PHASE TRANSFER CATALYSIS

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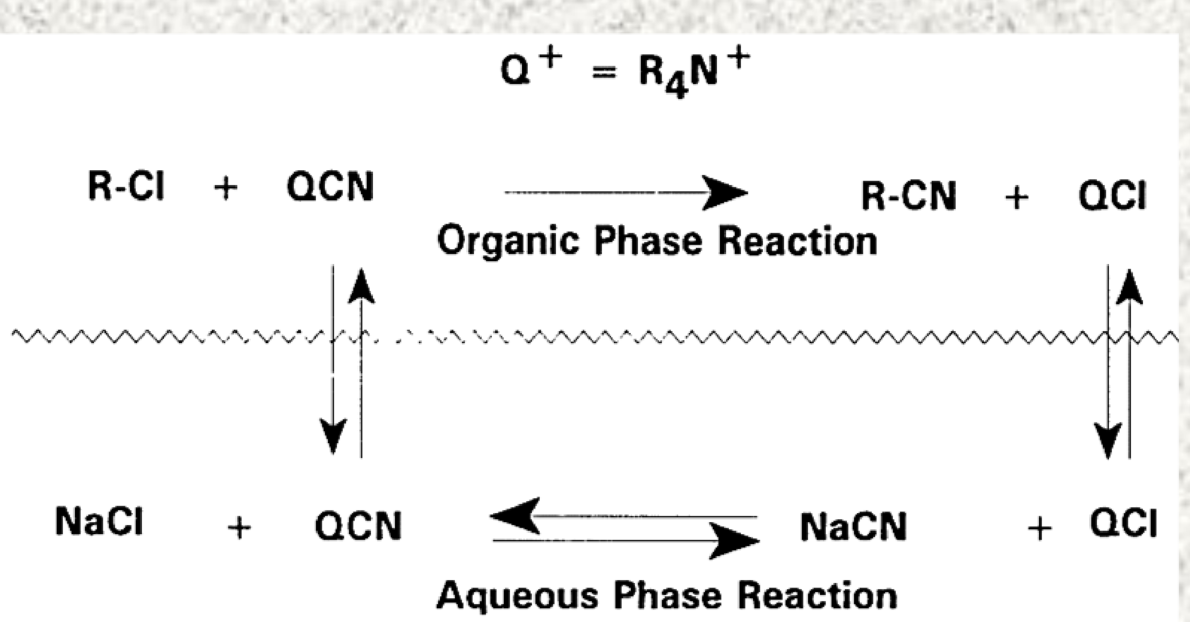
Definition

Phase-transfer catalysis (PTC) accelerates reactions by facilitating the movement of a reactant from one phase to another, where the reaction occurs. It is a form of heterogeneous catalysis that relies on phase-transfer agents to transport a reagent between immiscible phases, enabling the reagents to interact. The transferred species remains active for effective catalysis and is regenerated during the reaction.



BASIC STEPS
1) Anion transfer or delivery of anion from aqueous to organic phase
2) The intrinsic reaction or organic-phase displacement reaction step

Understanding the two steps in PTC reactions is essential because different variables impact each step differently. For example, agitation is crucial for the transfer step but not for the intrinsic displacement reaction. To optimize the reaction, focus on variables that enhance the slower step.

Relationship with Green and Sustainable Chemistry

PTC are crucial in green chemistry, enabling the use of water and reducing organic solvents. PTC reactions proceed usually in high yields and selectivity, whereas undesired side-products are produced in low quantities. These technologies require less investments, consume less energy, and generate much less industrial wastes as compared to the traditional ones.

- Elimination of organic solvents
- Elimination of dangerous, inconvenient, and expensive reactants
- Low energy consumption
- Minimization of industrial wastes

3. Less Hazardous Chemical Synthesis

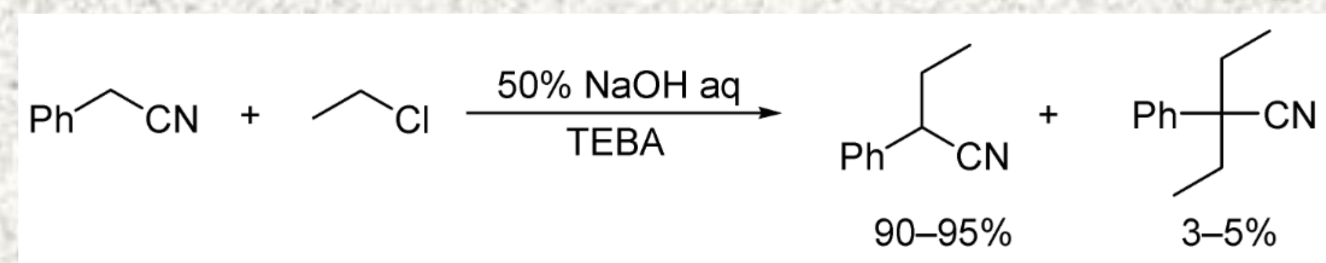
5. Safer Solvents & Auxiliaries

6. Design for Energy Efficiency

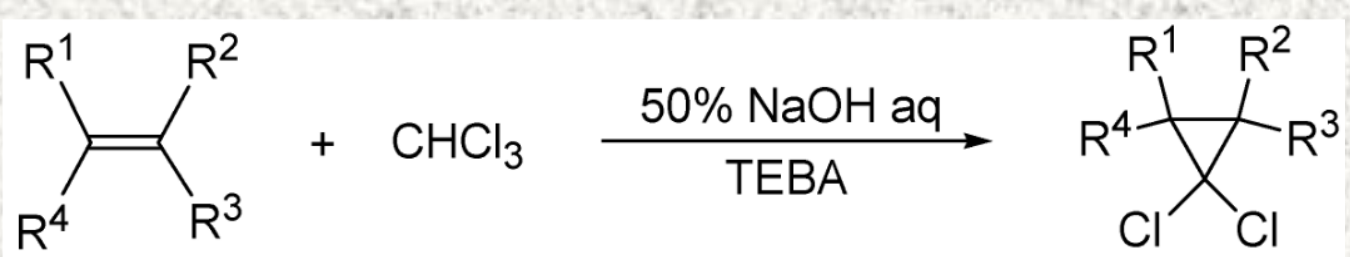
9. Catalyst

History and Development

The first example of PTC being applied in industry was in 1962 at a Polish company, Isopharm, where they were manufacturing 2-phenylbutyronitrile.



In 1969, dichlorocarbene was shown to be generated and reacted with alkenes, while treating chloroform and alkenes with concentrated aqueous NaOH in the presence of benzyltriethylammonium chloride. This convinced the chemical community that this approach using a two immiscible solvents was an efficient way to generate carbanions.



In 1971, Charles Starks coined the term *Phase Transfer Catalysis,* when he reported reactions of inorganic anions and nonpolar organic compound proceed in two-phased systems when catalyzed by tetraalkylammonium salts.

$$n\text{-}C_8H_{17}Cl + NaCN \xrightarrow[R_4N^+Cl^-]{H_2O} n\text{-}C_8H_{17}CN$$

The extraction mechanism was also formulated by Starks in this same publication.

The importance of PTC and its development is evident through the market for PT catalysts exceeding 1 billion USD.

References

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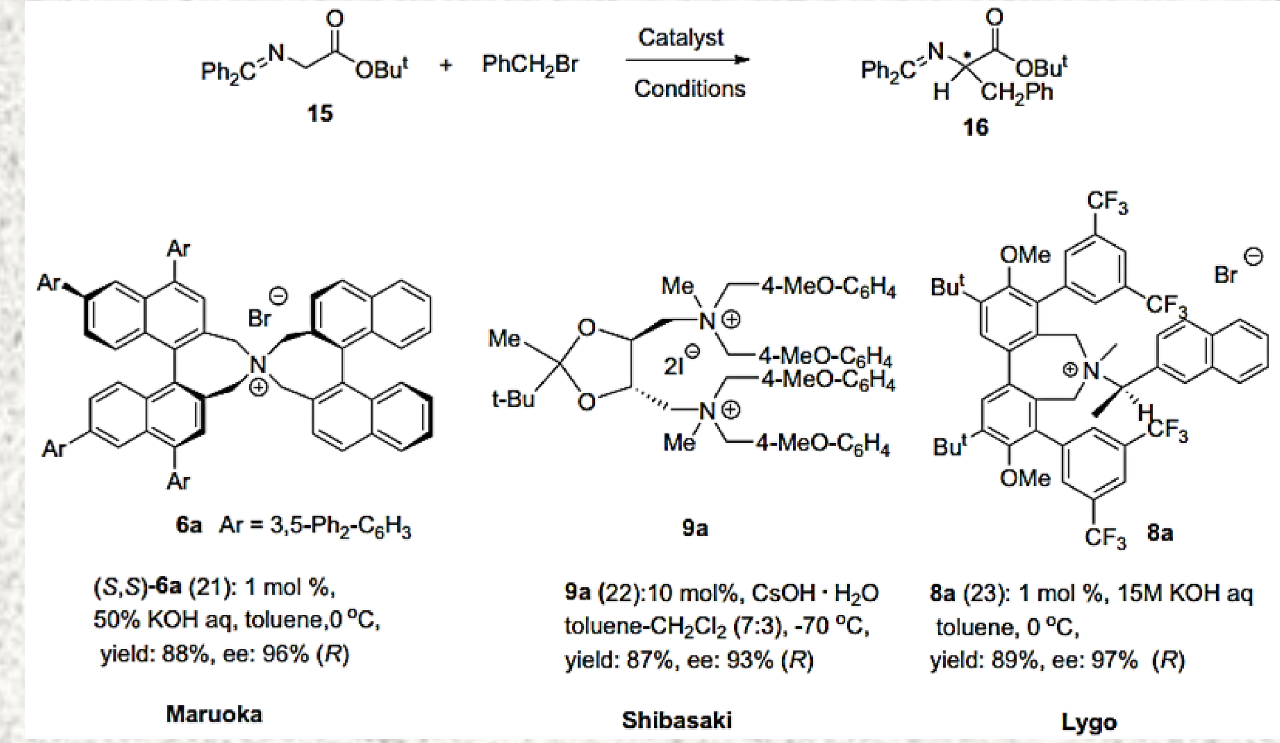
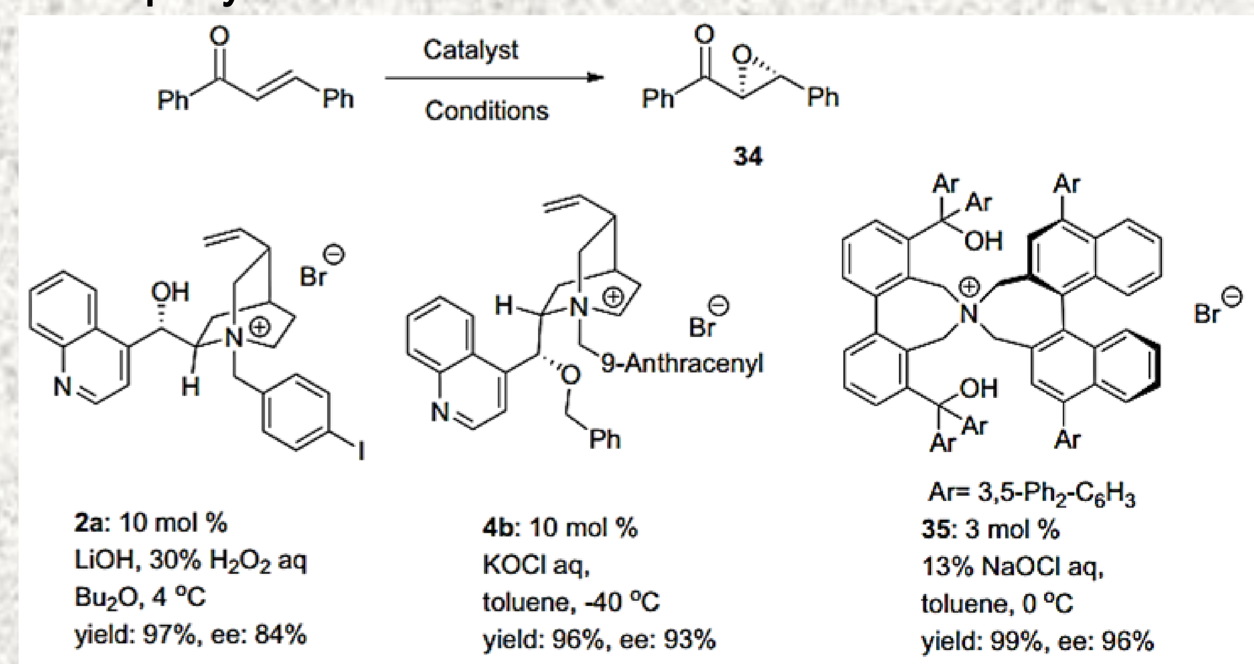
Examples of Successful Applications

Catalysts based on chiral quaternary ammonium salts derived from cinchona alkaloids have found the most widespread applications

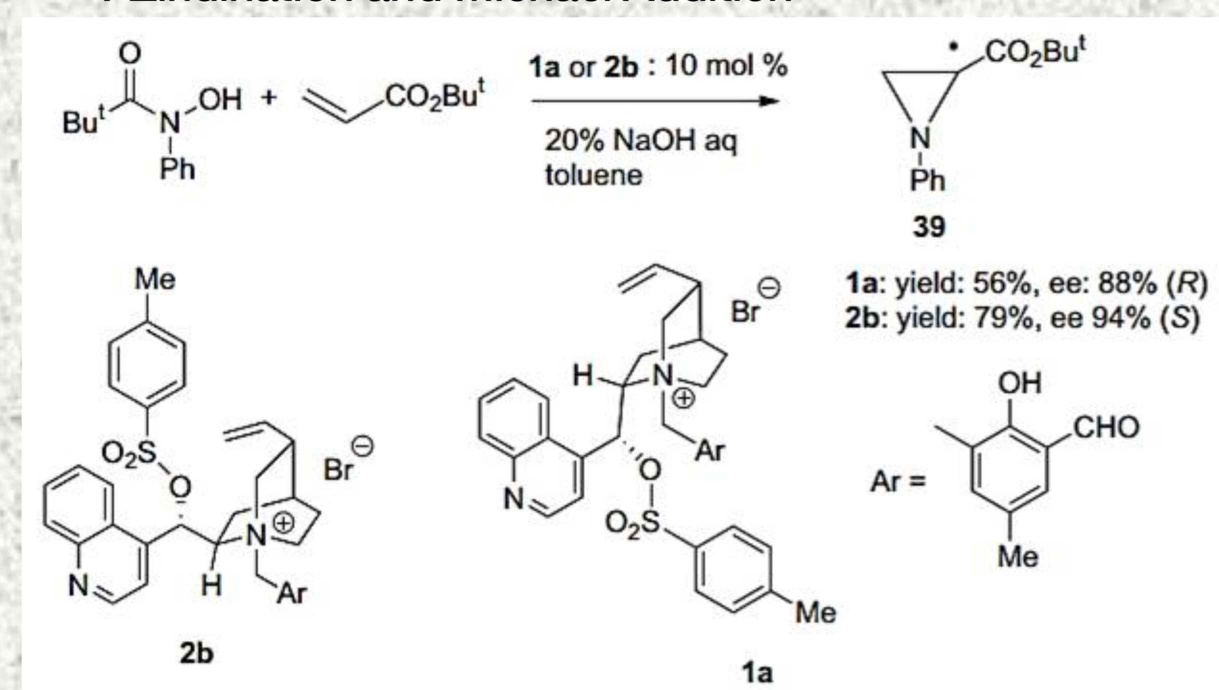
- Asymmetric Alkylation



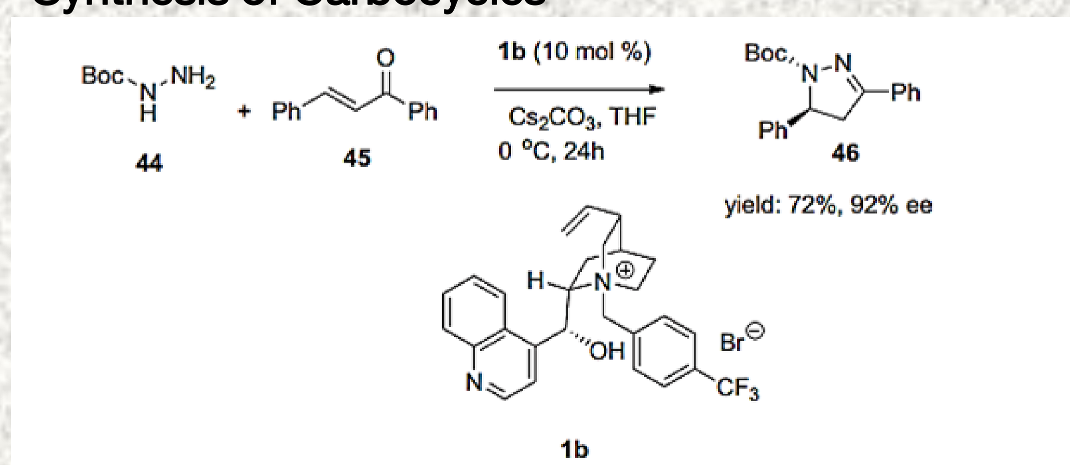
- Epoxydation



- Aziridination and Michael Addition



- Synthesis of Carbocycles



Advantages and Challenges of Implementing PTC

Advantages

- Reduces the need for high temperatures and vigorous reaction conditions
- Allows for the use of cheaper and more readily available catalysts (such as replacing harsh catalysts like LDA for bases like KOH)
- Decreases the use of harmful organic solvents and expensive aprotic solvents
- Eliminates solvent drying steps as there is no need for using anhydrous solvents
- Is easily scalable and cheap due to the use of aqueous solvents

Challenges

Table 1. Commonly Used PT Catalysts

Catalyst	cost	Stability and Activity	Use and Recovery of Catalyst
Ammonium salts	Cheap	Moderately stable under basic conditions and up to **100°C.** Decomposition by **Hofmann** elimination under basic conditions. Moderately active.	Widely used. Recovery is relatively difficult.
Phosphonium salts	Costlier than ammonium salts	More stable thermally than ammonium salts, although less stable under basic conditions.	Widely used. Recovery is relatively difficult.
Crown ethers	Expensive	Stable and highly active catalysts both under basic conditions and at higher temperatures up to even**150−200°C.**	Often used. Recovery is difficult and poses environmental issues due to their toxicity.
Cryptands	Expensive	Stable and highly reactive, except in the presence of strong acids.	Used sometimes despite high costs and toxicity, due to higher reactivity.
PEG	Very cheap	More stable than **quaternary** ammonium salts, but lower activity.	Often used. Can be used when larger quantities of catalyst cause no problems. Relatively easy to recover.

PTC is not an inherently green method, solvent selection is very important. For example, some reactions may proceed better with solvents such as DMF and DMSO. These solvents are, however, expensive, hard to separate, and have high environmental impact

It is also often difficult to separate the catalyst and products from the two phases

Catalyst selection can be challenging and requires looking at many factors. It may also be difficult to regenerate the catalyst

Mechanisms are also often very complicated and kinetic modeling is difficult, due to the many different interactions between phases, reactants, products, and the catalyst.

Like any synthetic tool, it is essential to implement PTC where it is contextually relevant and perform an appropriate life cycle assessment to find the environmental impact.