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► **To cite this version:**

Jean-François Betzer. Inverse Phase-Transfer Catalysis. I. Reduction of Ketones in a Micellar Two-Phase Medium. *New Journal of Chemistry*, 1995, 19, pp.807-811. hal-04218431

HAL Id: hal-04218431

<https://hal.science/hal-04218431>

Submitted on 26 Sep 2023

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Inverse phase-transfer catalysis.

I. Reduction of ketones in a micellar two-phase medium

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Alain LEYDET and Jean-Pierre ROQUE*

Abstract. – The reduction reaction of ketones by sodium borohydride has been investigated in a two-phase medium using an inverse phase-transfer catalysis (IPTC) technique in the presence of surfactants (monomeric and polymeric species). The phase transfer process is always catalyzed by micellar aggregates. The main role of the surfactant is to promote the transfer of the lipophilic substrate into the water phase.

Résumé. – **Catalyse par transfert de phase inverse. I. – Réduction de cétones dans un milieu biphasique micellaire.** L'étude de la réaction de réduction des cétones par le borohydrure de sodium a été réalisée dans un milieu biphasique selon un procédé de catalyse par transfert de phase inverse (CTPI) en présence de tensioactifs (monomères et polymères). Dans tous les cas, le procédé de transfert de phase est catalysé par les agrégats micellaires. Le rôle principal joué par le tensioactif est de faciliter le transfert du substrat lipophile dans la phase aqueuse.

Introduction

Phase-transfer catalysis (PTC) has been intensively investigated in the past 20 years. It has been widely used in organic synthesis to promote reactions involving a lipophilic substrate with a hydrophilic reactant using two-phase water-organic solvent media¹⁻⁶.

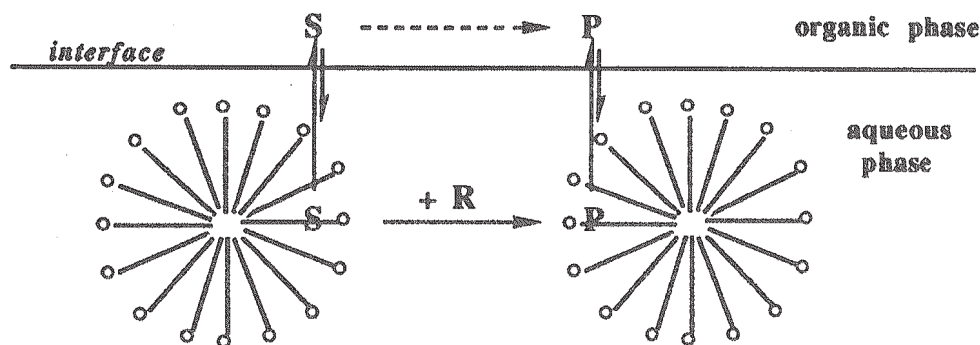
The usual procedure consists of transporting an anionic reactant from the water phase into the organic phase in the form of ion pair with a quaternary onium cation^{1,3,4}. The anionic reactant reacts with the lipophilic substrate in the organic phase. The possibility of transferring a cationic reactant to the organic phase with a lipophilic non-nucleophilic anion has also been mentioned⁷⁻⁹.

Recently, another methodology was described by Mathias et al.¹⁰ as "inverse phase-transfer catalysis" (IPTC). This involves the conversion of the organic substrate into an ionic derivative suitable for transportation into the water phase, where it reacts with the hydrophilic reactant^{10,11}. The reaction studied involved the acylation of aqueous alanine with organic-soluble acid chlorides. In the presence of 4-(dialkylamino)pyridine, the acid chloride was converted to an *N*-acylpyridinium, a hydrophilic activated intermediate.

Although this approach is complementary of the normal PTC, it is difficult to generalize. It is not always feasible to convert a substrate into an ionic derivative and retain its specific reactivity.

We present here preliminary results dealing with a methodology which we can term as IPTC but which is applicable to any reaction occurring in biphasic medium. Its principle consists of transporting the lipophilic substrate from the organic phase to the aqueous phase by means of amphiphilic aggregates. In the aqueous phase, the substrate reacts with the hydrophilic reactant in the micellar microenvironment. If the product of the reaction is hydrophobic, it is progressively transferred into the organic phase as it is formed (Scheme 1).

It is worth noting that apart from the transfer phenomena, the chemical step is actually controlled by a micellar catalysis process. If the reaction between the substrate (S) and the reactant (R) provides a negatively charged transition state, a cationic surfactant can increase the chemical reaction rate by the micellar effect. In contrast an anionic surfactant would lead to a decrease in the rate¹².



Scheme 1.

Results and discussion

We checked the validity of this approach by studying the reduction of acetophenone and benzophenone¹³ by sodium borohydride in a water/heptane medium (scheme 2).



Scheme 2.

First we measured the influence of either a cationic surfactant, docecyltrimethylammonium bromide (DTAB), or an anionic surfactant, sodium dodecyl sulfate (SDS), on the reduction rate of the acetophenone in a homogeneous aqueous medium. The results are represented in Figure 1 and are consistent with positive

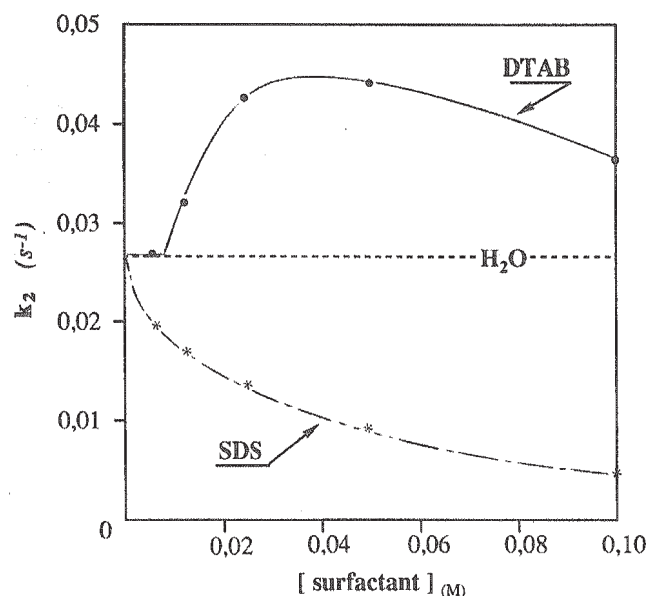


Figure 1. - Rate constant variations for the reduction of acetophenone in homogeneous media as a function of surfactant concentration at 25°C.

micellar catalysis (enhancement) by DTAB and negative micellar enhancement (decrease) with SDS. As expected, the catalytic effect only appears for concentrations higher than the critical micellar concentration (cmc): 1.44×10^{-2} M for DTAB and 0.8×10^{-2} M for SDS¹⁵.

We also studied the reduction reaction in biphasic conditions (water/heptane). The acetophenone or benzophenone was dissolved in heptane and the borohydride in water. The reaction was carried out with and without surfactant in the aqueous phase ([DTAB] or [SDS]=0.05 M). The reaction mixture was vigorously stirred (1200 rpm) at 25°C. The reaction progress was followed by measuring the absorbance of an aliquot diluted in heptane, at the wavelength corresponding to the maximum absorbance of ketones ($\lambda = 287$ and 291 nm for the acetophenone and benzophenone, respectively).

Absorbance variations with no surfactant or with DTAB or SDS are reported as a function of time in Figures 2 (acetophenone) and 3 (benzophenone).

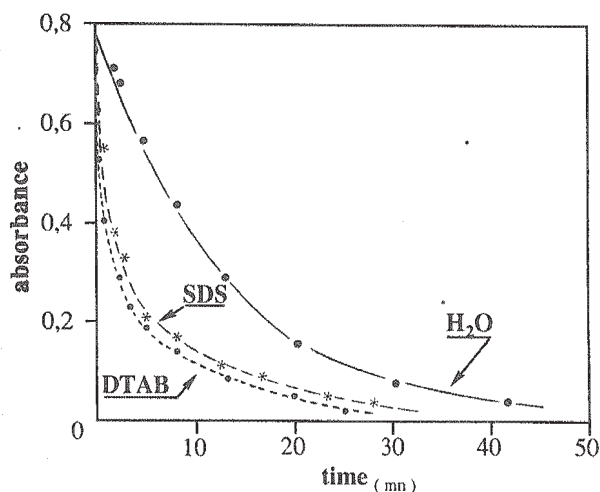


Figure 2. - Acetophenone reduction in biphasic media (heptane/water 1:1): plot of absorbance versus time (without surfactant, SDS 0.05 M, DTAB 0.05 M).

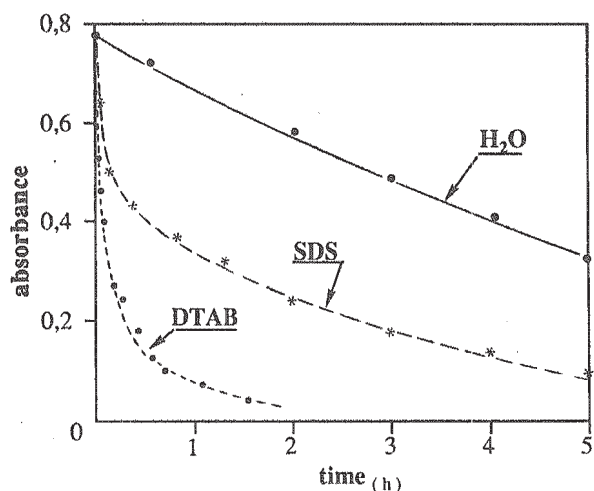


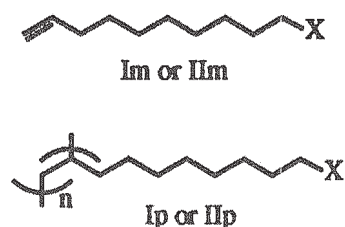
Figure 3. – Benzophenone reduction in biphasic media (heptane/water 1:1): plot of absorbance versus time (without surfactant, SDS 0.05 M, DTAB 0.05 M).

The half-life values determined graphically are reported in Table I. From the results, it is worth noting that the addition of either cationic (DTAB) or anionic (SDS) surfactant favors the reaction. Furthermore, this effect is more pronounced with benzophenone. These results prove the validity of a phase-transfer procedure catalyzed by micellar aggregates.

Table I. – Half-life for the reduction of acetophenone and benzophenone in biphasic media (heptane/water 1/1): without surfactant or in the presence of DTAB or SDS (0.05M).

Surfactant	Acetophenone		Benzophenone	
	$t_{1/2}$ (s)	$t_{1/2}$ (rel)	$t_{1/2}$ (s)	$t_{1/2}$ (rel)
none	450	1	15 800	1
DTAB	45	0.10	235	0.015
SDS	104	0.23	1 800	0.11

In 1988, Jursic¹⁴ showed that the oxidation reaction of alcohols by the chromate ion in a two-phase system (water/chloroform) was catalyzed by hexadecyltrimethylammonium bromide. He supposed that this



Scheme 3.

onium salt acted as a normal phase-transfer catalyst by transferring chromate ions to organic phase in the form of ion pairs. In our opinion, this explanation is not appropriate. Indeed, although this idea may be convenient to account for the increase due to DTAB (a cationic surfactant which could transfer the anionic reactant BH_4^-), it is inadequate to explain the increase observed by the addition of SDS (an anionic surfactant).

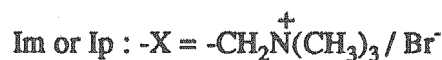
The main role played by the surfactant is to ensure the transfer of the lipophilic substrate to the water phase. Without any doubt, we have observed an IPTC procedure. On this basis, we can make the following comments:

(i) The cationic surfactant (DTAB) is more efficient than the anionic surfactant (SDS). Both favor the reaction in facilitating the transport of the ketone into the water phase. However beyond the transfer phenomena, DTAB increases the chemical step by micellar catalysis while SDS decreases it (see Fig. 1). Globally, the IPTC procedure is more important than the micellar catalysis.

(ii) The enhancing effects are larger in the case of the benzophenone. This observation must be related to the water solubility of these two ketones: 47.1 mM for acetophenone at 25°C and 0.41 mM for benzophenone¹⁵. The more hydrophobic the substrate, the more efficient the IPTC procedure.

In a recent work, we showed that polymerization of unsaturated surfactants amplifies some of their micellar properties, such as solubilizing power or micellar catalysis¹⁶⁻¹⁹. We wanted to see how the IPTC was influenced by the use of polymerized amphiphiles. We have thus studied the reduction of benzophenone in the same conditions and in the presence of monomeric surfactants undec-10-enyltrimethylammonium bromide (Im) and sodium undec-10-enylcarboxylate (IIm), and their polymerized analogs Ip and IIp^{15,16}, the structures of which are given in Scheme 3.

Absorbance variations at 291 nm are indicated in Figure 4 as a function of time. As previously shown, the addition of a cationic surfactant (Im or Ip) enhances the reaction more than an anionic surfactant (IIm or IIp). Furthermore,



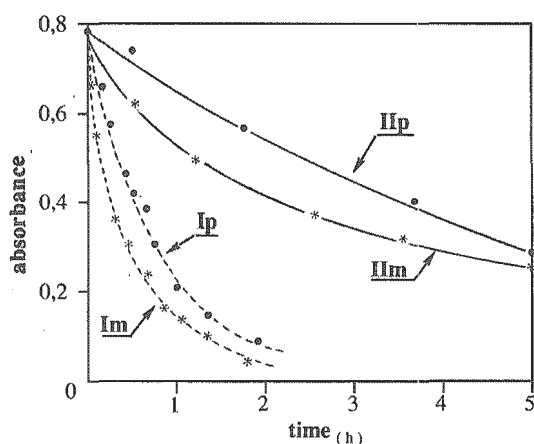


Figure 4. – Benzophenone reduction in biphasic media (heptane/water 1:1): plot of absorbance versus time (Im; Ip, IIm; IIp).

whatever the nature of the surfactant, the polymeric form is less efficient than the corresponding monomeric form, contrary to what was observed in monophasic aqueous media¹⁶. The contribution of the surfactant polymerization to micellar catalysis in homogeneous media is probably compensated in two-phase media by the fact that the polymerized species is less prone to transfer the lipophilic substrate from the organic to the water phase.

We showed that the polymerized form of an amphiphile had no significant effect on the surface tension¹⁹ because of the difficulty it has to form a monolayer at the interface. During the reaction of benzophenone in a stirred biphasic medium, a polymerized surfactant leads, to a lower interface area than its unpolymerized analog and so to a weaker transfer efficiency.

In summary, a polymerized surfactant is more prone to catalyze the chemical step¹⁶, but less prone to promote substrate transfer, which predominates over the catalysis. However, the difference in reactivity between the monomeric and the polymeric surfactant is relatively low. In practice, although the polymeric species is slightly less efficient it is particularly interesting. Effectively, due to its weak surfactive properties, the phase separation is complete less than one minute after stirring is stopped. In the case of unpolymerized surfactants, the phase separation takes several hours. Polymerized surfactants

may play an important role as part of preparative methods. Further investigations are under way to extend IPTC to other reactions.

Experimental section

Surfactant synthesis

Sodium dodecyl sulfate (SDS) and dodecyltrimethylammonium bromide (DTAB) are commercially available. Undec-10-enyltrimethylammonium bromide (Im) and sodium undec-10-enylcarboxylate (IIm), were prepared according to a previously described procedure¹⁵. Polymerization was performed by γ -irradiation of 0.1 M aqueous solutions^{15, 20}.

Kinetic studies

– Reactions in monophasic aqueous media

A 1.00 cm cuvette was filled with 1 mL aqueous sodium borohydride (0.08 M) and 1 mL water or aqueous surfactant solution and equilibrated in a thermostated cell holder (25°C) of an SAFAS DES-170 spectrophotometer. A methanolic solution of acetophenone (20 μ L, 0.625 M) was then added. The rate of the acetophenone reduction was determined by monitoring the disappearance of the ketone at 287 nm as a function of time.

In all cases, first-order plots were linear, even above 80% reaction. The observed rate constants (k_{obs}) were evaluated from the absorbance/time data using a least-squares fit computing method. Knowing the sodium borohydride concentration, the bimolecular rate is expressed as $k = k_{obs}/4[BH_4Na]$. Each rate reported is the mean of at least three independent determinations differing by 3% or less.

– Reactions in two-phase media

Aqueous 2 M BH_4Na (1 mL), surfactant 0.1 M (1 mL) or water (1 mL) and ketone (0.125 M) in heptane (2 mL) were quickly mixed and stirred in a jacketed reactor thermostated at 25°C. At a chosen time, 40 μ L of the emulsion was withdrawn and placed in a tube containing heptane (2 mL). The tube was shaken vigorously for 1 min and then allowed to stand for a few minutes to allow the two phases to separate. The organic phase was then analyzed by UV to follow the variation in absorbance. Absorbance was monitored as a function of time.

References

- 1 Starks C. M., *J. Am. Chem. Soc.*, 1971, **93**, 195.
- 2 Starks C. M., Liotta C., *Phase Transfer Catalysis, Principle and Techniques*, Academic, New York, 1978.
- 3 Brändström A., *Adv. Phys. Org. Chem.*, 1977, **15**, 267.
- 4 Dehmlow E. V., Dehmlow S. S., *Phase Transfer Catalysis*, 2nd ed., Verlag Chemie, Weinheim, 1983.
- 5 Makosza M., Fedorynski M., *Adv. Catal.*, 1985, **35**, 375.
- 6 Freedman H. H., *Pure Appl. Chem.*, 1986, **58**, 857.
- 7 Ellwood M., Griffiths J., Gregory P., *Chem. Commun.*, 1980, 181.

- ⁸ Iwamoto H., Sonoda T., Kobayashi H., *Tetrahedron Lett.*, 1983, **24**, 4703.
- ⁹ Kobayashi H., Sonoda T., Iwamoto H., *Chem. Lett.*, 1982, 1185.
- ¹⁰ Mathias L. J., Vaidya R. A., *J. Am. Chem. Soc.*, 1986, **108**, 1093.
- ¹¹ Fife W. K., Xin Y., *J. Am. Chem. Soc.*, 1987, **109**, 1278.
- ¹² Fendler J. H., Fendler E. J., *Catalysis in Micellar and Macromolecular Systems*, Academic, New York, 1975.
- ¹³ We have chosen these two aromatic ketones as solutes because they provide a low water solubility and a large UV molar extinction coefficient (ϵ) which facilitates low concentration measurements.
- ¹⁴ Jursic B., *Synthesis*, 1988, 868.
- ¹⁵ Boyer B., Lamaty G., Leydet A., Roque J. P., Sama P., *New J. Chem.*, 1992, **16**, 883.
- ¹⁶ Boyer B., Lamaty G., Leydet A., Roque J. P., Sama P., *New J. Chem.*, 1992, **16**, 887.
- ¹⁷ André B., Boyer B., Lamaty G., Roque J. P., *Tetrahedron Lett.*, 1991, **32**, 1881.
- ¹⁸ Boyer B., Lamaty G., Moussamou-Missima J. M., Pavia A. A., Pucci B., Roque J. P., *Tetrahedron Lett.*, 1991, **32**, 1191.
- ¹⁹ Boyer B., Durand S., Lamaty G., Moussamou-Missima J. M., Pavia A. A., Pucci B., Roque J. P., Rouvière J., *J. Chem. Soc., Perkin Trans 2*, 1991, 1311.
- ²⁰ Larrabee C. E., Sprague E. D., *J. Polymer Sci., Lett. Ed.*, 1979, **17**, 749.