

Phase-Transfer Catalysis Communications

Increasing Plant Profits by Phase-Transfer Catalysis Retrofit

by Marc Halpern

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Summary: Enormous profit opportunity currently exists and is ready to be taken advantage of at hundreds of chemical manufacturing facilities by retrofitting existing processes with phase-transfer catalysis. The primary benefits which have been realized by chemical companies in recent years include:

- **Reduce Cycle Time**
(up to 50%; debottleneck plants)
- **Increase Yield**
(usually 5-10%; sometimes more; debottleneck plants)
- **Eliminate, Reduce or Replace Solvent**
- **Pollution Prevention**
by drastically reducing the volumes of waste streams and by converting more raw material into salable product
- **Enhance Safety**
by reducing usage of hazardous materials, using alternate less hazardous raw materials and/or controlling exotherms better
- **Reduce Raw Material Costs**
by using alternate raw materials or reducing charges of existing raw materials
- **Increase Selectivity**
ambident alkylation; minimizing hydrolysis; dozens of other crucial selectivity situations for organic chemicals and polymers

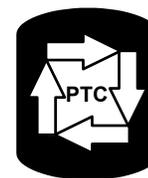
Challenges which were overcome when chemical companies actually successfully implemented PTC Retrofit in the plant related to the catalyst, process recertification and organizational resistance to change. More chemical companies would do better by focusing on using process chemistry departments to reduce variable costs (e.g., cost of manufacture) instead of focusing on reducing fixed costs (e.g., R&D headcount). Criteria are presented for identifying those plants which have great potential for gain from PTC Retrofit. The gains already reaped from PTC Retrofit are real. **Does your plant meet the criteria for PTC Retrofit?**

PTC Retrofit - Introduction

In the quest for improved profits, chemical companies have successfully implemented PTC Retrofit projects in real world operating plants and have achieved greatly reduced variable costs and improved plant operability. This article will describe (1) the benefits of PTC Retrofit, (2) how to determine if your plant is a good PTC Retrofit candidate and (3) provide practical information to help you implement PTC Retrofit and increase your company's profits. *continued on page 2*

Breakthrough Process Development

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Relating Plant Variable Cost to PTC Theory

Although there are a multitude of reasons why PTC helps plant operations, the major compelling underlying factor is **REDUCED SOLVATION**. The inherent nature of PTC systems provides the opportunity to bring reactants together in an environment in which solvation barriers are reduced. When the solvation of a nucleophilic reactant, base or oxidant is reduced, its nucleophilicity, basicity or activity is greatly enhanced. **When reactivity is increased, reaction cycle time is reduced and/or yield is enhanced.** Cycle time reduction and/or yield improvement are two major components of plant profitability. Alternatively, one can maintain the reaction time constant and reduce temperature to achieve **greater selectivity** and minimize noncatalyzed side reactions. Improved selectivity can sometimes be the difference between a process achieving commercial viability or not. In some cases, improved selectivity can eliminate costly separation steps if the improved selectivity in the reaction itself results in meeting customer specification without a separation step (recrystallization, distillation, etc.). **Pollution Prevention** is achieved by eliminating or replacing undesirable solvents and by drastically reducing waste for every increment of yield increase or cycle time reduction. All of the above benefits result in some fashion from reduced solvation, which is one of PTC's strengths as a synthetically useful process technology. In addition, PTC provides many opportunities for replacing or reducing the usage of expensive, hard to handle or hazardous raw materials. Indeed, there are many highly desirable, implementable and pragmatic driving forces for considering and executing PTC Retrofit and they relate directly to the fundamental foundations of PTC technology.

How Does a PTC Retrofit Project Typically Get Started in a Real Chemical Company

The PTC Retrofit project typically begins when a process chemist, a process engineer, a plant manager or a marketing manager recognizes the opportunity to proactively improve plant productivity, quality, safety or environmental performance. Sometimes, the improvement in any or all of these areas is forced upon the plant by external market, government or community forces.

At this point, as usual, it is the knowledgeable and pragmatic process chemist or process engineer who initiates the idea (and possibly skunkworks) to use phase-transfer catalysis to achieve the lofty corporate goal or meet the imposed corporate need. This individual now needs to sell the idea to colleagues and managers. The following discussion will illustrate the factors involved in successfully initiating and implementing the PTC Retrofit.

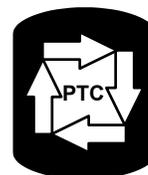
An Example of a PTC Retrofit

Following is an example of a PTC Retrofit presented as an exercise at the Short Course "Phase-Transfer Catalysis In Industry."¹ The process includes two consecutive reactions,

¹ "Phase-Transfer Catalysis In Industry," PTC Interface Inc., Starks, C.; Liotta, C.; Halpern, M.; 1990-1995

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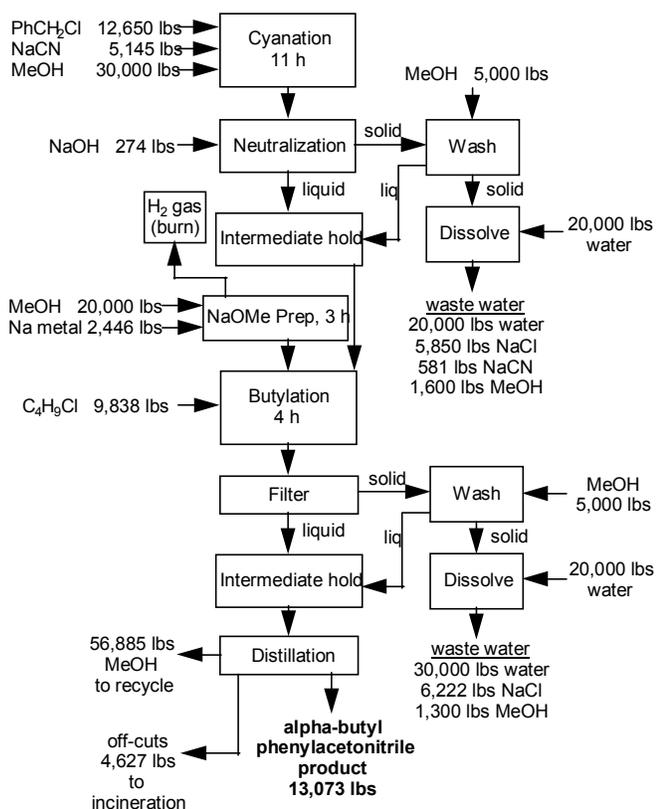
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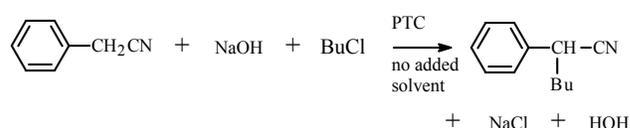
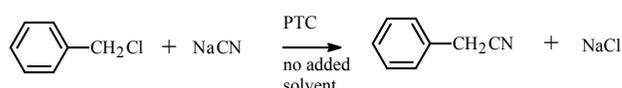
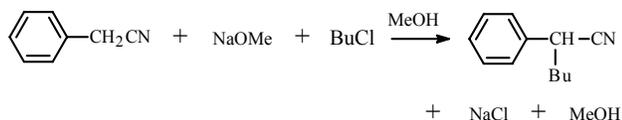
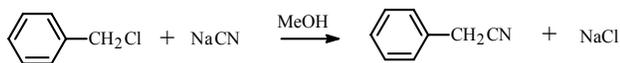
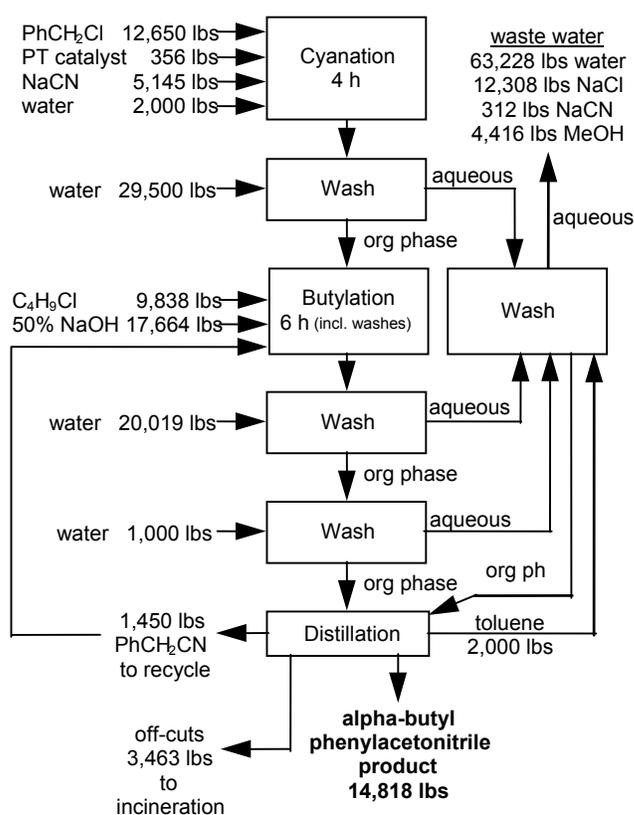
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The Pre-PTC Process: Cyanation & C-Alkylation



The PTC Retrofit Process: Cyanation & C-Alkylation



both of which are excellent candidates for PTC Retrofit. In the first step, benzyl chloride is converted to phenylacetone nitrile (benzyl cyanide) by nucleophilic attack of cyanide. The subsequent reaction is the C-alkylation of the deactivated methylene group (being benzyl and α to the nitrile) by butyl chloride using sodium methoxide as the base. PTC excels in cyanation reactions. In addition, base promoted reactions constitute the largest class of PTC commercial applications. In fact, replacement of organic bases, such as methoxide, with NaOH and PTC, is one of the best targets for PTC Retrofit (take note if you are using alkoxides, sodamide, hydride or even LDA!).

The "conventional" non-PTC cyanation uses methanol as a co-solvent to force the inorganic cyanide and the benzyl chloride to come in contact. The methanol forms strong hydrogen bonds with the cyanide and greatly reduces its nucleophilicity.

In the PTC cyanation, there is no methanol. There is a much smaller quantity of water, but the water is present as a second immiscible phase. A small amount of water of hydration accompanies the cyanide into the organic phase, but overall, the solvation of the cyanide in the PTC process is much smaller than the solvation of the cyanide in the "conventional" non-PTC process. **The result is that the cycle time of the cyanation reaction only, is reduced by 64% (!)** due to the PTC Retrofit. In addition, the cyanation was converted to a "solvent-free" process (no added solvent). Thus, emissions and recovery of the volatile methanol (otherwise requiring a high energy consuming chiller/scrubber?) were eliminated!

According to the Halpern pKa Guidelines for the evaluation and optimization of new PTC applications,^{2,3} the optimal catalyst for

² Halpern, M.; PTC Comm., 1995, 1, 1

reactivity of cyanation is likely to be organophilic. As such, the catalyst remains in the organic phase and is ready to catalyze the next step.

In order to C-alkylate phenylacetonitrile, a base is required to deprotonate the substrate. The pre-PTC process used sodium methoxide. The methoxide was prepared by reacting the very hazardous and difficult to handle sodium metal, which liberated explosive hydrogen gas in the process. The cost and safety aspects of making sodium methoxide were obviously unfavorable. In contrast, **the PTC Retrofit process replaced the sodium methoxide with the inexpensive and readily available NaOH, which liberates water as the by product, and totally avoids the generation of hydrogen gas and handling metallic sodium.** Safety was greatly enhanced, the cost of the base was substantially lowered and the unit operations, time and plant operability issues associated with NaOMe production were eliminated, all due to the PTC Retrofit. The second step, as the first step, is a solvent-free process (i.e., no added solvent). Again, there is less opportunity for methanol emissions.

The key additional tradeoffs for using PTC for the C-alkylation are an increase in the cycle time of the C-alkylation (6 h includes wash operations; may have been optimized further), the introduction of a toluene wash and an increase in the quantity of water used.

In this case, the final distillation of the product, which was already in place for the pre-PTC process, was sufficient to separate the catalyst from the product, thus no extra capital was required for catalyst separation.

Since by-products were minimized in the PTC Retrofit process, a distillation cut of the intermediate phenylacetonitrile was able to be recovered and recycled. This recycle stream was responsible for an overall **10% yield increase** relative to the pre-PTC process.

This particular PTC Retrofit process offered multiple attractive and highly significant benefits in all of the following crucial plant parameters: reduced cycle time, increased yield, safety and environmental performance! One cannot expect to obtain all of these simultaneous advantages from each PTC Retrofit, but this example does illustrate what can be achieved.

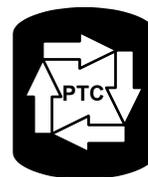
By the way, according to the Halpern pKa Guidelines, the C-alkylation would be predicted to be best performed using an accessible quat, whereas the cyanation would work best with an organophilic quat. In this two step process, more development work may have been warranted to determine if one compromised quat structure was best or possibly two quats should have been used to optimize the cycle time of each reaction separately.

A summary of the comparison between the "conventional" process and the PTC Retrofit process is shown in Table 1.

³ Starks, C.; Liotta, C.; Halpern, M.; "Phase-Transfer Catalysis: Fundamentals, Applications and Industrial Perspectives," Chapman & Hall, New York 1994

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Table 1: Key Benefits of PTC Retrofit Example - Comparison of Pre-PTC and PTC Retrofit Processes

| KEY BENEFITS | | | |
|------------------------------|--|-----------------------------|--------------------------------------|
| | <u>Methanol Process</u> | <u>PTC Retrofit Process</u> | <u>Comments</u> |
| Overall Yield | 75.3% | 85.3% | 10% yield advantage |
| Total Cycle Time | 18 h | 10 h | 44% cycle time reduction |
| Total Variable Cost | \$3.08/lb | \$2.19 | 29% cost reduction |
| Plant Capacity | 5.8 MM lb/yr | 11.8 MM lb/yr | 105% capacity increase |
| Base | Na metal/MeOH (H ₂ by prod) | NaOH (water by prod) | major safety improvement |
| Reaction Solvent | methanol | no added reaction solvent | "solvent-free" (toluene wash) |
| TRADE OFFS | | | |
| | <u>Methanol Process</u> | <u>PTC Retrofit Process</u> | <u>Comments</u> |
| Catalyst | none | 2.8 wt% organophilic quat | represents 2.3% of total |
| Catalyst Separation | none | distillation of product | variable cost |
| OTHER ASPECTS | | | |
| | <u>Methanol Process</u> | <u>PTC Retrofit Process</u> | <u>Comments</u> |
| Distillation (incl. product) | 5.8 lb/lb product | 1.5 lb/lb product | difference mostly MeOH solv |
| waste water generated | | | |
| aqueous | 5.0 lb/lb product | 5.3 lb/lb product | |
| organic | 0.22 lb/lb product | 0.30 lb/lb product | |
| waste organic generated | 0.35 lb/lb product | 0.20 lb/lb product | |
| cyanide in waste stream | 0.04 lb/lb product | 0.02 lb/lb product | |

Benefits of PTC Retrofit

Reducing Cycle Time:

In the industrial world of process chemistry, PTC Retrofit is often considered in order to debottleneck a plant which has already has high yield, just too low a nameplate capacity. In addition, debottlenecking a multi-purpose plant also provides greater flexibility for producing other products and/or scheduling campaigns in that plant. PTC provides this benefit by reducing cycle time.

The capital investment required to expand a plant is usually large. Even if a company is willing to invest capital, the engineering time and the additional construction time is very significant and the market timing window of opportunity may diminish. In addition, the nature of fluctuating markets for certain products introduces an element of risk and uncertainty regarding the long term utilization and justification of the plant expansion. For all of these reasons, plant managers and/or executives in charge of profit and loss usually request (or hand down an edict) to debottleneck

the plant using some clever process chemistry or process engineering trick. If you are an experienced process chemist or process engineer, you probably are not only familiar with this situation, you may have built your career on such heroic improvements.

A PTC Retrofit offers the opportunity to reduce cycle time, thus debottlenecking the plant, especially if your reaction is listed in Table 3. As will be discussed below, this plant expansion/debottlenecking is likely to be low-capital or even capital-free. Moreover, in order to exploit a market opportunity in a timely manner, an accelerated PTC Retrofit project could be implemented in a fraction of the time that a plant expansion would require. The dream of debottlenecking the plant may well be worth a development program (or call PTC Organics at 800-PTC-7118 or +1 856-222-1146 for process improvement by the Industrial PTC Experts). The author has personally been involved in debottlenecking plants which added more than \$10 million/year incremental profit implemented within several months of conceptualization.

Increasing Yield:

Even though most industrial processes already enjoy high yield, some industrial processes can actually be run profitably at yields under 85%. Market demand, profit margins and other factors can justify these processes. If your commercial reaction is within a reaction family listed in Table 3, there is a non-negligible possibility that high to very high yield can be obtained by PTC retrofit. How much profit could your plant add if it enjoyed 10% yield increase?

Sometimes, cost of manufacture is only a small component of the final sales price (e.g., certain high value added specialty chemicals). In such cases, reducing cycle time or increasing yield may be considered, at first glance, to be of limited value. However, when a surge in market demand occurs and extra capacity is needed, PTC Retrofit should be considered as a method for increasing plant capacity.

For large volume plants, sometimes a 1-3% yield increase may be large enough to justify the entire R&D budget for years. The competitiveness of some of the largest plants may be maintained on a fraction of a percent of yield. It should be noted that there are several plants which use PTC to produce products in the range of 100 million to one billion pounds per year. The process chemists and engineers certainly had yield in mind when they initiated and executed the PTC development project.

Eliminating, Reducing or Replacing Solvent:

An exhaustive review of the academic PTC literature from the 1970's and early 80's would reveal methylene chloride to be the solvent of choice for many PTC syntheses. In the 1990's and beyond, solvents like methylene chloride are being publicly reported to government agencies and their emissions have been dropping. Some companies issue press releases to announce significant reduction in emissions and solvent usage of certain solvents, such as methylene chloride. One of the advantages of PTC is great **flexibility** to avoid undesirable solvents and choose a reaction solvent based on any combination of factors such as regulatory requirements, boiling point, polarity (non-polarity), recovery, toxicity, flammability, cost, availability, etc. Today, PTC Retrofits are helping companies eliminate solvents such as methylene chloride, DMSO, NMP, DMF and others. A solvent gaining popularity in commercial PTC processes is xylene. It is a recoverable, low emissions solvent which affords good reactivity in most PTC systems in which a solvent is needed. A discussion of choosing a solvent for industrial PTC processes is given in reference 3.

One of the areas of PTC which has gained tremendous momentum in the academic literature as well as in industry is "**solvent-free PTC.**" The example described at the beginning of this article illustrates solvent-free PTC. In that case, the starting material and product were liquids. Since PTC works well in a very wide range of polarities of organic phases, then typical organic products or reactants can serve as the reaction solvent. If only one of the reactants or the product is a liquid at the reaction temperature, then *it* can be used as the solvent. For example, if only the product is a

liquid, then the reaction mixture charged to the reactor can be spiked with some product. This will create a small organic phase (and possibly help fluidity) in which the reaction can take place. The liquid organic phase will then "grow" as the reaction proceeds. Alternatively, if the reaction uses the excess of a liquid reactant, such as an alkylating agent, *it* can be used as the solvent. If the alkylating agent is used as the solvent, and the reaction is intrinsic reaction rate limited,² the reaction may enjoy reduced cycle time since the concentration of that reactant will contribute greatly to the rate of "second order kinetics" reaction. Recovering the excess alkylating agent may require an additional unit operation such as distillation. However, sometimes the pre-PTC process may already have a recovery system for the alkylating agent (for cost or emissions reasons). In such a case, extra capital will not be required to recover the reagent.

In general, though not always, PTC Retrofit processes will **require less solvent** than pre-PTC processes. This is because the reaction only needs some organic phase to commence and therefore, the quantity of solvent (or "solvent-free" reactant) can be chosen to meet fluidity requirements. So, if you can use less solvent, you can fill the reactor with more reactants and obtain more product. This is yet another method to debottleneck the plant.

During a recent exploratory PTC Retrofit conversation with a plant manager, he prioritized his needs by saying that he already had high yield and he preferred to reduce cycle time, but secondarily, it would be nice to eliminate the polar solvent from his process. I responded by saying that a non-polar solvent might actually be the best solvent for the PTC Retrofit process to reduce cycle time.

Some plants can realize enormous gains in plant capacity if the PTC Retrofit provides simultaneous cycle time reduction, increased yield and replacing reactor volume with reactants instead of solvent.

Pollution Prevention:

Pollution prevention is the rapidly becoming the preferred approach and replacing *pollution treatment* as a focus in process development. If you don't generate "non-product output" then you don't have to treat it. PTC Retrofit enhances pollution prevention through increased yield, reduced solvent and by using alternate raw materials.

When PTC Retrofit results in increased yield, the impact on pollution prevention is very great. If, for example, a PTC Retrofit increases a yield from 90% to 94% then the non-product output due to one of the starting materials alone, is reduced from 10% to 6%. This represents a 40% reduction in non-product output of that raw material. Moreover, the costs for treating the 10% yield loss have probably been reduced by 40% and more salable product was produced.

When a PTC Retrofit results in the elimination, reduction or replacement of solvent, emissions and other solvent related issues are often dramatically reduced.

Table 2: Process Triggers for Considering PTC Retrofit of Existing Plant Processes

- Using NaOMe, NaOEt, KOBu^t, NaNH₂, NaH or LDA as base?
- Using DMSO, DMF, NMP or a halogenated hydrocarbon as solvent?
- Reaction yields < 85%?
- Desire to reduce cycle time or increase plant capacity?
- Desire to eliminate, reduce or replace solvent?
- Desire to reduce emissions?
- Using large excess of reactant to achieve reactivity or selectivity?

Sometimes, the driving force for the PTC Retrofit is to use an alternate raw material. For example, if a transition metal, used in an oxidation, either as a reagent or as a catalyst, is replaced by using PTC and hypochlorite, then metal usage (such as the heavily regulated chromium from dichromate) can be eliminated. The use of NaOH in place of sodium methoxide, shown in the example, generates water as the by-product (environmentally acceptable) instead of methanol. Other TPCA chemicals can be eliminated or reduced by PTC Retrofit.

Enhancing Safety:

PTC Retrofit can enhance safety controlling exotherms and by reducing the usage of hazardous chemicals.

Many reactions are exothermic and pose safety challenges to engineers. PTC Retrofit can exploit two factors to control exotherms. These factors are catalyst level and agitation.

Agitation: The very nature of PTC systems is that they contain two (or more) phases and the reactants are fully or partially separated by the phases. Even when the catalyst is present in a PTC system, if there is no agitation, reactivity is usually very low due to mass transfer limitations of the reactant between the phases. As agitation is increased, from very low efficiency to higher agitation efficiency, the mass transfer will increase accordingly and the reaction rate will increase until it becomes intrinsic reaction rate limited. Since exothermicity depends on reaction rate, as long as the reaction rate can be controlled by agitation in the transfer rate limited regime (take care with volatile solvents), then exothermicity can be controlled by staying in that regime.

Catalyst Level: If one of the reactants is not soluble by itself in the reaction phase, then the amount of catalyst will determine how much transferred reactant is in the reacting

phase. If the reaction is intrinsic reaction rate limited, then the rate usually is first order in reactant. Thus, the amount of catalyst will control the reaction rate by controlling the reactant concentration in the reaction phase. Since the reaction rate of an exothermic reaction determines how much heat is generated, then the catalyst level can be used to attenuate exothermicity.

Catalyst level and agitation can be used together to control exotherms such that the rate of heat generation is designed to be well within the ability of the reactor's cooling system to remove heat.

Reducing Raw Material Costs:

PTC Retrofit can reduce raw material costs by using less raw materials or by using alternate raw materials.

PTC Retrofit often results in less usage of raw materials. For example, when inorganic nucleophiles are reacting with organic substrates under PTC conditions, the reduced hydration results in higher nucleophilicity of the anion. Often, this results in reducing the amount of excess salt of the nucleophile required to be charged to the reactor. The two phase nature of PTC systems also protects sensitive secondary reactants from undesired reactants not located in the organic phase. For example, if one desires to perform an alkylation with dimethyl sulfate or an acylation with benzoyl chloride in the presence of strong aqueous base, one would usually have to use a large excess of the alkylating or acylating agent. Under PTC conditions, one can choose an organic solvent (possibly the substrate itself) which is highly immiscible with water, but is an excellent solvent for the alkylating or acylating agent. In such cases, hydrolysis is minimized and the alkylating or acylating agent is saved and ready for reaction (with enhanced reactivity) when the nucleophilic reagent is ready in the organic phase.

Table 3: Reaction Triggers for Considering PTC Retrofit of Existing Plant Processes

- Etherification of phenols
- Etherification of alcohols
- C-Alkylation
- N-Alkylation
- S-Alkylation
- Aldol Condensation
- Polymerization using Etherification or Esterification
- Dehydrohalogenation
- Michael Addition
- Cyanation
- Halide Exchange (F⁻, Cl⁻, Br⁻, I⁻)
- Esterification/Transesterification
- Oxidation (H₂O₂, O₂, ClO⁻, MnO₄⁻)

Other reactions amenable to PTC Retrofit include: Nucleophilic Aliphatic or Aromatic Substitution using N₃⁻, SCN⁻, NO₂⁻, SO₃⁻², etc., Wittig, Carbene Reactions, Thiophosphorylation, Darzens Reaction, Carbonylation and other transition metal catalyzed reactions. These reactions can also be performed to modify polymers.

Many (though not all) alkylations and acylations are performed with stoichiometric or near stoichiometric quantities of alkylating or acylating agents! Reducing the excess of these reagents, for cost or safety reasons, can be a strong driving force for PTC Retrofit.

As in the example above, using alternate raw materials can reduce the cost of those raw materials. One of the most common and advantageous applications of PTC Retrofit is using NaOH with a phase-transfer catalyst and non-polar solvent to replace classic organic bases.

Increasing Selectivity:

Hundreds of examples have been published which use PTC to enhance selectivity. Many examples may be found in reference 3. The proliferation of PTC applications for enhancing selectivity is very understandable. The more handles one has to affect relative reaction rates, the more selectivity is achieved. PTC conditions offer more handles than conventional systems. In order of importance they are:

a) Hydration

Hydration dramatically affects reactivity. Hydration affects reactivity of different nucleophiles, bases and oxidants to varying degrees. The variation in effect on different reactants leads to altered selectivity. Hydration levels in the organic phase can be controlled in PTC systems. Tuning alkylation ratios of ambident anions is an example of altering selectivity by varying hydration.

b) Temperature

As noted earlier, reduced hydration in PTC systems can be utilized to lower reaction temperature. Lower reaction temperature is very often used in PTC as well in conventional chemistry to alter selectivity, due to differential dependencies of competing reaction rates on temperature. For example, PTC Retrofit can be used to reduce tar formation or color by reducing temperature.

c) Catalyst Structure

Since the catalyst is usually in close proximity to the substrate during the product-determining step, it affects selectivity. The catalyst is usually not a passive observer since it is cationic or very polar and it generally has significant interaction with the anionic nucleophile or polar substrate. The cation-anion interaction has been used to significantly alter alkylation ratios of ambident anions or for chiral PTC syntheses.

d) Solvent

Solvation by organic solvents can be utilized in PTC systems similar to conventional systems to alter selectivity. A wider variety of polar and non-polarsolvents can be used in PTC systems. For example, most conventional nucleophilic substitutions cannot be performed in toluene (not polar enough to solubilize most anionic nucleophiles), but can be readily performed in toluene using PTC. Therefore, PTC offers more control of selectivity than conventional systems, when choice of solvent can affect selectivity.

e) Agitation

As discussed above, agitation can significantly affect side reactions in PTC systems. For example, reactions with benzoyl chloride are best performed at the transition regime between transfer rate limitation and intrinsic reaction rate limitation, since excessive agitation will selectively enhance non-catalyzed hydrolysis. Hydrolysis by-products can lead to further undesired side reactions. Agitation can also affect the relative rates of two competing PTC reactions if one is transfer rate limited and the other is intrinsic reaction rate limited. This trick may be enough to justify a PTC Retrofit.

f) Catalyst Level

It is possible to simulate high dilution in cases where it is needed to obtain selectivity. If the anion is water soluble only, and if a low level of catalyst is used, then only a low level of anion will be transferred into the organic phase. Even though the total reactor may be charged with stoichiometric quantities of reactants, the anions in the organic phase (reaction phase) may be effectively swimming in an excess of substrate due to the restriction resulting from the limiting catalyst level. This is useful, for example, in the selective preparation of oligomers with > 99% electrophilic end groups for use as a reactant for block copolymers.

g) Order of Addition

O'Donnell and coworkers found that order of addition dramatically affected the enantiomeric excess of a chiral reaction in a chiral PTC reaction.⁴

h) Choice of Reactant

If one is performing alkylation of ambident anions, one can often choose to use a different alkylating agent than when using conventional methods. Different alkylating agents afford different alkylation ratios.

Increasing selectivity can be a big profit generator. SPC and other quality methods track parameters to measure product quality. Assay and/or impurity levels are common measures for organic chemicals. Charting these parameters, followed by process tweaking are popular methods for continuous improvement. What if you could significantly reduce a major impurity by PTC Retrofit so that it was "in spec" all of the time? How much off-spec material could you avoid? How many added late shipment could be avoided by being in-spec a greater percentage of the time? Could you avoid a costly recrystallization previously required to remove a key impurity by implementing a successful PTC Retrofit? These are important selectivity-profit questions.

Chemical Companies Should Focus on Reducing Variable Costs Instead of Fixed Costs

The staggering multitude of benefits described above for implementing PTC Retrofit in a plant should be overwhelming. Millions of dollars of incremental profit have been realized by chemical companies which implemented PTC Retrofits. These companies were in the "cost cutting" mode. Millions of dollars of incremental profit are waiting to happen in hundreds of

⁴ O'Donnell, M.; Esikova, I.; Fang, Z.; Ma, X.; Mi, A.; Wu, S.; Zhou, C.; Pacificchem 95 Meeting, Hawaii, 1995, ACS Symposium Series #659, 1997, Halpern, M. editor

organic chemical and polymer plants around the world. Most of the companies and plants waiting for PTC Retrofit are not aware of it and are also in the "cost cutting" mode. One executive remarked "we are cutting costs...we can't afford to examine a PTC Retrofit." Depending on the potential gain to the company, could the executive afford *not* to evaluate the PTC Retrofit? The answer obviously depends on the net benefit.

Reductions of fixed costs have received much public attention. However, gains resulting from reducing variable costs, achieved by retrofitting processes with better technology, are generally only published internally within an organization due to the proprietary nature of the gains. The exception to this is when environmental gains are achieved, which are often published for public relations advantage.

Chemical companies continue through the mid-90's with "fixed cost reduction" which more often than not means "headcount reduction." R&D departments have not escaped the fixed cost reductions. It is true that all fixed cost reductions, involving R&D or not, reduce the ability of the organization to function in the short term. However, the combination of PTC Retrofit and gainfully employed R&D departments can lead to enormous "variable cost reductions" (i.e., reducing cost of manufacture). Moreover, these variable cost reductions can often be achieved within the attention span of top executives. So, let's use the politically correct cost reduction argument to champion PTC Retrofit.

Triggers for Considering PTC Retrofit of Existing Plant Processes

There are very many situations which warrant PTC Retrofit. Each opportunity is unique and has unique needs and a unique setting. Within the variety of opportunities which should "trigger" the PTC Retrofit project within a chemical company, several compelling triggers stand out. These triggers are summarized in Table 2.

Does your company or plant meet any of the PTC Retrofit triggers shown in Table 2? Does your company or plant meet *all* of the PTC Retrofit triggers shown in Table 3? If so, cost cutting stardom may be in your future. Now let's identify which reactions are best suited for PTC Retrofit.

Reactions Amenable to PTC Retrofit

Although many reactions are amenable to PTC conditions, some reactions are particularly suited to benefit from PTC Retrofit. For example, it would be difficult to think of reasons to perform the etherification (O-alkylation) of phenols under basic conditions other than using PTC. Or in the case of S-alkylation, thiolates are easily transferred by PTC to the organic phase (due to their high polarizability and organophilicity) and once they are in the organic phase, they are naturally excellent nucleophiles.

The most outstanding PTC Retrofit opportunities are generally, though not exclusively, for base promoted reactions and nucleophilic substitutions.

Challenges to be Overcome to Successfully Implement a PTC Retrofit

It is important to be aware of and take into account the tradeoffs and additional costs involved in implementing a PTC Retrofit. In all cases the additional costs must be weighed against the net incremental benefit. Sometimes the net incremental benefit is measurable, as in the case of trying to achieve a 1% yield increase or a 4% cycle time reduction for the production of a large volume commodity chemical. In other cases, it may be difficult to quantify the net incremental benefit, such as implementing a PTC retrofit to control the exotherm of a reaction which had an erratic excursion history due to exothermicity.

Following are some of the issues which must be properly addressed. Once these issues are accounted for, the viability of the PTC Retrofit will be more obvious.

Catalyst Separation:

Phase-transfer catalysts are usually separated from the product by extraction or distillation.

When distillation of the product is already included in the existing pre-PTC process, PTC Retrofit may be capital-free. In such cases, the catalyst remains in the residue (bottoms) which is generally incinerated or repurified. Small quantities of catalyst decomposition products are removed in the off-cut(s) of the distillation. When required, the catalyst structure can almost always be "designed" (i.e., a commercially available catalyst can be found) such that if there are any decomposition products they do not co-distill with the desired product.

When the product of the pre-PTC process is not distilled, then the catalyst in the PTC Retrofit process is usually separated from the product by extraction. The extraction adds cost to the process because it is a unit operation which requires time and equipment. The extraction will not increase cycle time if it is not the bottleneck, but it adds complexity to the process and every added unit operation has the potential of affecting plant operability. The equipment required for the extraction is generally a simple tank outfitted with an agitator, a bottom drain and a sight glass. If the reaction to be retrofitted with PTC is one of several unit operations and is not the plant bottleneck, then the reactor itself is often used as the extraction vessel/separator. If a separate vessel is required, most plant sites can resurrect a vessel "from the graveyard" of vessels that accumulate in an obscure corner of the plant. Regardless of whether an old vessel is reinstalled or whether a new separator is purchased, some engineering/maintenance time will need to be allocated. The total cost of the separator should be weighed against the net benefit from the PTC Retrofit. Remember, the PTC Retrofit would have not been considered in the first place unless it held promise for very significant improvement in productivity, quality, operability, safety and/or environmental performance.

Catalyst Cost:

Another cost which must be offset by the net benefit of the PTC Retrofit is the cost of the catalyst. As a rule of thumb, the cost

of the catalyst is 0.1-5% of the total variable cost and is often in the 1-2% range. Obviously, the degree to which catalyst cost is a significant factor in determining viability, varies greatly from situation to situation. Due to the situational nature of the benefit, one should not rule out catalysts at the outset based on their cost per kg. There are even known cases in which crown ether is more cost effective than a common ammonium quat. It is recommended that catalysts be evaluated on performance without prejudice during the screening stages of the PTC Retrofit project. A later stage of economic evaluation, is a more appropriate time to compare the relative cost of the catalyst to the net incremental benefit. Again, this evaluation within a PTC Retrofit project for optimizing a process for a commodity chemical is likely to be different than that for increasing the selectivity for a pharmaceutical intermediate and yet again different for coping with mandatory emissions reduction regulations by implementing a PTC Retrofit.

Recertification of Process:

Certain chemical processes may be subject to recertification if the process is changed. Examples include many pharmaceutical processes and processes for performance chemicals such as photographic chemicals, fragrances and polymers. Recertification is usually required when there is the possibility that the impurity profile may change ("purer" is not necessarily "better"). The expense of recertification can be significant and is sometimes prohibitive. Nevertheless, pharmaceutical processes have been retrofitted in such cases where improved selectivity was anticipated to become a requirement or in cases where the modified reaction was far enough back in the synthetic scheme that the impurity profile was unaffected by the process change. Even when recertification is required, the consistency of an impurity profile may be assured due to the nature of intermediate purification steps, especially if multiple distillations and/or recrystallizations exist in the existing pre-PTC process. Again, the recertification effort, as significant as it may be, must be weighed against the benefit of the PTC Retrofit, as significant as it may be.

Other Process Issues:

All chemical process development efforts address scale up issues. These issues include agitation, heat transfer, potential solids handling, potential rag layers during separation, potentially complex kinetics and potential need for additional storage. Following is a brief discussion of these issues.

As noted above, agitation may be an advantage to be utilized to control reactivity or selectivity. Nevertheless, the agitation requirements of a PTC Retrofit system are likely to be different than for the pre-PTC system and need to be reviewed. Likewise, the heat transfer properties of the two phase PTC system are likely to be different than those of the pre-PTC system (usually with a different solvent) and need to be accounted for. One must be particularly aware of the added reactivity which catalytic systems induce. Added reactivity and may result in added requirement for heat removal to control exotherms. Of course, as noted above, PTC offers the unique advantage of using agitation and catalyst level as good handles for controlling reactivity and the resulting heat generation.

Sometimes, there is great advantage to using solid-liquid PTC conditions to enhance reactivity, selectivity and/or reactor volume usage. In such cases, solids handling needs to be addressed.

The choice of catalyst is one of the most important factors to be evaluated in a new PTC system. The author is currently creating an advanced guideline for choosing catalyst which integrates the combination of reactivity, catalyst separability and catalyst stability. In most cases, one needs to be careful in choosing a catalyst which minimizes emulsions. Improper choice of catalyst can also result in nuisance rag layers during separation, if extraction is used as the method of catalyst separation.

Complex kinetics can sometimes add difficulty to predicting heat transfer and cycle time.

A modified process may require additional storage tanks due to change in the identity of the reactants, solvent or for the catalyst. Sometimes, the modified process will require less or replacement of storage tanks, especially if solvents are replaced or eliminated or if undesirable raw materials are substituted by more favorable raw materials.

Some or all of the above process issues may not be required to be addressed in every PTC Retrofit. It is always prudent to be aware of the issues in a proper evaluation. Note that the above discussion does not cover every possible situation and therefore, cannot be comprehensive. In all cases, one must always take proper safety precautions and perform the proper safety and environmental evaluations when performing chemical reactions and processes on any scale, including phase-transfer catalysis reactions and processes.

Resistance to Change (Individual and Organizational):

(To Retrofit or Not To Retrofit...That Is The Question!)

It is often said that chemical companies and onstream plants are resistant to change. Let's face it, the performance of production staff is often rated according to the quantity and consistency (not necessarily equivalent to quality) of product produced in a given period of time. Change represents short term risk. Of course, lack of change represents long term risk, due to competition. In reality, almost every existing chemical plant has not only undergone and survived many *intentional* changes, they have actually benefited from them. In addition, in enlightened organizations, one component of the performance rating of production staff may often be "continuous improvement." It is within the push-pull of *resistance to change* versus *continuous improvement* that the decision to proceed with a PTC Retrofit project is made or broken.

The question of PTC Retrofit should depend primarily on two factors: (1) what is(are) the *net* benefit(s) of the PTC Retrofit? and (2) is the PTC Retrofit technically achievable?

To answer the first question, in the name of continuous improvement, it is worthwhile investing 5-30 minutes doing a back-of-the-envelope calculation to see if the PTC Retrofit is worthwhile considering. Perform the mental exercise of

disregarding development constraints and list the specific and tangible benefits your plant could realize from a PTC retrofit. If the potential savings are hundreds of thousands or millions of dollars, or substantial pollution prevention or compliance with a new regulation can be achieved, then the return on investment of the PTC retrofit is very likely to be quite high. Management should then have large incentive for initiating or authorizing the PTC Retrofit project. Call PTC Organics (+1 856-222-1146) to initiate the PTC Cost Savings Program.

Once it is established that the benefits of the PTC Retrofit are significant (or even organizationally irresistible!), the race for profit should begin and the PTC Retrofit project should commence. Industrial process development departments are very effective in designing and executing process feasibility studies. Which raises the next cost to be addressed.

Development Cost:

Effective Utilization of In-House Resource and Expertise to Achieve Rapid and Effective PTC Retrofit

The proven ingenuity of the process chemists (see editorial: "The Pride of the Process Chemist" in this issue) and process engineers is the key to innovating ideas and reaching firm conclusions about their implementation. The process chemists and engineers are experts in the specific chemistry under evaluation for improvement. These individuals are the most likely to be the initiators, and heroes, of the PTC Retrofit. Since industrial PTC has many unique technical aspects, such as the interactions between optimal catalyst structure, anion, optimal solvent, the narrow range of optimum hydration, agitation effects and other key and unique PTC factors, it is recommended to supplement the process development team with the highly specialized expertise dedicated industrial PTC experts who have decades of experience in sorting out these factors and interactions. One must not overlook the incremental profit opportunity resulting from close but not quite optimal conditions. Usually, added gain can be realized from tricks of the trade that only dedicated PTC experts are aware of. The added gain compounds itself when the techniques are used in additional PTC Retrofits or development projects.

In most companies, the cost of one person-month of process development is \$15,000 to \$30,000 and even though the chemists are highly competent, they do not deal with PTC 80 hours a week for decades. Therefore, the larger real cost opportunity in the development process is the time-weighted realized profit from the PTC Retrofit. For example, \$1MM/yr profit means that a one month delay in development actually costs \$125K somewhere down the road. Therefore, reducing the development time by several weeks or months is usually well worth the outside highly specialized industrial PTC expertise. This is in addition to the higher performance process achieved (higher yield, reduced cycle time, expensive strong base replaced, etc.)

Once the PTC Retrofit is developed and implemented rapidly, the process development team can generate even more profit for the company by working on other projects in the development portfolio. The combined profit magnitude and number of profit-generating projects completed per unit time is

an important component in measuring productivity of process development departments.

Irrelevant Objections to PTC Retrofit: How to Convert an Objector Into a Champion

One last word about resistance to change. Do not succumb to irrelevant objections to PTC Retrofit which mask the underlying resistance to change. A common objection to PTC retrofit is "We already have 95% yield and we don't need anymore!" You would be surprised to see how many eyebrows are raised converting the objector into a PTC Retrofit champion when the follow up question is: "In that case, would you like to benefit from reduced cycle time/increasing plant capacity or how about solvent reduction?" If *you* think that PTC Retrofit is worth at least a second thought, help your colleagues visualize the key grand benefit(s) of the PTC Retrofit (or call 800-PTC-7118 and PTC Organics will be glad to help catalyze your achievement).

Conclusion

PTC Retrofit of an existing non-PTC plant process can potentially dramatically reduce operating costs (\$millions) and/or eliminate long standing operating problems. PTC Retrofit has been performed successfully for dozens of organic and polymer reaction families in commercial manufacturing plants and is being overlooked in dozens more. The process development departments have become the heroes in these cost savings and pollution prevention achievements. Challenges which need to be overcome for a successful PTC Retrofit relate primarily to the catalyst and possible recertification of the new process. The fear or organizational resistance to change should not outweigh the potential of the organization to realize significant profit. PTC Retrofit should be given serious consideration and evaluation when the potential benefits are high. PTC Retrofit is do-able and profitable. So, do it and profit!

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About the Author

Dr. Marc E. Halpern is a leading authority on **increasing profit** using phase-transfer catalysis (PTC) technology. Dr. Halpern is the founder of PTC Organics, Inc. the only company dedicated exclusively to enhancing customer profit and process performance by developing high-performance low-cost processes for the manufacture of organic chemicals using Phase Transfer Catalysis. Dr. Halpern helped companies save > \$150 million in process improvements and has provided PTC services at > 150 industrial sites in the US, Europe, the Middle East and Asia.

Dr. Halpern has authored or co-authored the classic books and training programs "*Phase-Transfer Catalysis: Fundamentals, Applications and Industrial Perspectives*" (Chapman & Hall, 1994) "*Phase-Transfer Catalysis: Mechanism and Syntheses*" (ACS Symposium Series #659, 1997), "*Practical Phase-Transfer Catalysis*" (320 chemists trained in the US, UK, Germany, Switzerland and Italy). Dr. Halpern founded PTC Communications, Inc., publisher of the journal "Phase-Transfer Catalysis Communications." PTC Communications, Inc. distributes this journal free of charge to industrial customers. Dr. Halpern innovated the guidelines for evaluation and optimization of new PTC applications and invented the accessibility parameter for characterizing the effect of phase-transfer catalyst structure on reactivity and selectivity. Dr. Halpern has an impressive track record as an Organic Process Chemist, a Supervisor of Process Chemistry Research and Director of Research and Development over a 18 year period in the chemical industry. Dr. Halpern currently dedicates his full time to phase-transfer catalysis.

Dr. Halpern would appreciate your comments and questions about this article and about industrial phase-transfer catalysis.

Proper safety precautions must always be taken when performing chemical reactions, including phase-transfer catalysis reactions.

The PTC Cost Savings Program

www.ptcorganics.com/CostSav1.htm

Editorial

The Pride of the Process Chemist

Do the following statements look like highlights from your annual performance review (or resume)?

Debottlenecked plant by increasing productivity of the esterification step by 12%, which resulted in added incremental profit of > \$1MMyr, achieved through catalyst modification and optimization of solvent and other chemical parameters.

Initiated and developed process improvements, based on lab and pilot plant development, in team with plant engineers, which reduced solvent usage by 30% and emissions by 50%.

Developed new process for new commercialized product, achieving overall 82% yield in two chemical steps and one purification unit operation, instead of 61% overall yield in four steps and numerous unit operations, as transferred from the Discovery Group.

Are you a process chemist?

If yes, **exactly how and when did you learn to be a process chemist?!?** You probably didn't learn to be a process chemist in college...have you heard of a course called Process Chemistry 101 (although some progressive universities actually offer a course in Industrial Chemistry)?

In my opinion, learning to be a process chemist requires a combination of self-taught problem solving complemented by guidance handed down from generation to generation. The fatherly guidance includes outstanding elegant and proprietary tricks. Unfortunately, this guidance also includes some outstanding myths. The myths might actually be good for your career, since you can enter the ranks of company stardom by dispelling an "unshakable truth" (i.e., myth), which results in increasing profit by \$1million/yr. You may even receive a \$25 piece of fashioned acrylic with the engraving "Organic Division Quality Award: Awarded to J. Smith."

If you are an organic process chemist, the first face-to-face encounter with process chemistry may have been during your first week in an industrial lab when you asked your new lab partner "where is the magnesium sulfate?" He/she then proceeded to lecture you that drying an organic solution is performed by choosing the right solvent for azeotroping the solution dry. Your colleague may even have helped you visualize the futility of asking two operators to add magnesium sulfate to an opaque metal reactor and swirling the reactor until they can see the powder become fluffy.

Now you yourself are mentoring new graduates. Be patient with them. Explain the elegant (i.e., simplified and clever) solutions you innovated on your own.

Describe how you ingeniously consolidated unit operations. Describe how you solved the emissions problem by eliminating the root cause of the problem by making slight changes in the chemistry as opposed to helping an engineer find the best scrubber liquid (as your boss initially instructed). Describe how you increased productivity by changing the pH (based on fundamental thinking) beyond what was previously considered to be the limit (because someone blamed a plant excursion in 1969 on pH...and we all *know that nothing has changed* since then!). Explain that the words "fix it, but don't change it" are equivalent to "welcome to the real world of process chemistry." Above all, instill in your new mentoree that he/she can be a process chemistry hero by **applying and integrating practical and theoretical thought** to solving the problem at hand, and of course, getting to know the operators on a first name basis.

You learned process chemistry the hard way and you are proud of it. You developed new chemistry and unit operations with the constraints of economic viability and succeeded. Nobody wrote a book called "What They Didn't Teach You About Process Chemistry in School." Maybe YOU should write that book. After all, you did figure out most of it by yourself!

Process chemists rarely spend their day executing predefined procedures which make the company run. Process chemists innovate the new procedures for others to execute which generate millions of dollars for their companies. All functions are essential for a chemical company to survive. Process chemists are essential for a chemical company to grow.

Marc Halpern