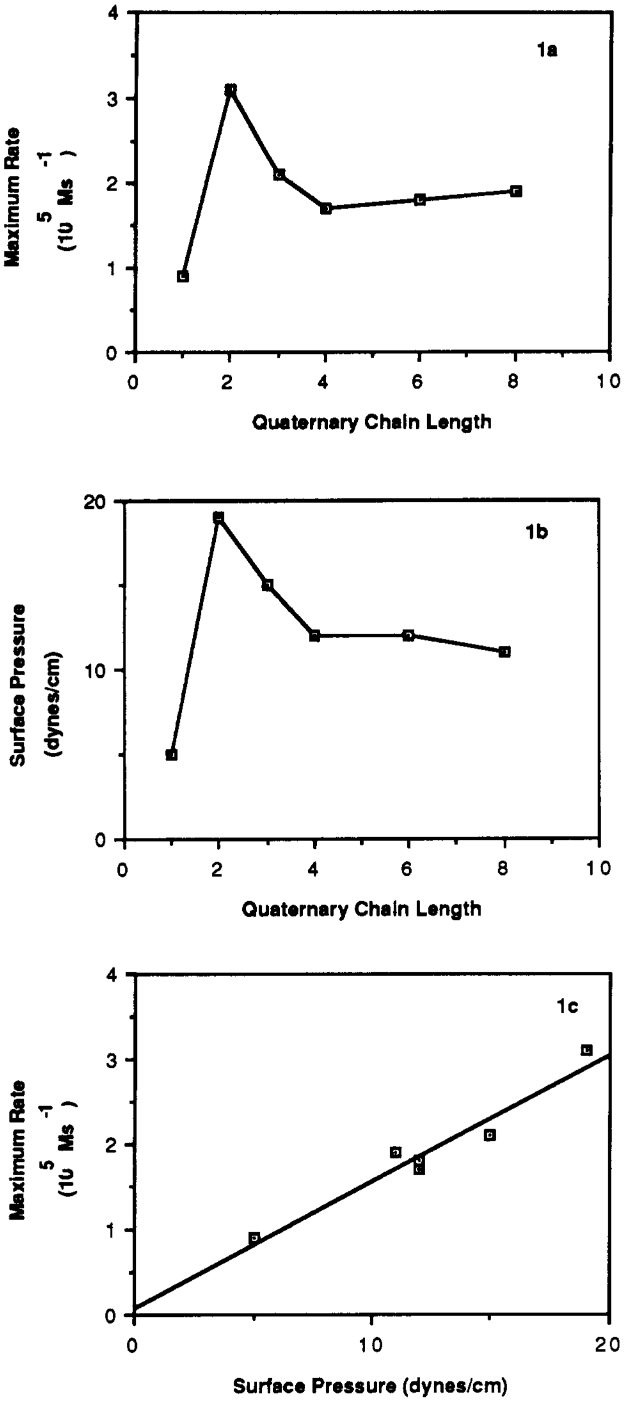

Figure 1. Symmetrical quaternary ammonium bromides in methylene chloride: (a) catalytic activity in ethylation of deoxybenzoin; (b) interfacial activity at solvent–50% NaOH interface; (c) correlation between catalytic and interfacial activities.

surfactant in commercial applications depends upon the nature of the phases. If the surface activity of the catalyst is indeed important then absolute and relative reactivities of different quats will vary with the solvent.

In methylene chloride as solvent reaction rate was found to increase as the catalyst was changed from tetramethylammonium (TMeAB) to tetraethylammonium (TEtAB) bromide and to fall off as the catalyst size was further increased (Figure 1a). The surface pressure of quat bromides at the methylene chloride–50% NaOH interface also showed a maximum for the tetraethyl salt with the larger salts being less active (Figure 1b). A clear correlation exists between catalytic and interfacial activity, such that the more interfacially active the quat the more catalytically active it is. Interestingly when reaction rate is plotted against surface pressure a straight line is obtained with a coefficient of regression of 97% (Figure 1c), although we cannot comment on the significance of this linearity at present.

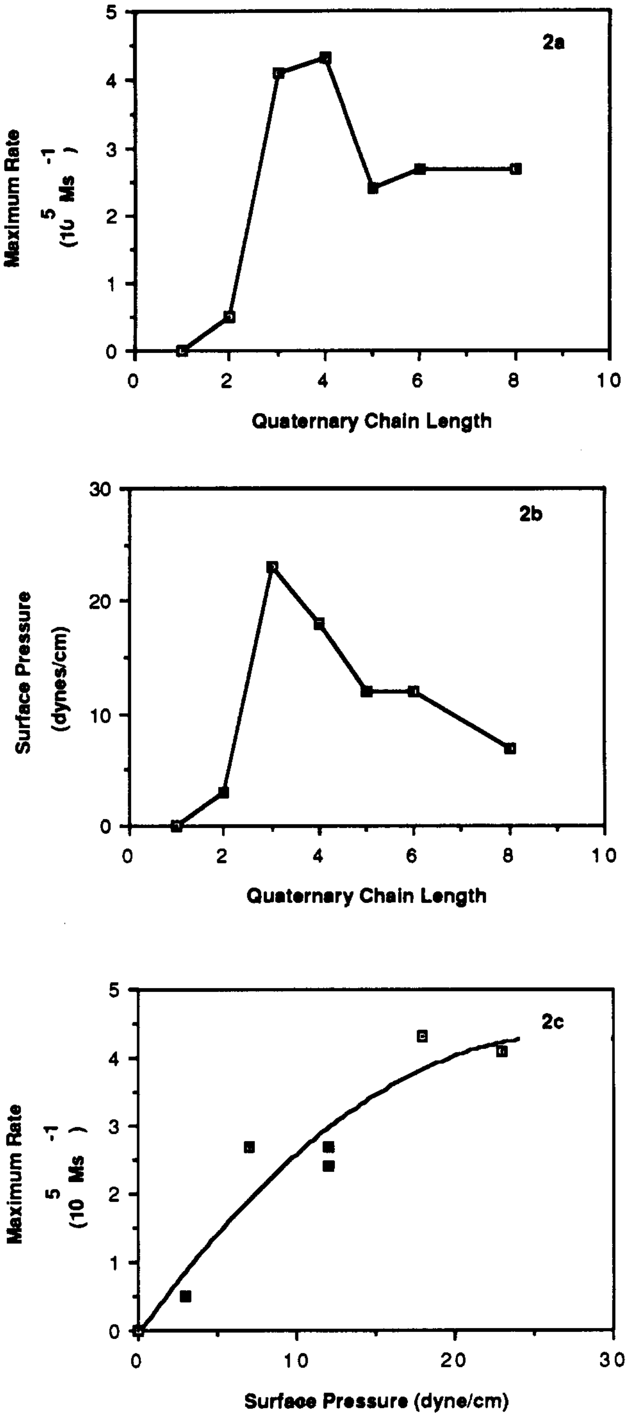

Figure 2. Symmetrical quaternary ammonium bromides in benzene: (a) catalytic activity in ethylation of deoxybenzoin; (b) interfacial activity at solvent–50% NaOH interface; (c) correlation between catalytic and interfacial activities.

Using benzene as the solvent, tetrapropylammonium (TPrAB) and tetrabutylammonium (TBuAB) bromides were the superior catalysts, the latter giving a marginally higher maximum reaction rate (Figure 2a). Both TEtAB and TPrAB were only partially soluble and showed induction times prior to reaction. Surface pressure measurements in benzene/aqueous NaOH showed TMeAB and TEtAB to be virtually nonsurfactant, TPrAB and

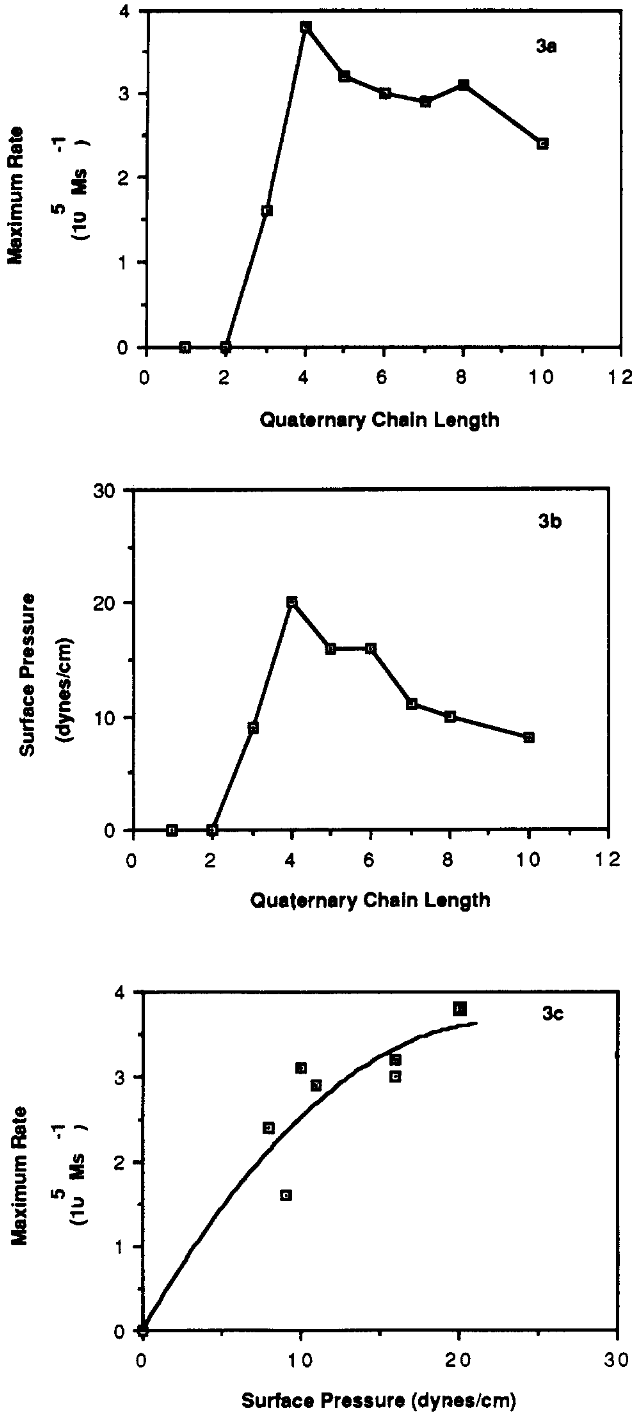

Figure 3. Symmetrical quaternary ammonium bromides in *p*-xylene: (a) catalytic activity in ethylation of deoxybenzoin; (b) interfacial activity at solvent–50% NaOH interface; (c) correlation between catalytic and interfacial activities.

TBuAB to be strongly surface-active, and the larger quats to be somewhat less effective (Figure 2b). Generally a good correlation between catalytic and interfacial activity was again obtained (Figure 2c), although the tetrapropyl salt might have been expected to be a better catalyst.

For the solvent *p*-xylene the peak of maximum activity was shifted still further toward the hydrophobic quats. Tetrabutylammonium bromide gave the fastest reaction rate, with catalytic activity dropping off mildly as quat size was increased and strongly as size was decreased (Figure 3a). Tetrapropyl was a much poorer and tetrapentyl a much better catalyst in xylene than in benzene. Tetrapropyl and tetrabutyl catalysts showed respectively considerable and slight induction times prior to reaction. Surface pressure measurements in *p*-xylene/aqueous NaOH (Figure 3b) showed a similar pattern to that of the rate behavior, namely TBuAB best, with a mild fall in activity for large quats and a sharp fall for small quats. A clear, somewhat curved correlation was once again obtained (Figure 3c).

At this stage it is important to consider some additional features of the system. The question might be raised that the surfactancy of a quat could physically increase reaction rate by virtue of a reduction in droplet size. In this context several classical surfactants were tested for surface and catalytic activity in our system. Using the same concentrations as for the quat catalysts the anionic surfactant sodium dodecyl sulfate gave a surface tension reduction of 11 dynes/cm but was totally inactive as a catalyst. The nonionic surfactant BRIJ 52 (ethoxylated(2) cetyl alcohol) was also not a catalyst although it reduced the interfacial tension to only 19 dynes/cm! The cationic surfactant cetyltrimethylammonium bromide caused some catalysis, but this is hardly surprising as it is itself a quaternary ammonium salt. These experiments showed that the surfactancy of the catalyst is not primarily of *physical* importance but rather that there is *chemical* significance to its concentration at the interface. This concept is consistent with our proposal that eq 2 above is kinetically important and should perhaps be rewritten in the form of eq 5.

$$R^-_{(\text{interface})} + QX_{(\text{interface})} \rightarrow RQ_{(\text{org})} + X^-_{(\text{aq})} \qquad (5)$$

While we cannot entirely discount the accessibility-hydrophobicity approach[5] to our system, we have shown that poorly accessible catalysts such as TBuAB may be optimum in several cases. Moreover in xylene TBuAB is very successful despite a very low bulk solubility. In fact in methylene chloride all except TMeAB are fully soluble at the level used, in benzene the three lowest quats are not fully dissolved, and in *p*-xylene only tetrahexylammonium bromide is fully dissolved. It is indeed remarkable that each correlation plot links points representing such differing bulk concentrations. We submit that the bulk of evidence indicates *interfacial concentration* of the catalyst as the key factor in our system.

Investigations are presently underway for other systems, including other alkylating agents and nonsymmetrical quaternary catalysts. In addition we are undertaking a kinetic characterization of the present system including the nature of the induction period sometimes observed.

Conclusions

The following major points emerge from the results described above. (1) Rate of reaction as a function of catalyst size passes through a maximum. (2) The quaternary catalysts are interfacially active, and surface pressure as a function of quat size also passes through a maximum. (3) In both cases the curve shifts toward larger quats across the solvent series methylene chloride, benzene, *p*-xylene. Tetraethyl quats are not necessarily the best catalysts for "interfacial" PTC. (4) There is a significant correlation between catalytic activity and interfacial activity, in all three solvents, the most surface active quats being the best catalysts. Therefore when choosing a catalyst for "interfacial" PTC its surface activity with respect to the reaction media should be considered carefully.

Experimental Section

Quaternary salts, deoxybenzoin, and ethyl bromide were commercial chemically pure grades (Fluka, Aldrich, and Merck, respectively). Sodium hydroxide was analytical grade. Sodium dodecyl sulfate and cetyltrimethylammonium bromide were chemically pure grades, while BRIJ 52 (ethoxylated(2) cetyl alcohol) was an Atlas commercial sample. Solvents were the middle fraction of redistilled analytical grade chemicals. This was a requirement of the interfacial tension work because trace impurities were found to reduce surface tension.

Reactions were carried out at 24 ± 1 °C (room temperature) in a 21-mm diameter glass tube, containing a 10 × 3 mm magnet. Stirring was achieved using a Cole–Parmer Magne-4 in which four stirrers are driven by a common belt. Catalyst was 5 mol % with respect to substrate and ethyl bromide was in 50% molar excess. Reaction volumes were 5 mL organic, 1 mL aqueous. Samples of 0.1 mL were withdrawn every 15–60 min according to the rate and extent of reaction and added to 0.1 mL of dilute HCl and 0.5 mL of toluene. The upper phase was injected onto a GC column (HP-1 crosslinked methyl silicone gum, 30 m × 0.53 mm) at 195 °C in a Hewlett-Packard 5890A instrument. Typical retention times were as follows: starting material, 3.3 min; C-alkylated product, 3.9 min; O-alkylated product, 4.5 min. Initial peak identification was confirmed by NMR spectroscopy. Each reaction profile was constructed from 5–8 samples.

Interfacial tension measurements were performed by the Du Noy ring method using a Lauda Tensiometer. Using the "prevented rupture" technique, in which the interface is not broken during the measurement, readings were taken every 5 min until a stable value was obtained. Ten minutes was usually sufficient.

Registry No. BRIJ 52, 9004-95-9; TMeAB, 64-20-0; TEtAB, 71-91-0; TPrAB, 1941-30-6; TBuAB, 1643-19-2; PhCH(Et)COPh, 16282-16-9; PhCH=C(OEt)Ph, 13676-20-5; tetrahexylammonium bromide, 4328-13-6; tetraoctylammonium bromide, 14866-33-2; deoxybenzoin, 451-40-1; ethyl bromide, 74-96-4; sodium dodecyl sulfate, 151-21-3; cetyltrimethylammonium bromide, 57-09-0.

Direct Observation of an Intermediate in the Oxygen Atom Rearrangement of 2-Cyclopropylnitrobenzene in a Strong Acid

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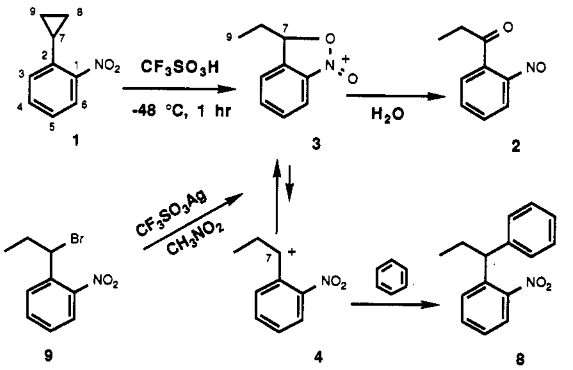
Direct spectroscopic observation revealed the formation of the 1,3-dihydro-3-ethyl-1-oxo-2,1-benzoxazolyl cation (**3**) from 2-cyclopropylnitrobenzene (**1**) in trifluoromethanesulfonic acid. This observation provided experimental evidence for the involvement of **3** as a discrete intermediate in the transfer of oxygen from nitrogen to carbon during the rearrangement of **1** to 2-nitrosopropiophenone.

The electron-donating effect of a cyclopropyl group on an aromatic ring is expected to stabilize a cation center more efficiently than that of a phenyl group.[1,2] This generalization led us to anticipate that a cyclopropyl group might exert a similar stabilizing influence on the cationic center NO_2H^+ (a protonated nitro group),[3] and we therefore undertook the investigation of the behavior of 2-cyclopropylnitrobenzene in a strong acid. 2-Cyclopropylnitrobenzene (**1**) in an excess of trifluoromethanesulfonic acid (TFSA) reacted to give *o*-nitrosopropiophenone (**2**) in 79% yield after aqueous workup (Scheme I). The reaction catalyzed by sulfuric acid has been reported,[4] and the involvement of the cyclic intermediate **3** in the formation of **2** has been proposed although no experimental evidence was provided. We present herein direct spectroscopic evidence for the involvement of the cyclic intermediate, 1,3-dihydro-3-ethyl-1-oxo-2,1-benzoxazolyl cation (**3**), in the oxygen atom rearrangement of 2-cyclopropylnitrobenzene to *o*-nitrosopropiophenone. The cyclic intermediate **3** was a discrete chemical species, stable enough to be observed spectroscopically in TFSA at −30 °C. The ^1H and ^{13}C NMR data for **3** are summarized in Tables I and II, together with the data for the neutral precursor **1**. In the ^1H NMR spectrum of **3**, the H_7 proton was observed at 7.40 ppm as a double doublet, and in the ^{13}C NMR spectrum (Table II) the C_7 carbon atom resonated at 98.4 ppm. These chemical shifts are more readily interpreted in terms of formation of the C_7–O bond rather than the formation of the *free* cation center at the 7-position (**4**).[5] From structural considerations, **3** can be

Scheme I



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