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Phase-Transfer Catalysis in a Segmented Flow Assembly. Study of Transfer and Reaction Rates

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Abstract

A study has been made of the appropriateness of a combined semented flow/phase-splitter assembly for examining the kinetics of liquid/liquid phase-transfer catalysis reactions. Using hydrazobenzene and oestrone as oil-soluble substrates, permanganate as the oxidizing ion, and tetrabutylammonium ion as the pairing ion, the influence of reaction rate on the rate of permanganate transfer from an aqueous phase to an oil phase has been determined. Results indicate that the given assembly is suitable for the study of fast reactions occurring in two-phase systems.

INTRODUCTION

Phase-transfer catalysis (PTC) is a method for greatly increasing the distribution of ionized molecules from a polar to a nonpolar phase by use of small amounts of carrier pairing ion. The phenomenon is frequently used in synthetic organic chemistry and in extraction science, and has been shown to have possibilities for on-line postcolumn HPLC detection, and for aiding in the penetration of drug ions through biological membranes. PTC effects are generally studied using classical shake-flask techniques, which can seriously limit their elucidation (*1*). Continuous extraction systems, both with (*2–5*) and without (*6–12*) segmentation of the two phases with air, have been described for effecting ion-pair extraction of charged solutes, and recent studies (*12, 13*) have described the determination of ion-pair extraction constants using a segmented flow method. In this present contribution we

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describe our work on the examination of phase-transfer catalysis phenomena studied using a two-phase segmented flow assembly.

EXPERIMENTAL

Materials

Water was double-distilled from an all-glass still. All other solvents were at least of spectroscopic grade and were obtained from Merck (Merck Holland, Amsterdam, The Netherlands) and were used as received, except for chloroform which was shaken twice with water to remove ethanol. Potassium permanganate, tetrabutylammonium bromide, and hydrazobenzene were obtained from Merck Holland. Hydrazobenzene was recrystallized from 95% ethanol prior to use. Oestrone was from Brocacef (Maarsen, The Netherlands) and was used as supplied.

Apparatus

The design of the segmented-flow/phase-splitting assembly (SEGSPLIT), is shown by Fig. 1. It comprises five principal parts: a solvent delivery system, a sample injector (optional), a segmentor, a mixing coil, and a splitter device [as described previously by us (*12*)]. Further, on-line detection and registration are included. Aqueous and oil phases are pumped separately from a thermostatted reservoir by two pumps: the aqueous phase by a peristaltic pump, (Gilson Miniplus 2), using Tygon pump tubes (Technicon Inc., Tarrytown, New York), and the oil phase by a high-pressure liquid chromatography pump (Waters 6000) equipped for pulse-free flow. The coil (i.d. 1.4 mm) and segmentor are made from polytetrafluoroethylene. The phase of interest was withdrawn from the phase-splitter through the spectrophotometer (Pye-Unicam SP 8-100) using a peristaltic pump.

When contamination of phases with particulate matter was suspected, a small glass-wool filter was placed between the phase-splitter and the cell of the spectrophotometer. The relevant parts of the assembly (Fig. 1), were thermostatted by immersion in a temperature-controlled water bath ($\pm 0.1^{\circ}C$) (Lauda, Tauber, West Germany). All solvent pairs studied were presaturated with each other at the temperature of the experiment.

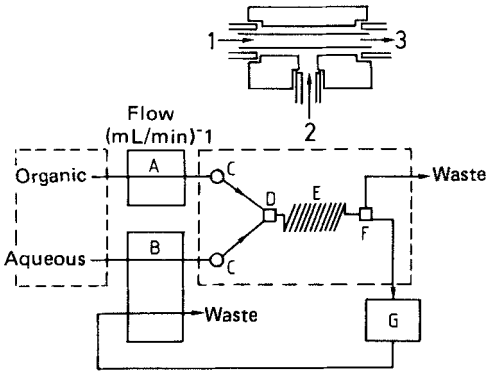

FIG. 1. Construction of the segmented flow/phase-splitter assembly. (A) Double-reciprocating pump; (B) peristaltic pump; (C) injection valve; (D) polytetrafluoroethylene T-piece, (see detail, where flows 1, 2, and 3 refer to aqueous, oil, and segmented phases, respectively); (E) extraction coil; (F) phase-splitter; (G) flow cell of spectro-photometer. The apparatus enclosed by the dashed line was thermostated.

RESULTS AND DISCUSSION

To examine phase-transfer catalysis phenomena using a segmented flow assembly, permanganate transfer has been chosen. PTC has been used frequently (*1, 14, 15*) in organic chemistry for transferring permanganate ion to an organic phase, wherein it can act as an efficient oxidant for solutes having low aqueous solubilities. The reaction is considered then as being independent of the interfacial area between the two phases and of the orientation of molecules therein (providing that phase-transfer is fast relative to oxidation). The literature shows us that permanganate transfer may be achieved using, for example, crown ethers or quaternary ammonium salts. Upon transfer and reaction of the permanganate ion, the complexing agent (sic) returns to the aqueous phase, complexes again with permanganate ions, and the catalytic cycle is therupon repeated (Fig. 2). Permanganate ion was chosen because of its ease of detection in both aqueous and oil phases, and because neither long reaction times nor severe reaction conditions are required.

Initial studies have been performed to establish the extracting efficiencies of a number of organic solvents. Figure 3 gives the results for the extraction of permangante ion as the tetrabutylammonium ion pair with benzene, chloroform, and dichloromethane. (2,2,4-Trimethylpentane was also examined but gave no extraction of the ion pair.) It is seen that the halogenated hydrocarbons lead to far higher extraction of the formed ion pair than does

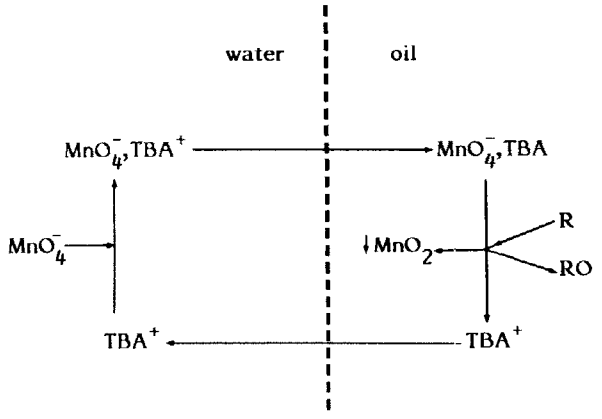

FIG. 2. Catalytic cycle of tetrabutylammonium (TBA) in the MnO_4–TBA phase-transfer catalysis system, using a substrate R being oxidized to RO. (Stoichiometry not shown.)

benzene. Since dichloromethane gave rise to gas bubbles at the liquid/liquid interface, further studies on the extraction of permanganate were carried out using chloroform as the extracting phase.

Kinetics of PTC

It is possible to use the permanganate–tetrabutylammonium system for examining whether the present segmented flow assembly is suitable for the study of rates of extraction. This is carried out by adding oxidizable solutes having a high liquid/liquid distribution coefficient ($\log K_d > 3$) to the organic phase. Figure 2 indicates that differing rates of oxidation in the oil phase would lead to different apparent rates of phase transfer. With the assembly described by Fig. 1, it is has been found that the addition of 1.15×10^{-3} mol/dm^3 hydrazobenzene ($\log K_d = 3.1$ (chloroform/water)) to either a benzene or chloroform organic phase resulted in the loss of all permanganate (original concentration in the aqueous phase of 4×10^{-5} mol/dm^3) from an aqueous phase containing (initially) 6.25×10^{-5} mol/dm^3 tetrabutylammonium ion. (In the absence of tetrabutylammonium, the losses of permanganate were, for benzene and chloroform, 16 and 11%, respectively; without hydrazobenzene the losses were 2 and 48% of the original amount of permanganate.) These results clearly indicate that for tetrabutylammonium the PTC cycle is completed many times within the period of contact between the two phases (100 s). The effect of altering the initial concentration of

hydrazobenzene in chloroform on the loss of permanganate from the aqueous phase is given by Fig. 4. The abscissa value of this figure shows that 1 mole of hydrazobenene substrate has reacted with 3.57 equivalents of permanganate. An experiment performed with a simple shake-flask method and using the same phases, phase volume ratio, and solute concentrations, and with a time of shaking of 15 min, gave a value of 2.91 equivalents. This difference may be explained by the spurious entry of oxygen when using the shake-flask procedure. Gerritse (*16*) has found that polytetrafluoroethylene tubing has a high permeability for oxygen, and this could explain why no integer equivalent number was found with the segmented flow system, suggesting that the use of glass or metal tubing would have avoided this problem. Table 1 gives the influence of varying both the concentrations of tetrabutylammonium and hydrazobenzene on the loss of permanganate from

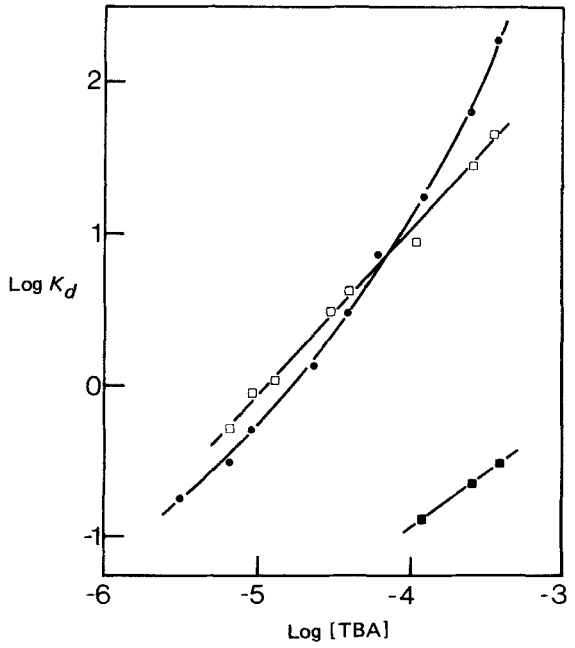

FIG. 3. Apparent distribution coefficients (K_d^{app}) for the transfer of the permanganate–tetrabutylammonium ion pair from water to various organic phases using differing initial concentrations of TBA (molar). Initial MnO_4 concentration, 2×10^{-4} mol/dm^3; $R = 1.87$ to 2.08; phase-contact time, 100 s. (Open and closed squares and closed circles refer to benzene, dichloromethane, and chloroform, respectively).

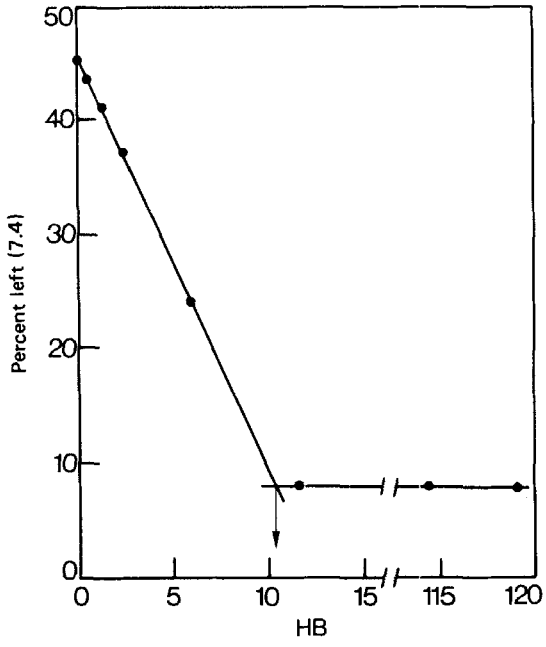

FIG. 4. Amount of permanganate ion remaining in the aqueous phase (as a percentage of the initial concentration, 4.0×10^{-5} mol/dm^3) using tetrabutylammonium (6.25×10^{-4} mol/dm^3) as the pairing ion, upon the addition of hydrazobenzene (HB) (in mol/dm$^3 \times 10^5$) to the chloroform phase. Contact time between phases, 100 s; phase-volume ratio, 0.60.

the aqueous phase. It is demonstrated that higher concentrations of both lead to increased losses of permanganate.

To examine the effect of substrate lability on observed rates of permanganate loss, oestrone has been chosen. This compound is far more stable than hydrazobenzene under oxidizing conditions, and has a log K_d of greater than 3 in the water/chloroform system. Figure 5 gives the results found for the loss of permanganate from the aqueous phase in the presence of tetrabutylammonium and these two substrates for differing reaction times (this being achieved using different lengths of reaction coil). The loss of permanganate from the aqueous phase may be expressed as

$$K_d^{app} = [(A_0 - A_e)/A_e]R^{-1} \quad (1)$$

where A_0 and A_e are the aqueous phase UV absorbances before and after contact with the organic phase, and R is the phase–volume ratio. It is seen

from Fig. 5 that in the absence of substrate (hydrazobenzene or oestrone) the maximum loss of permanganate is reached after 40 to 60 s. The addition of oestrone leads to a maximum loss after some 140 s (K_d^{app} includes both reacted and nonreacted permanganate in the organic phase). With hydrazobenzene as substrate, a maximum loss greater than that found with oestrone is reached after ~75 s. The data given in Fig. 5 may be represented by a first-order plot (Fig. 6) from which the first-order rate constants (k) can be calculated using

$$k = (\ln A_\infty - \ln A_t)/t \qquad (2)$$

where A_∞ and A_t represent, respectively, the maximum loss of permanganate achieved (moles), and the loss of permanganate (moles) after reaction time t (seconds). The rate constants determined in this way for the systems examined are given in Table 2, where it is seen that the rate of phase-transfer in the absence of substrate is higher than that found using oxidizable substrates in the organic phase. As expected, the use of the more unstable substrate hydrazobenzene results in a higher overall rate constant than does oestrone.

TABLE 1

Influence of Hydrazobenzene (HB) and Tetrabutylammonium (TBA) Concentrations on the Apparent Liquid/Liquid Distribution Coefficient (K_d^{app}) of Permanganate between Water and Chloroform at 25°C (initial permanganate concentration, 2.0×10^{-4} mol/dm^3; phase-volume ratio = 2.08; reaction time = 100 s)

TBA[a]	HB[a]	log K_d^{app}
6.0×10^{-7}	2.1×10^{-5}	−0.67
9.0×10^{-7}	2.1×10^{-5}	−0.57
3.0×10^{-6}	2.0×10^{-5}	−0.12
3.0×10^{-6}	3.9×10^{-5}	0.26
3.0×10^{-6}	4.1×10^{-4}	1.19
6.0×10^{-6}	2.1×10^{-5}	0.31
6.0×10^{-6}	8.1×10^{-5}	0.40
6.0×10^{-6}	4.1×10^{-4}	1.37
3.0×10^{-5}	2.1×10^{-5}	0.69
3.0×10^{-5}	1.0×10^{-3}	1.69
3.0×10^{-5}	—	−0.27

[a] In mol/dm^3.

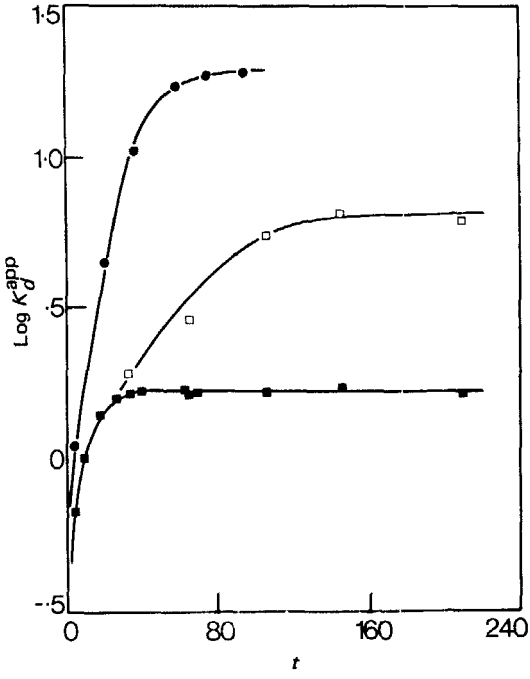

FIG. 5. Apparent liquid/liquid distribution coefficients for transfer of permanganate ion (initial concentration, 4×10^{-5} mol/dm^3) using tetrabutylammonium ion (initial concentration, 6.25×10^{-4} mol/dm^3) as the pairing ion, in the absence (closed squares) and presence of either hydrazobenzene (1.17×10^{-3} mol/dm^3) or oestrone (1.0×10^{-3} mol/dm^3) in the chloroform phase, at the various phase contact times t (seconds). Circles and open squares refer to hydrazobenzene and oestrone, respectively. (Phase-volume ratio = 0.60.)

CONCLUSIONS

The results presented here indicate that the segmented-flow assembly described by Fig. 1 is readily applicable to the study of phase-transfer catalysis and other fast reactions in two-phase systems. Due to the construction and method of use of the assembly, reactions may be examined that could not normally be considered.

The assembly can have a particular use for the study of reactions intended for pre- and/or postcolumn detection use in high-performance liquid chromatography, and we are currently examining this feature in greater detail.

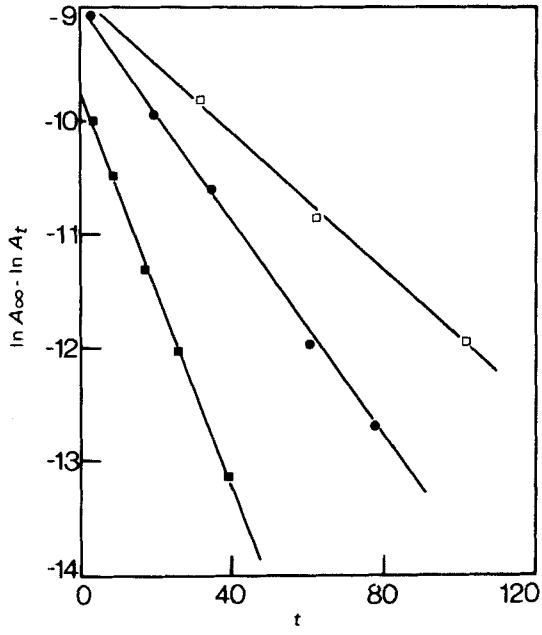

FIG. 6. First-order representation of Fig. 5. (See text for meaning of terms.)

TABLE 2
Apparent Phase-Transfer Rate Constants (s^{-1}) for the Transfer of Permanganate from Water to Chloroform at 25°C as the Tetrabutylammonium Ion Pair in the Absence and the Presence of Substrate in the Chloroform

System	Rate constant[a]
MnO_4–TBA	0.1034
MnO_4–TBA–HB	0.0457
MnO_4–TBA–oestrone	0.0297

[a] Calculated using the relationship given by Eq. (2) and Fig. 6.

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