CHAPTER 12

PHASE-TRANSFER CATALYSIS

CHAPTER 12 OBJECTIVES

- Introduction
- Catalysts for PTC
- Mechanism and Benefits of PTC
- PTC Reactions
- Selected Industrial Processes with PTC

PHASE-TRANSFER CATALYSIS Introduction

- Phase-transfer catalysts accelerate reactions of two immiscible reactants.
- Phase-transfer catalysis (FTC) is useful for performing reaction between anions (and certain neutral molecules such as H_2O_2 and transition metal complexes such as $RhCl_3$) and organic substrate.
- PTC is needed because many anions (in the form of their salts, such as NaCN) and neutral compounds are soluble in water and not in organic solvents, whereas the organic reactants are not usually soluble in water.

PHASE-TRANSFER CATALYSIS
Introduction

- PTC is not likely to be involved in the manufacture of large tonnage heavy organic chemicals but is an unusual and elegant catalytic technique that is energy sparing and gives high yields at low-residence times under mild conditions.
- It is therefore typical of the methods that will be attractive in the future.

PHASE-TRANSFER CATALYSIS
Catalysts for PTC

- Suitable catalysts for PTC are those which have a highly lipophilic cation (i.e. have strong affinity for an organic solvent). Catalysts used most extensively are quaternary ammonium or phosphonium salts (quats). Examples are:
  - Tetra-n-butylammonium bromide (TBAB)
  - Triethylbenzylammonium chloride (TEBA)
  - Methyltrioctylammonium chloride (Aliquat 336 or Adogen 464); $PhCH_2NEt_3Cl$ (TEBA,TEBAC)
  - Cetyltrimethylammonium bromide ("cetrimide") for basic PTC

PHASE-TRANSFER CATALYSIS
Catalysts for PTC

- Neutral complexing agents for organic cations, e.g. crown ethers, polyethylene glycols (PEGs), crvptands, etc., are also suitable catalysts open chain PEGs (e.g. PEG 400) are the least expensive catalysts and may be preferable to quats in some processes.

PHASE-TRANSFER CATALYSIS
Catalysts for PTC

- Crown ethers and cryptands can solubilize organic and inorganic alkali metal salts even in nonpolar organic solvents; they form a complex with the cation, and thus act as an “organic mask”.

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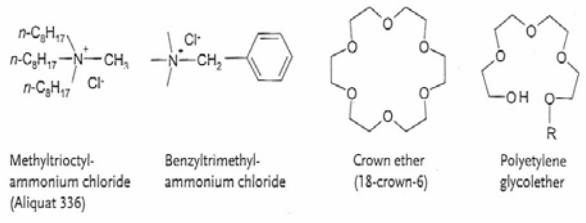
Catalysts for PTC



Methyltrioctyl-ammonium chloride (Aliquat 336)

Benzyltrimethyl-ammonium chloride

Crown ether (18-crown-6)

Polyetylene glycolether

PHASE-TRANSFER CATALYSIS
Catalysts for PTC

- Most commonly used organic solvents in liquid/liquid PTC are toluene and other hydrocarbons, chlorobenzene, and in the lab-chlorinated solvents such as CH_2Cl_2 and $CHCl_3$. For solid / liquid FTC the more polar acetonitrile and even DMF are employed, too.

PHASE-TRANSFER CATALYSIS
Catalysts for PTC

- Some newer variants of PTC are:
  - Triphase catalysts (in which the catalyst is anchored to a polymer for ease of removal)
  - Inverse PTC: extraction of cations for electrophilic reactions by large lipophilic catalyst anions
  - Extraction of uncharged species into organic media by onium salts. These include transition metal salts (complex formation with, e.g. CuX, $PdCl_2$), and acids,
  - H_2O_2 and amines which form weakly hydrogen-bonded complexes with quats

CHAPTER 12
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PHASE-TRANSFER CATALYSIS
Mechanism and Benefits of PTC

- Since the catalyst is often a quaternary ammonium salt (e.g. tetrabutyl aminoniuna, $[C_4H_9]_4N^+$, also called the "quat" and symbolized by Q^+, the ion pair Q^+X^- (X^- being the anion to be reacted) is a much looser ion pair than say Na^+X^-.
- This looseness of the ion pair is a key reason for enhanced reactivity, which will ultimately lead to increased productivity (reduced cycle time) in commercial processes.

PHASE-TRANSFER CATALYSIS
Mechanism and Benefits of PTC

- At the end of the reaction, an anionic leaving group is usually generated.
- This anionic leaving group is conveniently brought to the aqueous (or solid) phase by the shuttling catalyst, thus facilitating the separation of the waste material from the product.
- This mechanism is called the “extraction mechanism” of PTC.

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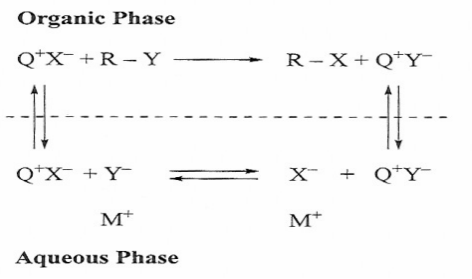
Mechanism and Benefits of PTC



The extraction mechanism of phase-transfer catalysis

PHASE-TRANSFER CATALYSIS
Mechanism and Benefits of PTC

- Due to process improvements, some benefits have been realized through phase- transfer catalysts, which can Increase productivity: increase yield, reduce cycle time, reduce or consolidate unit operations, increase reactor volume efficiency.
- Improve environmental performance: eliminate, reduce or replace solvent, reduce non-product output

PHASE-TRANSFER CATALYSIS
Mechanism and Benefits of PTC

- Increase quality: improve selectivity, reduce variability
- Enhance safety: control exothermic reactions, use less hazardous raw materials
- Reduce other manufacturing costs: eliminate workup unit operations, use alternate less expensive or easier to handle raw materials

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PHASE-TRANSFER CATALYSIS
PTC Reactions

- PTC technology is used in a wide variety of applications. PTC reactions under neutral conditions include:
  - Substitutions with many ions
  - Reductions
  - Oxidations
  - Epoxidation
  - Carbonylation
  - Transition metal co-catalysis

PHASE-TRANSFER CATALYSIS
PTC Reactions

- More widely applicable are base-catalyzed phase-transfer reactions using aqueous concentrated or solid NaOH, KOH, K_2CO_3, NaH, etc. These include:
  - Alkylations
  - Isomerizations
  - Addition reactions
  - Condensations
  - Eliminations
  - Hydrolyses
  - Nucleophilic aromatic substitutions
  - Carbene reactions etc.

PHASE-TRANSFER CATALYSIS
Selected Industrial Processes with PTC

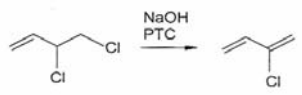
- There are hundreds of commercial applications of phase-transfer catalysis and they were commercialized due to the competitive advantages which they truly provide.

PHASE-TRANSFER CATALYSIS
Selected Industrial Processes with PTC

1. *Continuous Dehydrohalogenation to Produce the Large Scale Monomer Chloroprene*

   Dehydrohalogenation of 3,4-dichloro-l-butene with NaOH and the PTC cocoalkyl benzyl his [β-hydroxypropyl] ammonium chloride can be carried out in a reactor cascade of 3-8 stirred vessels.

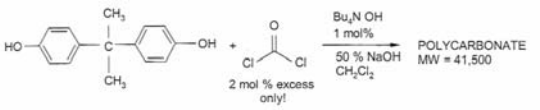
   Productivity ~16 t/hr, yield up to 99.2% and NaOH usage only 0.8 mole % excess.



PHASE-TRANSFER CATALYSIS
Selected Industrial Processes with PTC

2. *Polycarbonate Manufacture with Phosgene*

This process allows an outstanding reduction of excess hazardous high volume raw material such as phosgene. PTC provides 200 times less hydrolysis of phosgene/chloroformate than traditional catalysis.



PHASE-TRANSFER CATALYSIS
Selected Industrial Processes with PTC

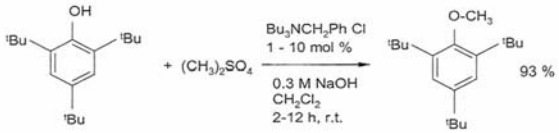
3. *Etherification (O-alkylation)*

A special Williamson ether synthesis can be carried. PTC usually provides the best Williamson ether synthesis. This reaction achieves:

a) High-yield etherification
b) No need for excess pre-formed alkoxide
c) Usually short cycle time and easy workup
d) Non-dry mild reaction conditions

PHASE-TRANSFER CATALYSIS
Selected Industrial Processes with PTC

3. *Etherification (O-alkylation)*



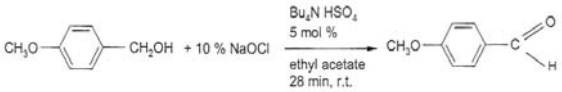
PHASE-TRANSFER CATALYSIS
Selected Industrial Processes with PTC

4. *Aldehydes by Oxidation of Alcohols with Hypochlorite*

This achieves a reaction with.

a) A high yield in short reaction time at room temperature

b) An inexpensive oxidizing agentlno transition metal with high selectivity (vs. over-oxidation)



PHASE-TRANSFER CATALYSIS
Selected Industrial Processes with PTC

5. *Carbonylation*

Phase-transfer catalysis offers a variety of conceptual and practical advantages. Among these advantages unique to PTC are the ability of quats to transfer the anionic forms of metal carbonyls in the organic phase, in which CO is about 20 times more soluble than in water, which thither leads to less hydrolysis of CO to formate and esters to acids

PHASE-TRANSFER CATALYSIS
Selected Industrial Processes with PTC

5. *Carbonylation*

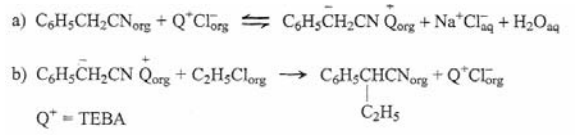
For example, malonic esters can be made by FTC carbonylation of ethyl chloroacetnte at 1 bar CO at 25°C in the presence of cobalt carbonyl.

$Ni(CN)_2$ was used for the PTC double carbonylation of alkynols, using PEG-400 as the phase-transfer catalyst, $LaCl_3$ as an additional co-catalyst, toluene as the solvent, and 0.5 M NaOH as the optimum base concentration. Yields of ene-dicarboxylic acids were up to 97%.

PHASE-TRANSFER CATALYSIS
Selected Industrial Processes with PTC

6. *2-Phenylbutyronitrile by Alkylation*

   An industrial process for the production of 2-phenylbutyronitrile consists of stirring phenylacetonitrile and an alkylating agent, preferably alkyl chloride, with aqueous 50% NaOH solution and a PTC benzyltriethylammonium chloride.



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