Industrial Phase-Transfer Catalysis

Pollution Prevention Using Phase-Transfer Catalysis

Technical and Market Perspectives

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Summary:

Phase-transfer catalysis is an extremely effective technology for improving environmental performance through pollution prevention, green chemistry and pollution treatment. PTC technology can help meet ever tightening environmental goals and maybe even help avoid the shutdown of a profitable production plant.

While it is true that phase-transfer catalysis excels at reducing the cost of manufacture of organic chemicals, many of the benefits of PTC have very direct and compelling impact on pollution prevention and green chemistry. Four of the many pollution prevention benefits of PTC include increasing yield, reducing excess reactants, conducting reactions under solvent-free PTC conditions and dramatically reducing reaction temperature. These benefits of PTC can often be absolutely crucial to reducing BOD, COD, TDS, air emissions and other forms of pollution.

This discussion will describe selected examples of how PTC is used to achieve real pollution prevention and pollution treatment. The article will conclude with a list of simple and practical questions to identify if phase-transfer catalysis should be considered as a potential solution for environmental problems or environmental opportunities.

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The use of PTC routinely helps companies meet their environmental performance improvement goals. In some cases, the use of PTC is much more dramatic when it can make the difference between shutting down a plant for lack of environmental compliance and keeping open a profitable job producing business.

Before discussing the technical aspects of the ability of PTC to affect environmental performance and pollution prevention, it is interesting to put into perspective the market ramifications of PTC on environmental compliance. More specifically, all eyes are on the unprecedented growth of the Chinese chemical industry and its potential dominance in various segments. This industrial revolution in China has huge impact on the local population as well as on the chemical companies all over the world that compete with Chinese chemical companies. How does PTC affect this global competition?

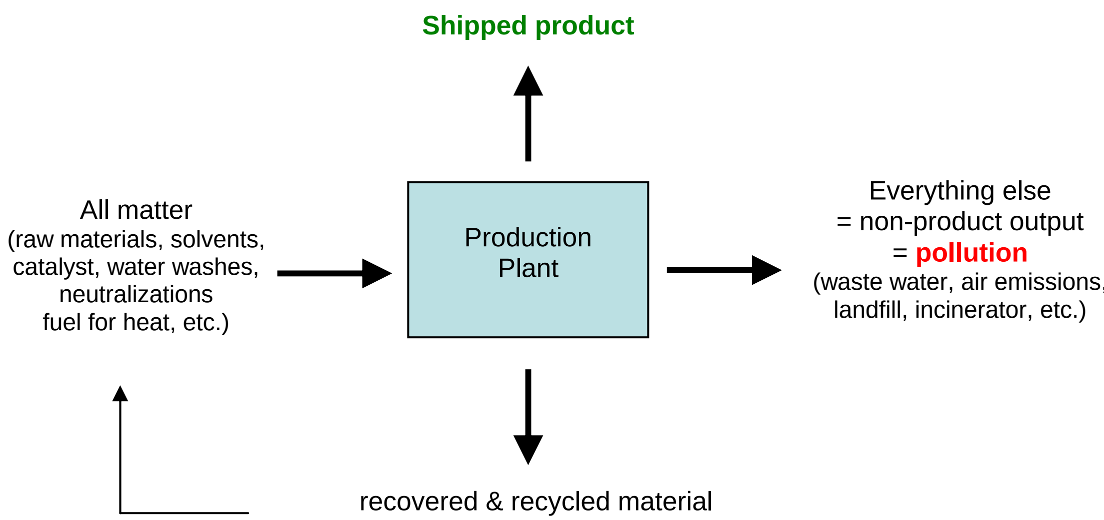
Interesting Thought: Environmental Impact of PTC on Chemical Companies in China and on Their Competitors

A reality which is being increasingly recognized in the West is that highly profitable chemical plants in China are being shut down due to increasingly stricter enforcement of tightening environmental standards by local Chinese authorities. The crackdown on safety and environmental compliance for quite a few industries in China (chemicals, pharmaceuticals, toys) accelerated in 2007 in light of widely publicized incidents.

It is rather interesting and almost amusing to consider the dual role that PTC plays in global competitive race in organic chemical industries. At the time of writing this article, PTC is actively helping companies in *North America, Europe and Japan compete with chemical companies in China by reducing cost of manufacture*. At the same time, PTC is helping *companies in China remain in operation* due to reductions in COD to within acceptable limits determined by local authorities. So, depending on who is reading this article, phase-transfer catalysis is either helping you chase low cost producers based on cost reduction or is helping you keeping your doors open based on environmental compliance...perhaps even both.

A Simplified Definition of Pollution

Pollution is defined as all "non-product output" which is essentially the difference between all materials that enter the plant and all materials that are shipped as product or recycled.



Strong Base Reactions * Nucleophilic Substitutions * Oxidations * Reductions

Achieve <u>Breakthrough</u> Process Performance

Using Phase-Transfer Catalysis

Route Selection * New Process Development

Process Improvement * Compete with Low Cost Producers

PTC Consulting

PTC Consulting enhances outstanding process R&D in two stages. First, after reviewing the Project Description, PTC Organics composes a written Design Report which includes [1] an in-depth discussion of the 4-6 key PTC process parameters (out of 14 possible factors) and underlying fundamentals likely to influence the successful outcome of your specific reaction for pre-defined target performance, plus critique of relevant PTC patents & literature and [2] the design of a resource-efficient experimental program to evaluate the PTC process option, including highly specialized PTC techniques (“tricks”). Secondly, PTC Organics provides up to 20 hours of analysis of results generated by the customer and additional input for the design, redesign, rationale, ramifications and recommendations for the experimental programs to assure the best process performance in the shortest time during development and scale up.

PTC Contract Research

PTC Organics dedicates its best efforts, highly specialized expertise in Phase-Transfer Catalysis and laboratory resources to design, redesign and execute an experimental program in PTC Organics’ laboratory, including highly specialized PTC techniques, to determine proof-of-concept and promising results for the PTC process option, typically within 1-2 months. PTC Organics composes a highly detailed report describing each and every procedure, results and rationale for the design of the experimental program as measured against the pre-defined Performance Targets.

Certain chemistries are not performed by PTC Organics, such as work with controlled substances, highly potent compounds, phosgene and lower mercaptans. Most other chemistries are acceptable, including work with cyanide, azide, epichlorohydrin, dimethyl sulfate, acrylonitrile, benzyl chloride, allyl chloride, PCl_3, fluoride and most standard organic and inorganic chemicals.

PTC Organics, Inc.

The Industrial Phase-Transfer Catalysis Experts

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Phase-transfer catalysis really does reduce non-product output in multiple ways. Four of the many pollution prevention benefits of PTC include increasing yield, reducing excess reactants, conducting reactions under solvent-free PTC conditions and dramatically reducing reaction temperature. These benefits of PTC can often be absolutely crucial to reducing non-product output, BOD, COD, TDS, air emissions and other forms of pollution. Following are selected compelling examples of pollution prevention.

Examples of PTC in Real Pollution Prevention

DMSO Cyanation Versus PTC Cyanation

Pollution prevention benefits: major reductions in wastewater volume, BOD/COD, TDS, TKN, sulfur and cyanide

One of the classical examples that illustrates the ability of phase-transfer catalysis to reduce non-product output is the replacement of a DMSO cyanation process with a PTC-toluene cyanation process. In this paper,[1] dimethyl sulfoxide was originally chosen as the solvent due to its outstanding ability to co-dissolve and react inorganic sodium cyanide and an organic benzyl chloride derivative. One major problem with the DMSO process is that the workup requires multiple and lengthy aqueous washes to separate the DMSO from the product. These washes not only create large volumes of aqueous waste, but the wastewater contains much DMSO (= problem with COD/BOD), entrains organic product due to the presence of DMSO (= yield loss & non-product output) and contains the excess cyanide from the reaction (TDS and major safety hazard that combines highly toxic cyanide with the effective skin penetrating DMSO solvent). Moreover, the DMSO procedure reported using a 70 mole% excess of sodium cyanide and afforded only 81% isolated yield. Clearly, there were multiple reasons to improve upon the DMSO process.

When the DMSO cyanation process was replaced with a PTC-toluene cyanation process, the following compelling environmental advantages were achieved:

1. 85% less aqueous waste!
2. 19% higher isolated yield which in addition to the major cost advantage means that all that organic material becomes product instead of non-product output!
3. 95% reduction of cyanide waste (70 mole% excess reduced to 2 mole% excess), which has huge impact on COD/BOD and nitrogen content!
4. The totally non-recoverable DMSO solvent (non-product output) with its huge cyanide load in the large volume of waste water was eliminated! In contrast, the toluene in the PTC process was used in the next step of the process and was fully recoverable.

So, it doesn't matter if your plant is in Houston, Leverkusen or outside of Shanghai, the high aqueous waste load and composition (carbon, nitrogen, sulfur) resulting from a DMSO cyanation is very likely to be highly undesirable compared to the low aqueous waste load and composition of a PTC-toluene cyanation.

<u>Other Polar Aprotic Solvents</u>: While we are on the subject of nucleophilic substitutions performed in high boiling polar aprotic solvents, we should note that DMF (dimethyl formamide), NMP (N-methylpyrrolidinone) and DMAc (dimethyl acetamide) are likely to suffer from similar waste characteristics as DMSO. These solvents are almost always preferentially replaced by PTC conditions. PTC generates much less waste achieving higher yield with much lower excess of nucleophile and uses easily recoverable solvents.

Polycarbonate

Pollution prevention benefits: major reductions of excess phosgene usage, resulting byproducts and TDS

Polycarbonate is one of the largest volume commercial phase-transfer catalysis processes. Since the global capacity of polycarbonate is more than 1 million tons/year, even small improvements in the efficiency of raw material usage can have a huge positive impact on environmental performance. GE Plastics (now

[1] Dozeman, G.; Fiore, P.; Puls, T.; Walker, J.; *Org. Proc. Res. Dev.*, **1997**, *1*, 137

SABIC Innovative Plastics) patented a PTC process that significantly reduces the excess of one of the highly hazardous raw materials which results in greatly reduced air and water emissions as well as cost savings.[2]

Polycarbonate is produced by the phosgenation of bisphenol A in the presence of base (to form the nucleophilic phenoxide). Prior to the use of PTC, triethylamine was used as the catalyst to activate the carbon-chlorine bond of phosgene and the chloroformate intermediate toward the nucleophilic attack of the phenoxide. However, that activation also promotes hydrolysis of these water sensitive compounds. To quote from the patent, "in a phosgene hydrolysis rate study, it was found that at a triethylamine concentration of 6.64×10^{-3} M, triethylamine affected phosgene hydrolysis at a relative rate of greater than 200 compared to a reference value of 1 without catalyst."

The GE patent describes a PTC procedure which avoids the use of triethylamine as the catalyst. This is turn dramatically reduces hydrolysis to the point that the process impressively uses only 1 mole% excess of phosgene to achieve the desired yield, molecular weight and other polycarbonate properties. This represents a reduction of the excess phosgene by at least 90% relative to the procedures using triethylamine described in previous patents. The reduced levels of phosgene and chloroformate hydrolysis result in much lower waste load in wastewater and air emissions and greatly enhanced safety.

[2] Boden, E.; Phelps, P.; Ramsey, D.; Sybert, P.; Flowers, L.; Odle, R.; (General Electric) **1995**, US Patent 5,391,692

The conclusion is that it is possible to achieve extremely significant improvements in phosgene utilization by retrofitting the non-PTC process with PTC and avoiding hydrolysis of the water sensitive compounds. This represents breakthrough performance from environmental, safety and cost standpoints.

p-Nitrophenetole

Pollution prevention benefits: major reductions in chlorinated aromatic waste & TKN

p-Nitrophenetole is an intermediate for dyes and other compounds of industrial importance. Prior to PTC, a British patent reported an attractive 90% yield for p-nitrophenetole produced by the reaction of p-chloronitrobenzene with ethanol in the presence of sodium hydroxide. However, the other 10% was the undesirable byproduct 4,4'-dichloroazoxybenzene. Separation of this chlorinated azoxybenzene not only requires much expenditure but it constitutes an environmentally undesirable non-product output. Furthermore, the purity of the p-nitrophenetole is insufficient for most application fields, especially that of dyestuff intermediates. So, there are multiple strong driving forces to improve this process that include pollution prevention, cost reduction and product quality improvement.

A PTC process reported in a patent[3] uses an inexpensive phase-transfer catalyst and achieves a 95% isolated yield with impurity levels of under 0.1% for 4,4'-dichlorazoxybenzene, p-chloronitrobenzene, 4,4'-diethoxy-azoxybenzene and p-nitrophenol.

In summary, this patent describes the use of phase-transfer catalysis to avoid the formation of hazardous and corrosive chlorinated aromatic waste while increasing yield and quality of the product.

Transesterification

Pollution prevention benefits: major reduction in fuel to heat large volumes of reactant

The production of 50,000 tons/year of monoglycerides and diglycerides for use as emulsifiers is performed at a temperature of about 250^{o}C. The reaction is a base-catalyzed transesterification that requires such a high temperature for two reasons: [1] to partially solubilize polar glycerol in nonpolar triglyceride (vegetable oil) and [2] to promote the reaction of the hydrogen-bonded hydroxyls of glycerol with the ester functional group. The amount of energy required to heat 50,000 tons to 250^{o}C is obviously great.

Halpern et al of PTC Organics patented a phase-transfer catalysis process[4] that reduces the reaction temperature by 150^{o}C to only 100^{o}C! This represents huge savings in fuel which in turn reduces greenhouse gas generation. The concept is based on the ability of PTC to transfer small amounts of the glycerol monoanion into the organic phase where there is no hydrogen bonding that could reduce the nucleophilicity of the glycerol monoanion. In fact, the reaction actually proceeds at 60^{o}C. Veterans in this field find this to be remarkable.

One lesson from this patent is that there are many potential applications waiting to be discovered that can use phase-transfer catalysis to reduce the temperature of high-temperature non-PTC reactions. The greatest environmental benefit is saving on burning of fuel, but there are also usually concurrent benefits for reducing reaction temperature by 20^{o}-150^{o}C such as better selectivity, better color and reduced pressure.

Use of PTC for Converting Waste Anion into Value Added Product

Environmental benefits: major reduction of waste organic and inorganic anions in aqueous waste streams

The previous examples illustrated the use of PTC for pollution prevention. Sometimes, it is difficult or impossible to avoid the generation of waste anions. In many of these cases, it is possible to leverage the strengths of PTC to simultaneously extract and react waste anions from an aqueous stream and produce

[3] Schubert, H.; Baessler, K.; (Hoecsht) **1984**, US Patent 4,454,355
[4] Halpern, M.; Crick, D. (PTC Organics) **2004,** US Patent 6,833,463

value added products that can be sold at a profit while cleaning up the waste stream. Sometimes this is called reactive separation.

Joyce, Bielski and Halpern of Value Recovery (formerly PTC Value Recovery Inc.) patented a phase-transfer catalysis process[5] which extracts waste anions from dilute aqueous waste streams and reacts them with a variety of alkyl halides or acyl halides to produce saleable product. The many examples described in the patent include effective reactive separation for many problematic waste anions including cyanide, phenoxide, acrylate, iodide, sulfide and others.

What's Next? There are hundreds of examples of the use of phase-transfer catalysis that achieve pollution prevention, green chemistry and pollution treatment. There are hundreds more potential applications that are waiting to be identified and developed by the creative and technically competent readers of this article. So, the question is how can you identify opportunities at your company to use PTC technology to achieve breakthrough improvements in environmental performance and maybe even save your production plant from closure due to non-compliance. The following section will provide some easy guidelines for identifying pollution prevention opportunities using phase-transfer catalysis.

The 5-Minute PTC Pollution Prevention Test

Following is a list of simple questions which can help you decide if phase-transfer catalysis should be considered when your company is trying to address environmental problems/crises or trying to achieve environmental performance improvement goals.

Your company should, at a minimum, consider phase-transfer catalysis for performing any **nucleophilic substitution, nucleophilic condensation, base-promoted reaction, oxidation or reduction if the answer to any one or more of the following questions is 'yes.'** Please note that questions 1-7 deal with pollution prevention whereas questions 8-9 deal with pollution treatment.

1. **Compliance**: Has your company at any time in the past year exceeded or come close to exceeding permissible limits in your waste water for any of the following?
   a. BOD (biological oxygen demand)
   b. COD (chemical oxygen demand)
   c. TDS (total dissolved solids)
   d. TKN (total Kjeldahl nitrogen)
   e. TOC (total organic content)
   f. sulfur or other organic or inorganic content limits (excluding heavy metals which PTC can usually not help).
2. **Excess Reactant**: Does your process use an excess of 10 mole% or greater of any reactant (e.g., alkyl halide, acyl halide, phosphoryl halide, sulfonyl halide, epichlorohydrin, phosgene, cyanide, azide, other inorganic or organic nucleophile, hydrogen peroxide, borohydride)?
3. **Yield**: Does your process have a molar yield of less than 90%?
4. **Solvent**
   a. Does a solvent take up more than 50% of your reactor volume?
   b. Does your process use DMSO, DMF, NMP, DMAC or HMPA?
   c. Does your process use any other water-soluble organic solvent (e.g., acetonitrile, acetone, ethanol)?
   d. Does your process use a volatile solvent that boils under 85^{o}C?
   e. Does your process use a chlorinated hydrocarbon as a solvent (e.g., methylene chloride, chloroform, dichlorobenzene)?
   f. Does your process use at least one reactant that is a liquid?
   g. Are you performing a solvent exchange between steps of a multistep process?
5. **Temperature**: Does your reaction require a temperature of more than 100^{o}C?

Continued on page 10

[5] Joyce, P.; Bielski, R.; Halpern, M. (Value Recovery) **2005,** US Patent 6,846,856

Wittig, Darzens
Carbene Reactions

Thiocyanate
Hydroxide, Hydrolysis
Other nucleophilic aliphatic & aromatic substitutions

Oxidation
- Hypochlorite
- Hydrogen Peroxide
- Permanganate
- Other oxidizing agents
- Epoxidation & Chiral Epox.

Reduction
- Borohydride
- Hydrogenation

Transition metal co-catalysis
- Carbonylation
- Other reactions

Course Manual

Each participant receives a 192 page well organized PTC reference manual which includes not only the updated applications and theory, but also includes the guidelines for identification, evaluation and optimization of new PTC applications. The manual includes more than 200 organic PTC reactions and 13 exercises. Additional subjects are covered of great interest to industrial chemists such as catalyst separation and recycle, resource-efficient PTC R&D and future patentable PTC technologies.

Facility Requirements

The hosting company provides a training room which will include tables for participants to take notes, an overhead projector and screen and a flip chart or a writing board with markers.

Course Schedule

Training on the first day is from 8:45 to 4:30 and from 8:45 to 4:00 on the second day. 15 minute breaks at 10:30 and 2:30. Coffee and/or refreshments should be provided by company for the participants for 15 the minute breaks. Lunch breaks will be 12:00-1:15. Logistics should allow for participants to return promptly to the training at 1:15, preferably, lunch should be provided by the company to the participants on both days in or near the training room. **An optional highly effective third day for reviewing current projects under secrecy agreement** may be contracted at additional charge. Direct application of the course material to current projects typically results in immediate R&D performance achievements!

Fees (2007)

$18,000 up to 20 participants
$24,000 for 21-30 participants.

In addition, the hosting company will reimburse reasonable travel expenses for Dr. Halpern (airfare, hotel, meals, other transportation, etc.). These fees include training and manuals. Course dates will be reserved upon prepayment of $1,000, at least 30 days before travel. Balance of fees and travel expenses will be paid within 30 days of course completion. Note: The fee per participant for "public" courses is $1,495 (excluding lodging).

Ratings by Course Participants

Twenty eight in-house and 14 public courses "Practical Phase-Transfer Catalysis" were conducted in the US, UK, Germany, Switzerland, Austria, Sweden, Holland, Italy, Hungary and Israel since 1996 with reported customer impact of several million $€! Overall course evaluations score an average of 4.5 out of 5.0 and >98% answer "yes" in response to the questions: "Would you have performed past projects differently if you took this course earlier?" and "Would you recommend this course to your colleagues?" Highly satisfied in-house course customers include well known pharmaceutical, agrochemical, dye and other specialty and fine organic chemical manufacturers.

Inquiries & Reservations

For reservations and information contact Dr. Marc Halpern at tel +1 856-222-1146, fax +1 856-222-1124, by E-mail at save@ptcorganics.com or complete the form at www.ptcorganics.com/ContactUs.htm and type in Comments Section "In-House Course Inquiry".

6. **Water-Sensitive Compounds**: Do you need to use a water-sensitive compound in the presence of water?
7. **Base**: Does your process use a base that is or generates undesirable volatile or hazardous compounds, such as triethylamine, pyridine, sodium methylate, sodium amide, sodium metal?
8. **'Unavoidable' Air Emissions**: Does your process generate an undesirable volatile byproduct as a necessary part of the stoichiometry of the reaction (e.g., methyl bromide, ethyl chloride)?
9. **'Unavoidable' Anions in Wastewater**: Does your process generate an undesirable salt/anion as a necessary part of the stoichiometry of the reaction (e.g., cyanide, phenoxide, acrylate, iodide, sulfide, thiocyanate)?

If the answer to any one of these questions is 'yes,' you should really invest at least five minutes thinking about the possibility that phase-transfer catalysis can help improve your environmental performance. If your production plant is in danger of non-compliance or even shutdown, you almost have no choice but to determine for sure whether phase-transfer catalysis can help you solve the problem. The easiest and quickest way to evaluate whether PTC can help is to contact Marc Halpern PTC Organics by E-mail (save@ptcorganics.com) or telephone (+1-856-222-1146). We should be able to provide an estimate of the probability of success within 24 hours.

Summary

Phase-transfer catalysis is an extremely effective and cost-effective technology for improving environmental performance through pollution prevention, green chemistry and pollution treatment. PTC technology can help meet ever tightening environmental goals and maybe even help avoid the shutdown of a profitable production plant. If you think there is any chance that phase-transfer catalysis may be able to help your company improve environmental performance, especially pollution prevention, you should not hesitate to request a free estimate of the probability of success from the industrial PTC experts at PTC Organics.

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Directory of commercial suppliers for all kinds of phase-transfer catalysts:

- quaternary ammonium salts
- quaternary phosphonium salts
- polyethylene glycols, glymes and other ethers
- crown ethers
- high-temperature phase-transfer catalysts
- chiral phase-transfer catalysts
- ionic liquids

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