Extraction of Highly Hydrophilic Anions in Low Polarity Media under Phase-transfer Catalysis Conditions: Dramatic Enhancement of the OH^- Reactivity by Reduction of its Specific Hydration

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In the chlorobenzene–aqueous NaOH two-phase system, an increase in NaOH concentration from 5 to 20 M reduces the OH^- hydration sphere of the tetrahexylammonium hydroxide (**1a**) dissolved in chlorobenzene from 11 to 3.5 molecules of water, thus producing a dramatic increase (up to 10^4 times) in OH^- reactivity.

Under liquid–liquid phase-transfer catalysis (P.T.C.) conditions anions associated with lipophilic cations (quaternary onium salts, macrocyclic and macrobicyclic polyethers, *etc.*) in the organic phase are solvated by a limited number of water molecules.[1] This hydration depends on the nature of the anion and appreciably decreases the reaction rates. By using concentrated aqueous alkaline solutions non-hydrated halides and pseudo-halides are transferred into the organic phase, thus giving rise to anionic reactivities identical with those found under anhydrous homogeneous conditions.[2]

Here we report that the same dehydrating effect is produced by concentrated aqueous alkaline solutions on the hydroxide

Table 1. Rate constants (k/s^{-1}) for the Hofmann elimination reaction of tetrahexylammonium hydroxide (**1a**) in chlorobenzene–aqueous NaOH two-phase systems[a] at 25 °C.

[NaOH] /(mol l^{-1})	Hydration state n of $(C_6H_{13})_4N^+OH^-\cdot nH_2O$[b]	10^6k/s^{-1} [c,d]	
4.8	11.0 ± 1.0	0.019[e]	(1)
6.5	9.0 ± 1.0	0.14[e]	(7)
10.0	5.0 ± 0.5	0.74[f]	(39)
15.0	4.0 ± 0.5	26	(1368)
20.0	3.5 ± 0.5	210	(11 053)

[a] 50 ml of a chlorobenzene solution of (**1a**) (1—4 × 10^{-2} M) and 50 ml of an aqueous solution of NaOH (4.8—20 M). Kinetics were measured by following the disappearance of the hydroxide ion (acid–base titration). [b] By Karl Fischer analyses of the organic phase; average of at least three determinations. [c] Relative rates in parentheses. [d] The rate constants are computer-generated from least-squares analysis. [e] Extrapolated values from measurements at 50, 60, and 70 °C *via* Arrhenius plot. [f] Extrapolated values from measurements at 40, 50, and 60 °C *via* Arrhenius plot.

ion transferred by quaternary onium cations in a low-polarity solvent. This effect causes dramatic enhancements of OH^- reactivity, much higher than those found for other anions.[2]

When a chlorobenzene solution of tetrahexylammonium hydrogen sulphate (**1b**) (1—4 × 10^{-2} M) was stirred with 15% aqueous NaOH (4.8 M) the corresponding onium hydroxide (**1a**) was quantitatively obtained. Titrimetric acid–base determinations and Karl Fischer analyses showed that, under these conditions, the quaternary hydroxide (**1a**) is entirely in the organic phase and that OH^- retains an hydration sphere (n) of 11 water molecules. By increasing the concentration of the base in the aqueous phase up to 50% (20 M) the conversion of hydrogen sulphate (**1b**) into quaternary hydroxide (**1a**) was, in all cases, quantitative; again, (**1a**) was entirely in the organic phase. At the same time the hydration number n of OH^- progressively diminished on increasing the concentration of the aqueous NaOH up to a value of 3.5 at the highest concentration of base (50% aqueous NaOH) (Table 1).

The enhancement of reactivity of OH^- as a function of its hydration sphere was studied in the Hofmann elimination. The tetrahexylammonium hydroxide is indeed unstable in chlorobenzene solution and decomposes quantitatively yielding trihexylamine and hex-1-ene [reaction (1)].

$$(C_6H_{13})_4N^+OH^- \xrightarrow[\text{aq. NaOH}]{\text{PhCl}} (C_6H_{13})_3N + \text{hex-1-ene} + H_2O \qquad (1)$$

(1a)

$$(C_6H_{13})_4N^+HSO_4^-$$

(1b)

The kinetics of reaction (1) were studied by stirring a heterogeneous mixture of a chlorobenzene solution of (**1a**) (1—4 × 10^{-2} M) and an aqueous solution of NaOH (4.8—20 M). In all cases reaction (1) followed the regular first-order kinetic equation rate = k[substrate] up to at least 70% conversion.

The rate constants, measured at or extrapolated to 25 °C, are in Table 1. In the range of NaOH concentrations examined they span up to 4 orders of magnitude and show the dramatic effect on the basicity of OH^- in non-polar media due to its specific hydration. The reactivity enhancements obtained by reducing the hydration of OH^- from 11 to 3.5 moles of water are much higher (10^3 times) than those previously found[1,2] in the dehydration of other anions.

Unfortunately, it was impossible to carry out reaction (1) under anhydrous conditions, since all attempts to dehydrate the quaternary hydroxide (**1a**) led to very fast decomposition [reaction (1)].† An aqueous solution of (**1a**) was unchanged after being heated at 80 °C for several days.

This means that in going from aqueous to the hypothetical anhydrous solution in a low polarity solvent the increase in reactivity of OH^- must be several orders of magnitude higher than that found in chlorobenzene by reducing the hydration sphere n from 11 to 3.5. The reactivity differences we found in the condensed phase are comparable with those measured by Bohme in reactions promoted by $OH^-\cdot(H_2O)_n$ (n = 0—3) in the gas phase.[3]‡

The data, as a whole, confirm[2] that, in anion-promoted reactions, reactivity conditions of the gas phase can be approached by desolvating the anions in a non-polar organic solvent. Moreover these results account for the dramatic effect that an increase of base concentration produces on the rate of reactions promoted by alkali hydroxides under liquid–liquid P.T.C. conditions: *e.g.* formation and alkylation of carbanions,[4] alkene isomerization,[5] H/D exchanges in carbon acids,[6] and acid–base equilibria,[7] for which only tentative explanations were given.

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† For example the addition of molecular sieves to a chlorobenzene solution of (**1a**), pre-equilibrated with 50% aqueous NaOH, led to decomposition of (**1a**) at a rate higher than that of its dehydration.

‡ It has been shown[3] that the rates of reactions promoted by non-hydrated OH^- in the gas phase are *ca.* 20 orders of magnitude higher than those measured in the aqueous phase.