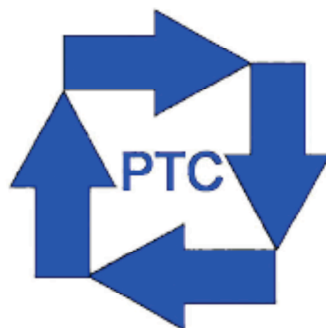

Phase-Transfer Catalysis



MacMillan Lab. Group Meeting
Anthony Mastracchio
April 10 2008

Phase-Transfer Catalysis (PTC)

Presentation Outline

■ Introduction

■ Mechanism and basic concepts of Phase-Transfer Catalysis

- Mechanism
- The Intrinsic Reaction Step
- The Transfer Step
- The PTC Matrix
- Reaction Variables

■ Phase-Transfer catalyzed transformations

■ Asymmetric Phase-Transfer catalyzed transformations

Relevant and Comprehensive Reviews:

Ooi, T., Maruoka, K., "Recent Advances in Asymmetric Phase-Transfer Catalysis." *Angew. Chem. Int. Ed.* **2007**, *46*, 4222-4226

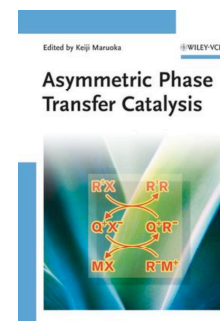
Lygo, B., Andrews, B. I. "Asymmetric Phase-Transfer Catalysis Utilizing Chiral Quaternary Ammonium Salts: Asymmetric Alkylation of Glycine Imines." *Acc. Chem. Res.* **2004**, *37*, 518-525.

Starks, C. M., Liotta, C. L., Halpern, M. E. *Phase-Transfer Catalysis*, Chapman & Hall, New York, **1994**, Ch. 1-3.

Phase -Transfer Catalysis: Mechanism and Synthesis (Ed.: Halpern, M. E.), American Chemical Society, Washington, DC, **1997** (ACS Symposium Series 659), Ch. 1-3.

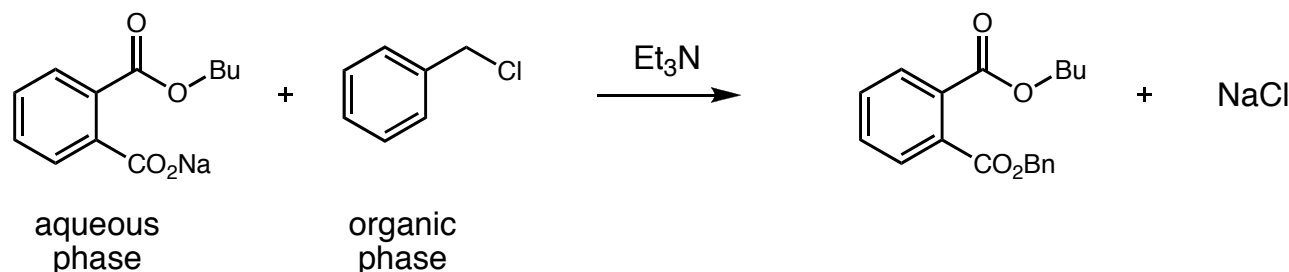
Encyclopedia of Catalysis Vol. 5 (Ed.: Horvath, I. T.), Wiley-Interscience, Hoboken, NJ, **2003**, 511-564.

Asymmetric Phase-Transfer Catalysis (Ed., Maruoka, K.), Wiley-VCH, Weinheim, Germany, **2008**.



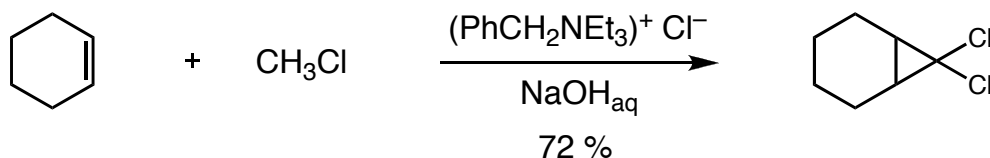
The Advent of Phase-Transfer Catalysis (PTC)

- 1946 - First clear-cut example of the commercial use of PTC (*Ind. Chem. Chem.*, **1946**, 38, 207.)



- The phase transfer catalyst, benzyltriethylammonium chloride, is formed *in situ* by addition of triethylamine

- 1969 - Formulation of the first mechanistic hypothesis on PTC by M. Makosza (*Tett. Lett*, **1969**, 10, 4659.)



Mieczyslaw Makosza

- Makosza postulated an ion exchange between the tetraalkylammonium chloride and aqueous NaOH to form the base that reacts in the organic phase

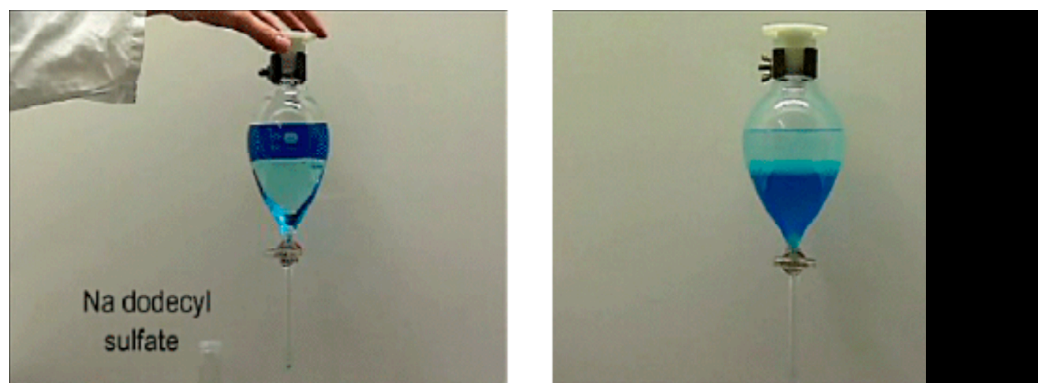
- 1971 - The concept of PTC is described by C.M. Starks (*J. Am. Chem. Soc.*, **1971**, 93, 195.)

- 1984 - First example of an asymmetric PTC by Merck Process (*J. Am. Chem. Soc.* **1984**, 106, 446)

Phase-Transfer Catalysis

■ Definition of a phase transfer catalyst

- A phase transfer catalyst is a catalyst which facilitates the migration of a reactant in a heterogeneous system from one phase into another phase where reaction can take place. Ionic reactants are often soluble in an aqueous phase but are insoluble in an organic phase unless the phase transfer catalyst is present



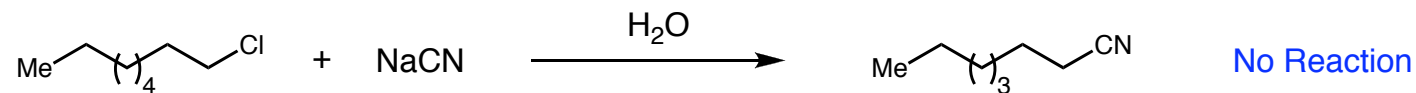
- Phase transfer catalysis or PTC refers to the acceleration of the reaction by the phase transfer catalyst.
- PTC for anions reactant are often quaternary ammonium salts. PTC for cations are often crown ethers

■ Advantages of PTC

- Elimination of organic solvents
- Use of simple and inexpensive reactants (NaOH, KOH, K_2CO_3 etc. instead of NaH, KHMDS *t*-BuOK, etc.)
- High yields and purity of products
- Simplicity of the procedure
- Highly scalable
- Low energy consumption and low investment cost
- Minimization of industrial waste

Phase-Transfer Catalysis

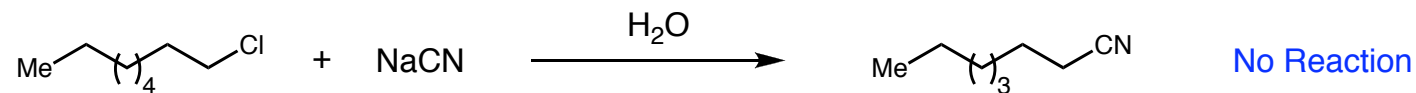
■ Consider the following reaction:



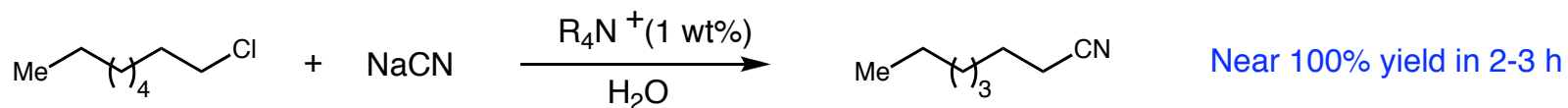
- The 1-chlorooctane and sodium cyanide solution form two separate layers. Heating of this two phase mixture under reflux and vigorous stirring for 1-2 days gives no reaction.

Phase-Transfer Catalysis

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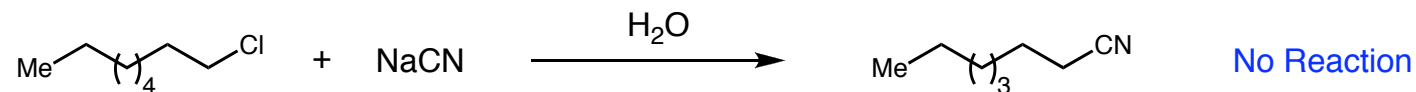
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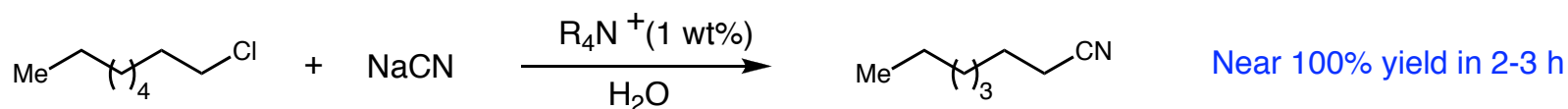
● When an appropriate quaternary ammonium salt is added, tetrahexylammonium chloride, the displacement occurs rapidly in near 100% in 2-3h.

Phase-Transfer Catalysis

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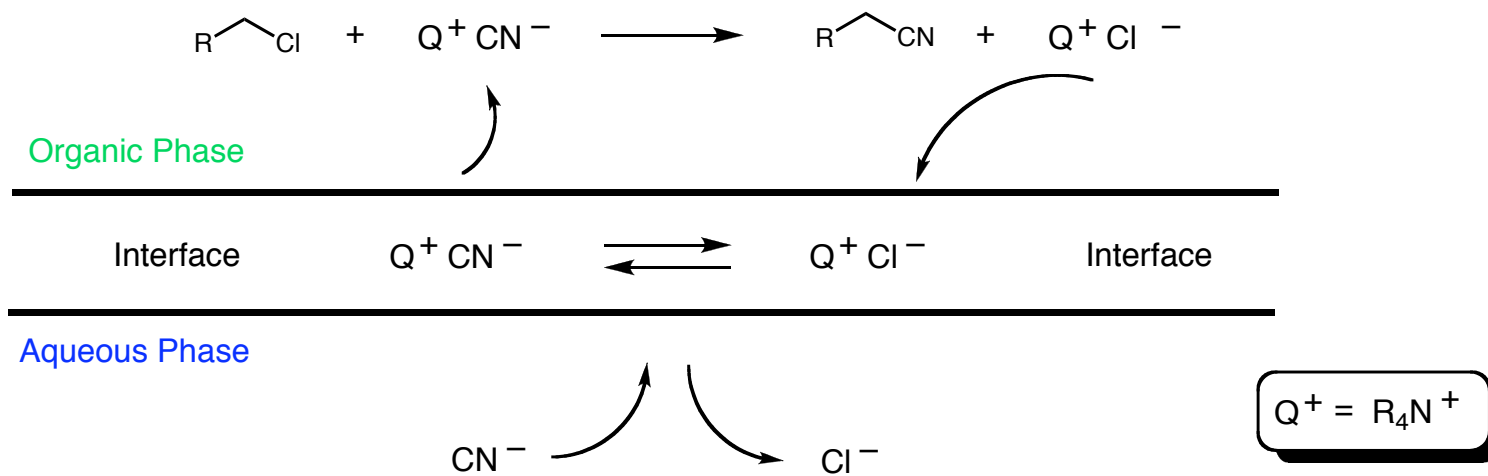
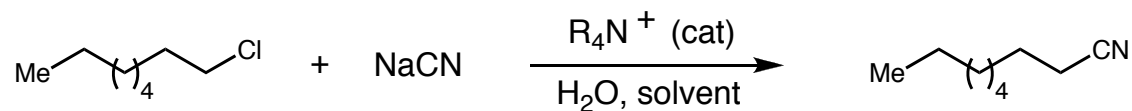
- When an appropriate quaternary ammonium salt is added, tetrahexylammonium chloride, the displacement occurs rapidly in near 100% in 2-3h.

■ In this process the ammonium salt catalyst:

- 1) Transfers the cyanide into the organic phase.
- 2) Activates the transferred cyanide for the reaction with the alkyl halide.
- 3) Transfers the displaced chloride anions back to the aqueous phase to start a new catalytic cycle

The Mechanisms of PTC

Case study: The PTC cyanide displacement reaction



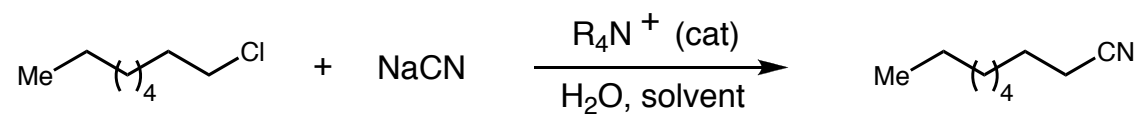
The reaction occurs in at least two steps

- Step 1: The intrinsic reaction or organic-phase displacement reaction step
 - If this step is rate determining \Rightarrow **Extraction Mechanism**
- Step 2: The transfer step
 - If this step is rate determining \Rightarrow **Interfacial Mechanism**

The Mechanisms of PTC

The Intrinsic Step

- The PTC cyanide displacement reaction.

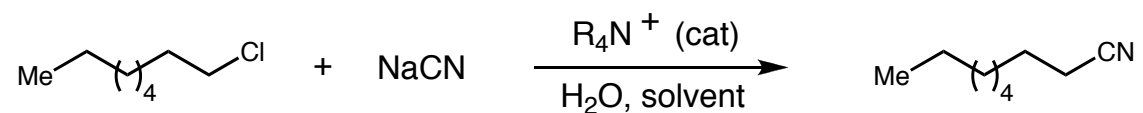


- Once in solution the cyanide anion must be sufficiently reactive to allow displacement to proceed.

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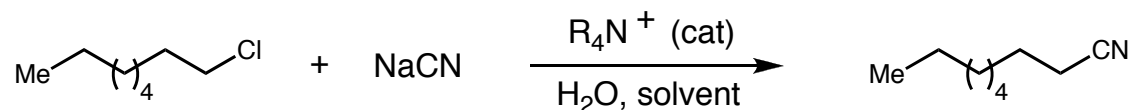


- The poor reactivity is due to the tight ion pairs of NaCN, or large interaction energy binding the two ions together.

The Mechanisms of PTC

The Intrinsic Step

■ The PTC cyanide displacement reaction.

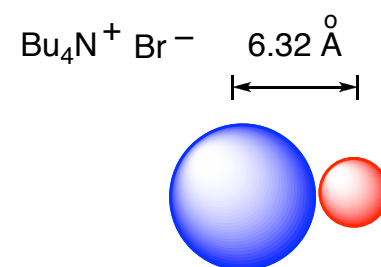
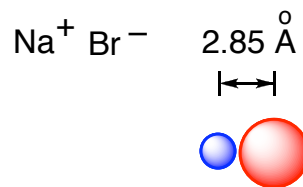


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- The poor reactivity is due to the tight ion pairs of NaCN, or large interaction energy binding the two ions together.

The difference in ionic radii can be translated into ionic interaction energies by simple Coulombic calculations.



Coulombic Interaction Energy (Kcal/mol):

11.4

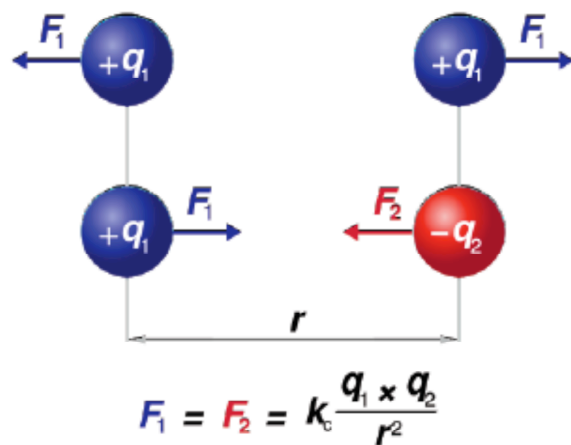
5.3

- By subtracting the tetrabutylammonium energy from the potassium energy, we can compare the calculated differences between ion pairs.
- If these differences in ion-pair energies are translated in reduction of kinetic activation energies then a 5 Kcal/mol difference in activation energy is equivalent to a 4400-fold changes in reaction rate.

The Mechanisms of PTC

The Intrinsic Step

■ Cation Size and Coulombic Interaction Energies of Bromide Salts



Cation	Cation Radius, Å	Coulombic Interaction Energy with bromide anion (Kcal/mol)
Li ⁺	0.6	12.8
Na ⁺	0.9	11.4
K ⁺	1.33	9.9
Rb ⁺	1.48	9.5
Cs ⁺	1.69	9
Me ₄ N ⁺	2.85	6.8
Et ₄ N ⁺	3.48	6.2
n-Pr ₄ N ⁺	3.98	5.5
n-Bu ₄ N ⁺	4.37	5.3

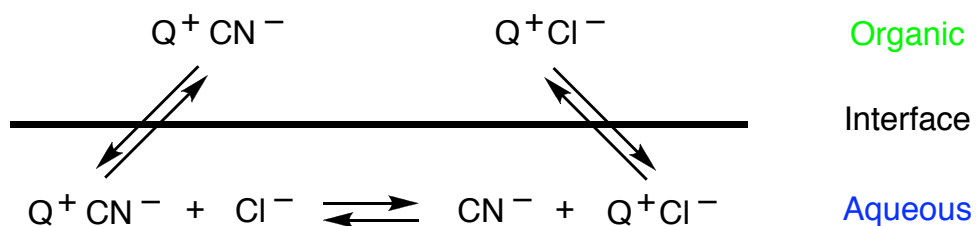
- As the cationic radius of the quaternary salt increases, the activating effect becomes larger
- However, the cationic radii does not grow indefinitely

The Mechanisms of PTC

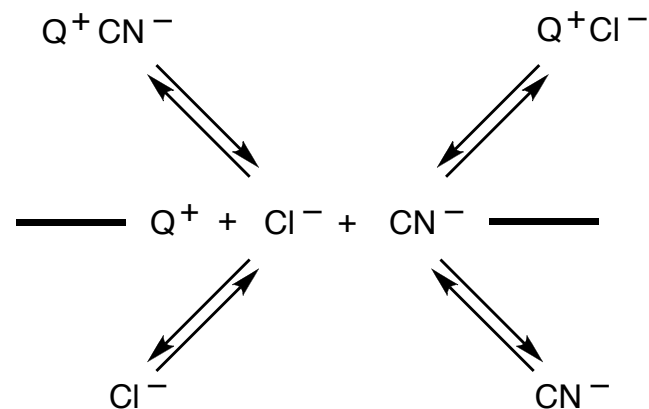
The Transfer Step

Two general mechanisms for the transfer step:

1. Quarternary salt extracted from the aqueous (Stark)



2. Quarternary salt stay outside the aqueous (Makosza)



● Both transfer mechanisms are probably correct depending on the quaternary catalyst, with the first being more likely with small to medium sized quaternary cations, while the second is more correct for medium and large quaternary cations

● For asymmetric PTC, most catalyst employed remains in the organic phase with transfer occurring at the interface (2nd mechanism)

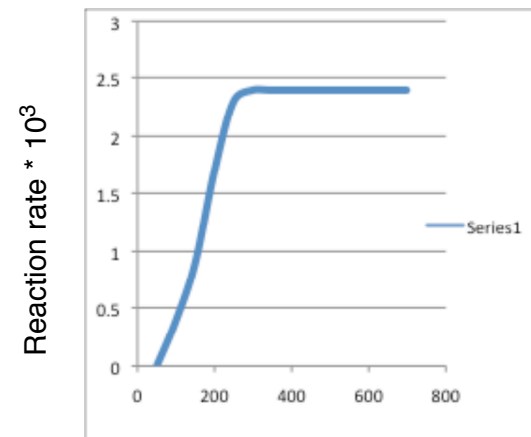
The Mechanisms of PTC

The Transfer Step

■ Factors governing the transfer step:

A. Interfacial area: An increase in the interfacial area helps the transfer step.

- The overall opportunity for any transfer in a two-phase system is governed by the amount of interfacial area available. Therefore, the dispersal of one phase as tiny droplets in the second phase is critical.
- Three important factors affecting the interfacial area:
 - *Interfacial tension*: More interfacial tension results in a decrease of the interfacial area. Highly nonpolar solvents and highly concentrated aqueous solutions have the highest interfacial tension.
 - *Presence of surfactants*: Surfactants increase the interfacial area by helping the formation of tiny droplets.
 - *Stirring*: At low stirring rates the interfacial area varies with the square of the stirrer speed (agitation energy = mass \times velocity²). The use of ultrasound can yield high levels of agitation.



Stirring rate, rpm

The Mechanisms of PTC

The Transfer Step

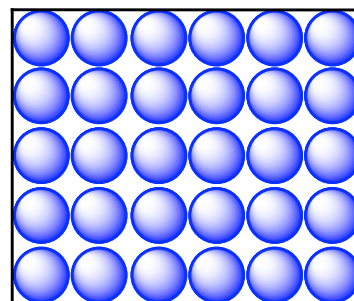
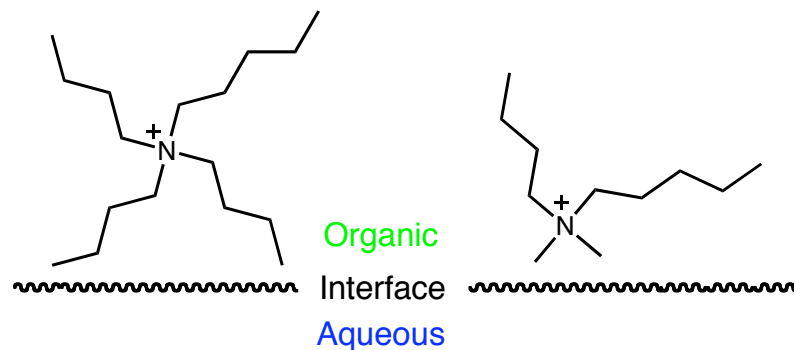
■ Factors governing the transfer step:

B. The nature of the anion:

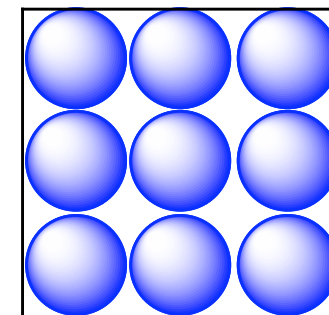
- Large weakly-hydrated or organic anions such as perchlorate, iodide and phenolate are easily transferred while small hydrated anions such as fluorides or hydroxide are poorly transferred

C. The Bulkiness of the quaternary cation catalyst

- As alkyl groups becomes larger and larger the rate of transfer becomes slower and slower
- The use of unsymmetrical quaternary cations much closer approach of the cationic center to the interface
- Catalyst's bulkiness also reduces transfer rates by lowering the maximum possible concentration at the interface.



Small quaternary cations

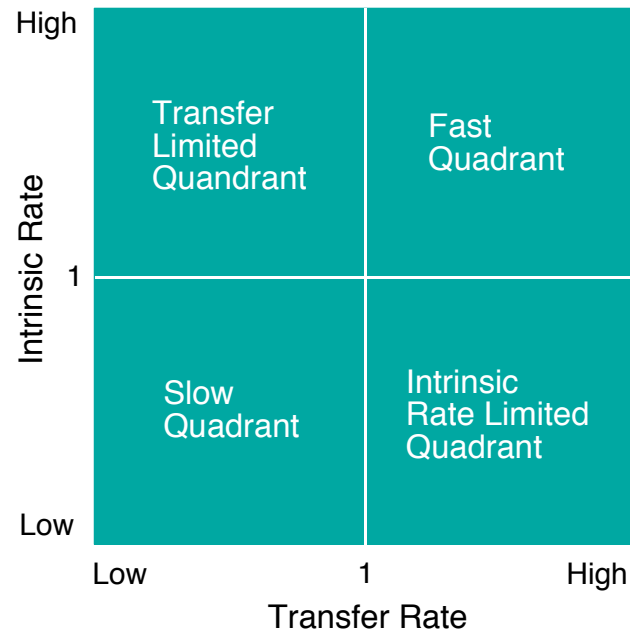


Bulky quaternary cations

The Mechanisms of PTC

The PTC Matrix

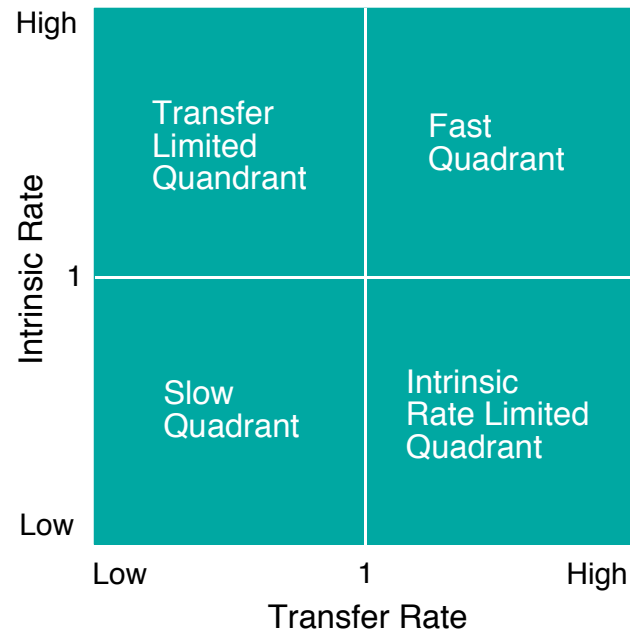
■ Selection of appropriate reaction conditions needs an understanding of how the two steps interact with each other. Use of the PTC Matrix help to sort out some important issues.



The Mechanisms of PTC

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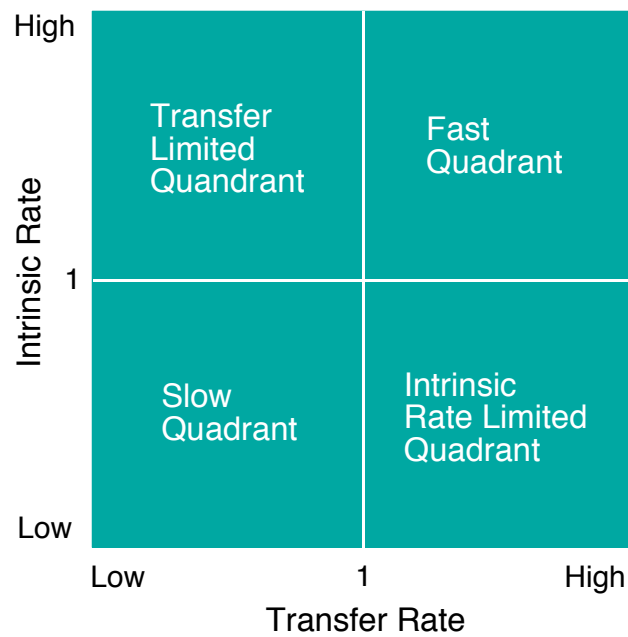


⇒ Both transfer and intrinsic reaction rate are fast. Work with almost any kind of catalysts
Ex: MnO_4^- oxidation of olefins

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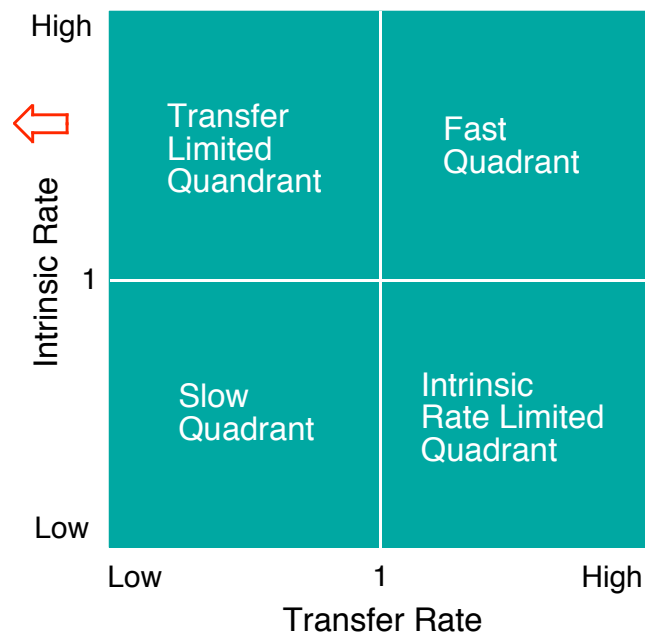
⇒ Reaction with fast transfer rate but slow intrinsic rate
Ex: cyanide displacement Rxns

The Mechanisms of PTC

The PTC Matrix

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Reactions where the transfer is the slow step.
Ex: Butylation of BnCN with NaOH



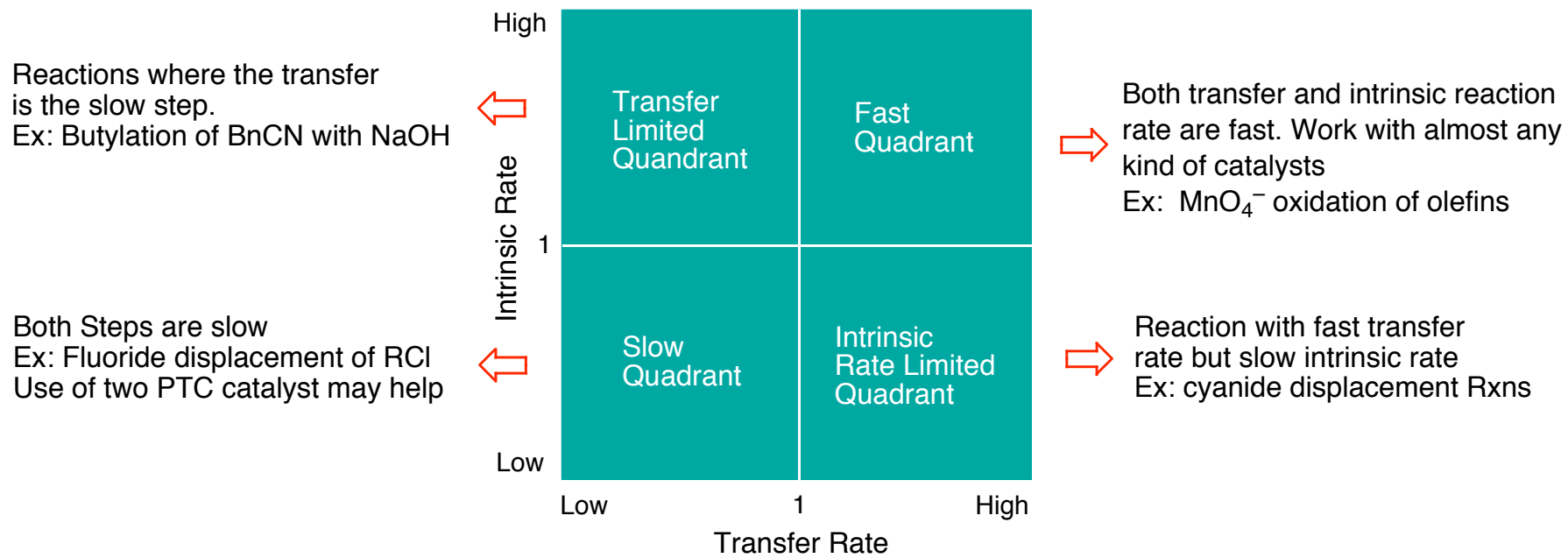
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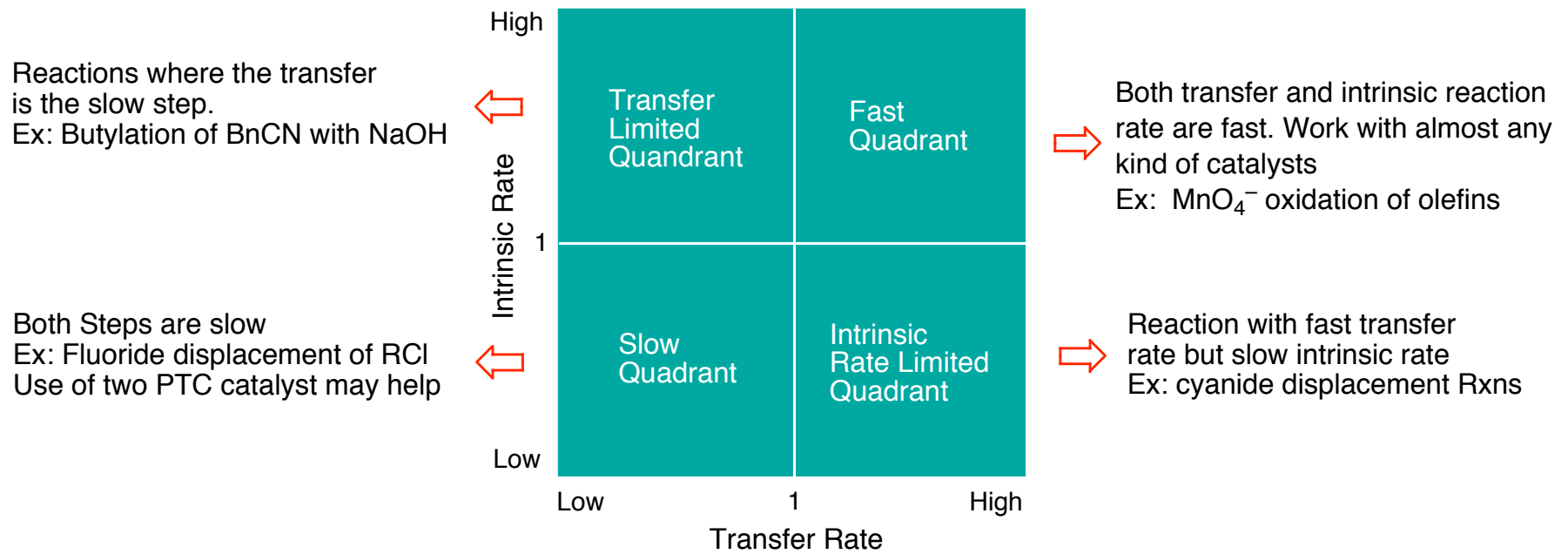
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The Mechanisms of PTC

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■ Effect of variables on PTC reactions

1. Agitation \Rightarrow Influence only the transfer rate

– Agitation speed should be high enough so that it has no influence on the overall reaction rate

2. Concentration of H_2O

– With anions difficult to transfer having saturated aqueous solution drives the equilibrium towards the catalyst substrate complex. Also, minimal amounts of water reduces the hydration of ions

The Mechanisms of PTC

Reaction Variables

■ Effect of variables on PTC reactions

3. Organic solvents \Rightarrow Can greatly influence the intrinsic reaction rate

- Affect the interfacial tension which influences the transfer rate
- CH_2Cl_2 is used extensively because of it dissolves most quaternary salts and is also hydrophobic
- For asymmetric PTC non-polar solvents such as toluene are used extensively because they maximize the interactions between the two counterions.

4. Temperature \Rightarrow Can greatly influence the intrinsic reaction rate

- Most quaternary ammonium salts decomposes at higher temperature, for examples 50-70 °C for systems containing KOH

5. Cocatalyst \Rightarrow Can influence both steps

- Often used to help one of the two steps. For example, addition of alcohols, particularly diols, significantly increase the ease of hydroxide anion transfer

6. Catalyst \Rightarrow The most important variable

- The size and shape affect the anion activation \Rightarrow Intrinsic reaction rate
- Bulkyness can slow the transfer rate (as seen earlier)
- Ability to solubilize the aqueous phase reagent into the organic phase \Rightarrow Transfer rate
- The stability of the catalyst under the reaction conditions
- The surfactant property of the catalyst \Rightarrow Transfer rate

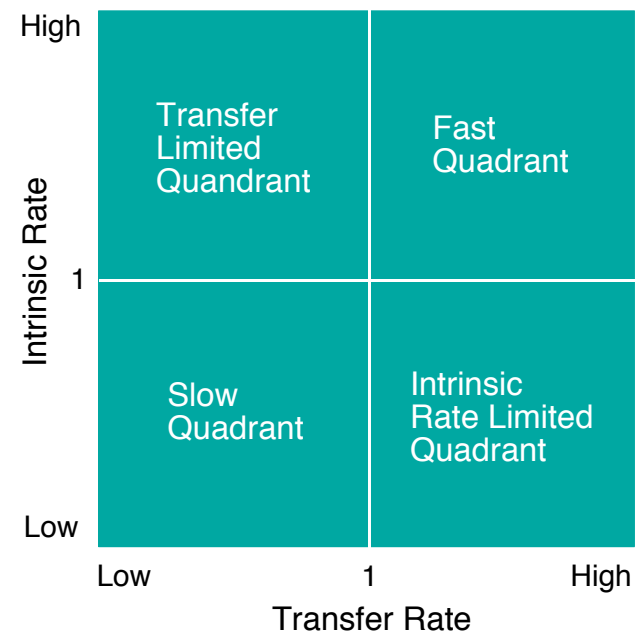
● Different reactions respond to these characteristics in different ways, thus not one catalyst structure is best for all reactions

The Mechanisms of PTC

The PTC Matrix

- Selection of appropriate reaction conditions using PTC matrix and variable diagram

Variable	Effect on transfer step	Effect on intrinsic reaction step
Catalyst structure	+++	+++
Agitation	++++	0
Type of inorganic anion	++++	++++
Water concentration	++	+
Organic solvent	+	++
Temperature	+	+++
Cocatalysts	++	+++
Organic reactant structure	0	++++



- Understanding and prediction of PTC reaction systems requires some knowledge of both the rates of transfer and the rates of the intrinsic organic-phase reaction. For new systems it is necessary to make some guesses and extrapolations from known systems

Practical Applications of PTC

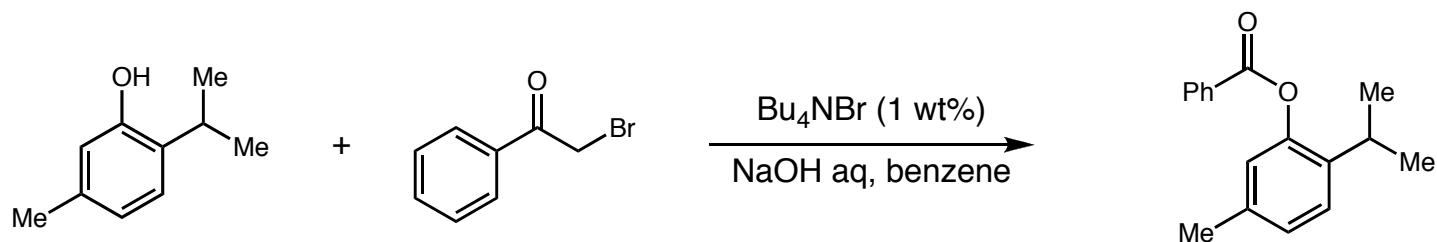
- PTC is particularly useful for reactions of organic anions with nonpolar organic reactants.

- PTC is also applicable for numerous reactions in which anions are intermediates for generating other active species such as carbenes, nitrenes and organometallic reagents.

- Reactions have been done in the following areas:
 - 1) Alkylations
 - 2) Substitutions
 - 3) Aldol and related condensations
 - 4) Carbenes reactions
 - 5) Oxidations and reductions
 - 6) Organometallic transformations

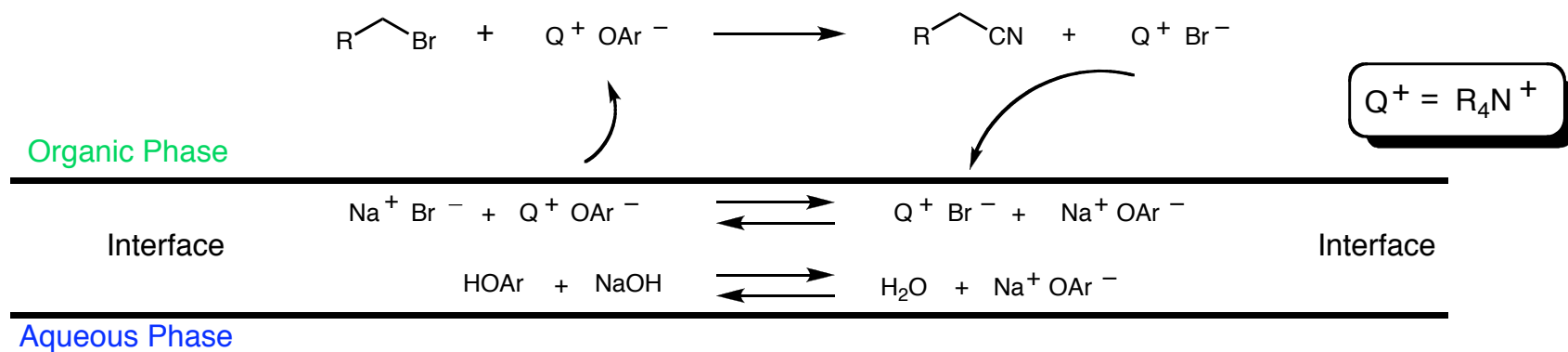
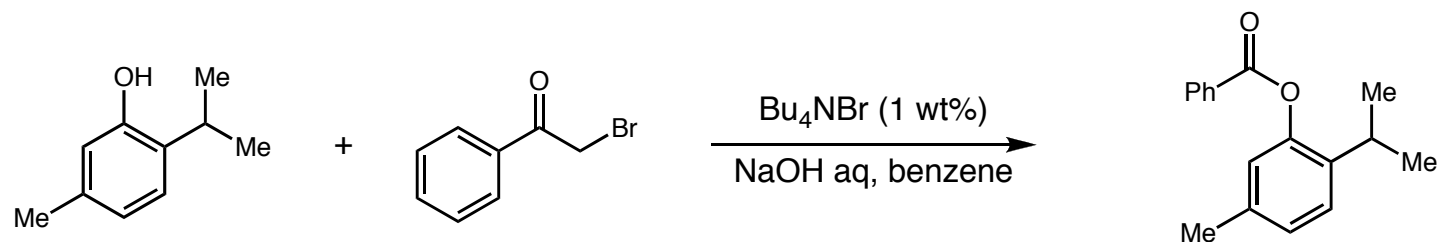
Practical Applications of PTC

- Alkylations are the most common application of PTC



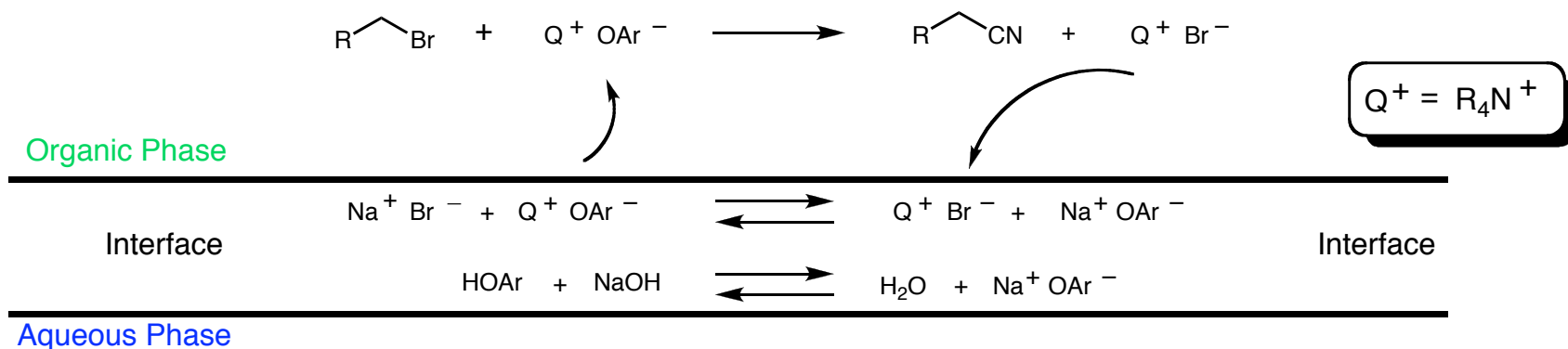
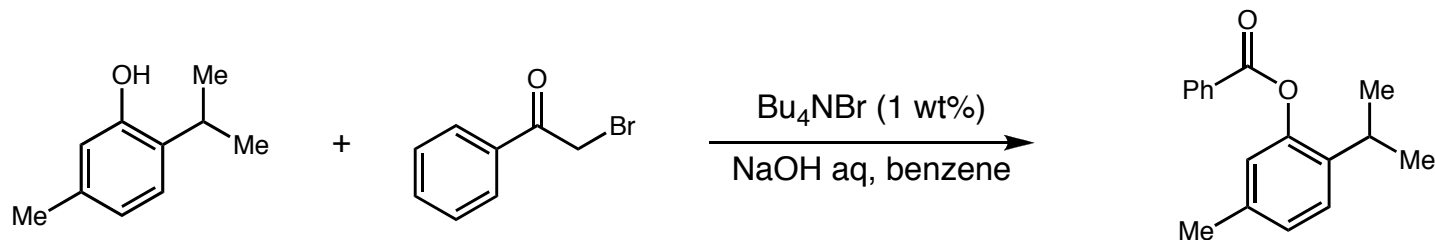
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Practical Applications of PTC

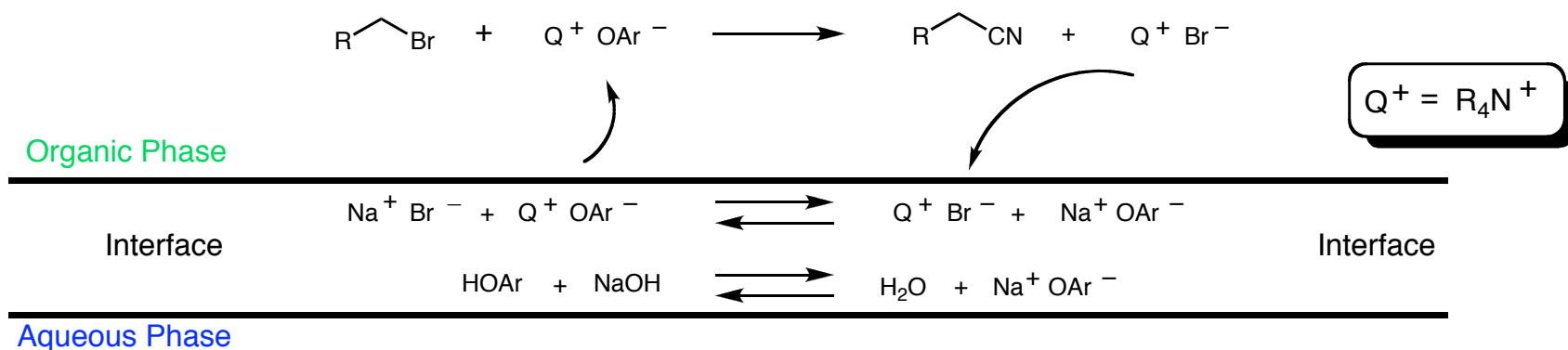
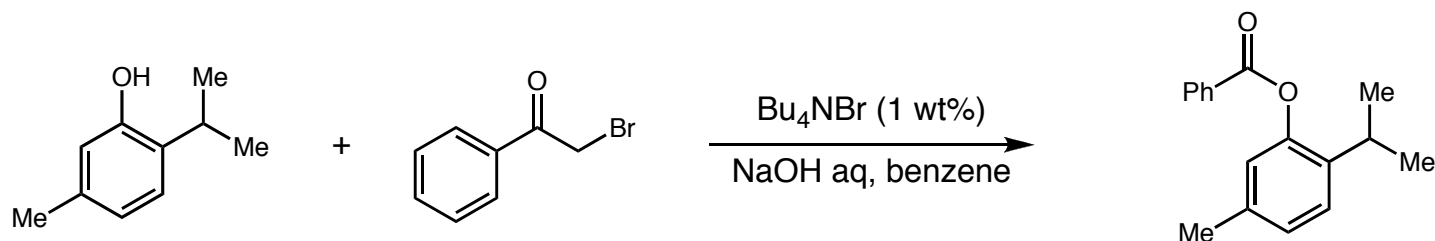
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- PTC in substitution reaction is govern by two major factors: equilibrium concentration of the reacting anions and the rate constant of the reaction.

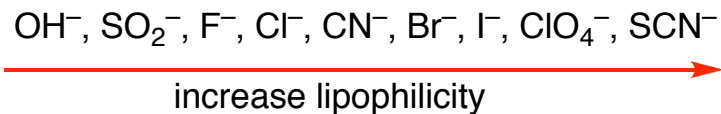
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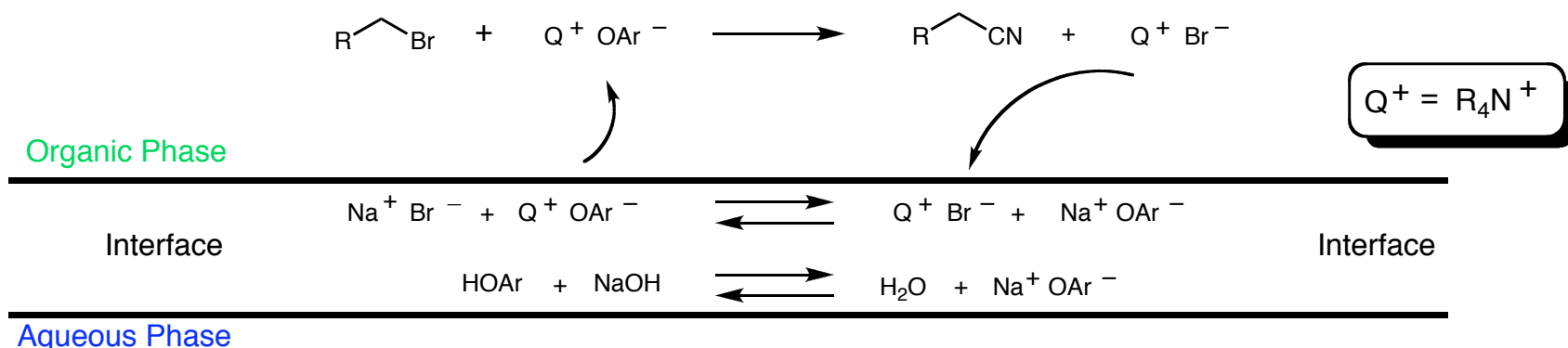
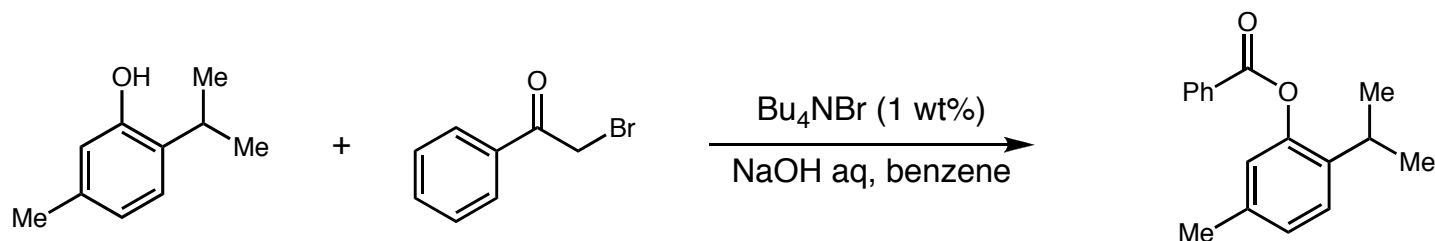
- More lipophilic anions will stay preferentially as quaternary ammonium pairs
- Anions of high hydration energy will preferentially stay in the aqueous



- Alkyl chlorides are often preferred as inhibitory effect of produced I⁻ or Br⁻ can be problematic

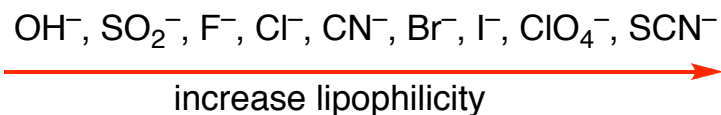
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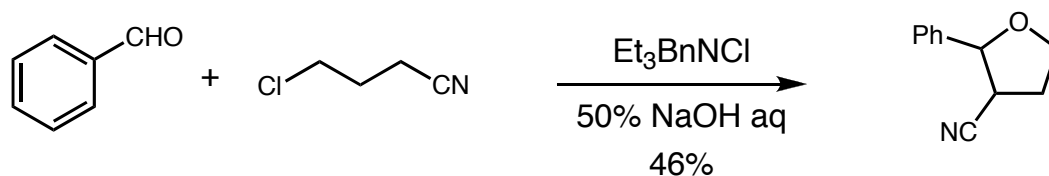
● A variety of other anion precursors can be deprotonated and efficiently alkylated under PTC conditions. The upper limit of $\text{p}K_a$ value of anion precursor is around 24

Practical Applications of PTC

■ Reactions of organic anions with electrophiles

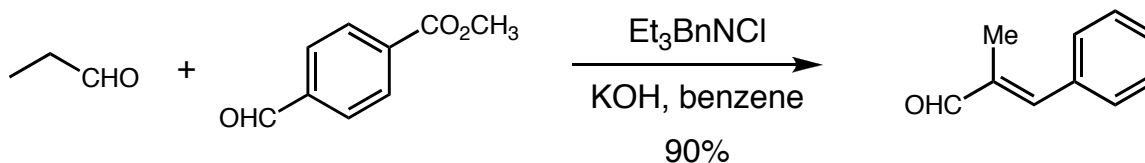
Reactions of organic anions with electrophilic sp^2 carbon atom.

- Reactions that produces aldol anions are usually not preferred since the retro aldol under PTC is favored.



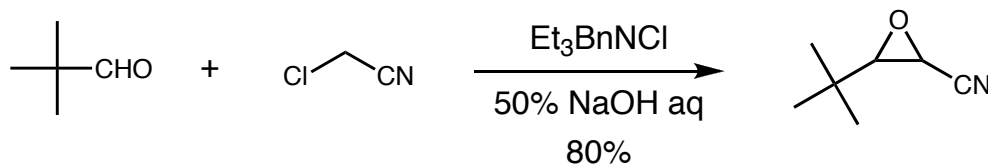
Alper, H., *Adv. Organomet. Chem.* **1981**, 19, 183

- The NaOH present can act as a dehydrating agent making the Knoevenagel proceed readily



Abbeyes, H. *et. al.*, *J. Organomet. Chem.* **1989**, 59, 205

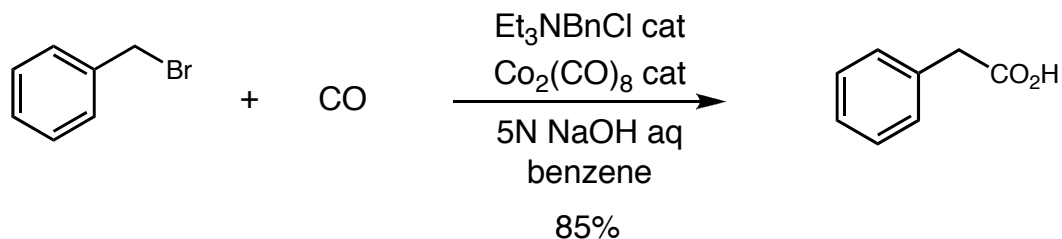
- PTC is of great effectiveness in the reaction of α -halocarbanions with aldehydes and ketones producing oxiranes (the Darzens reaction)



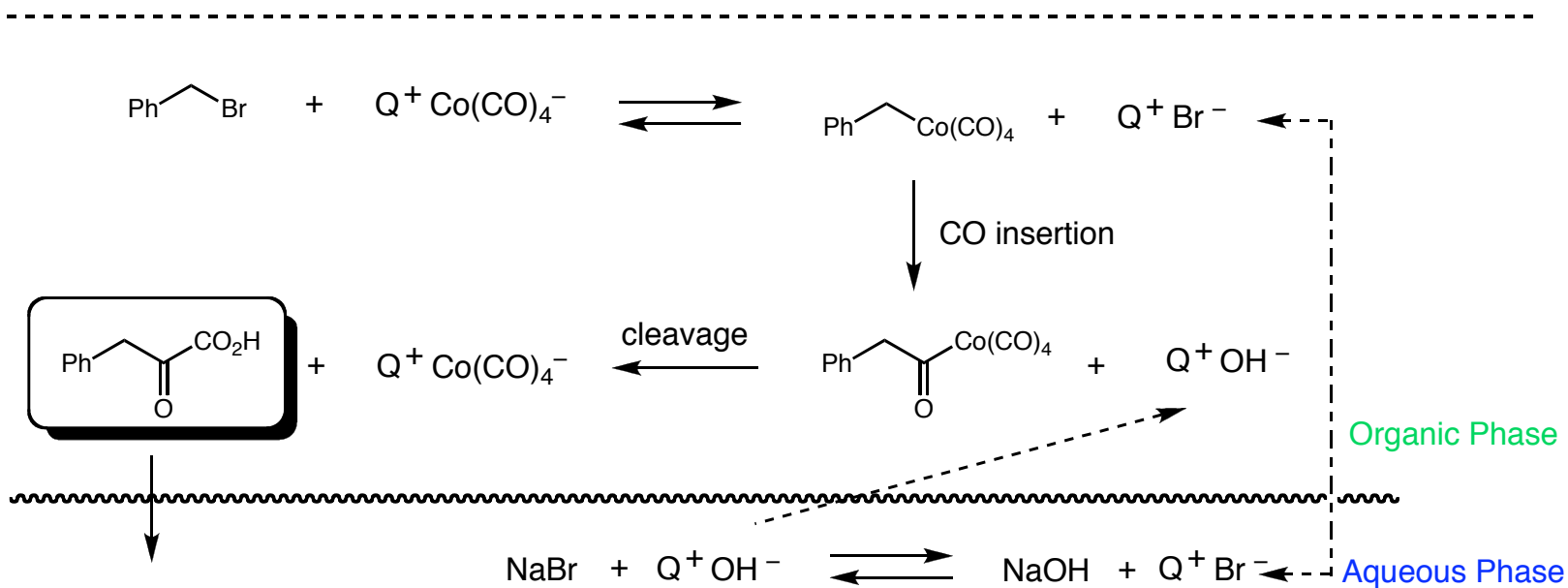
Amin, S. R., Sarkar, R. *Organometallics*, **1995**, 14, 547

Practical Applications of PTC

- PTC has found wide applications in organometallic chemistry
- PTC offers convenient conditions for carbonylations



Alper, H., des Abbayes, H., *J. Organomet. Chem.* **1977**, 134, C11

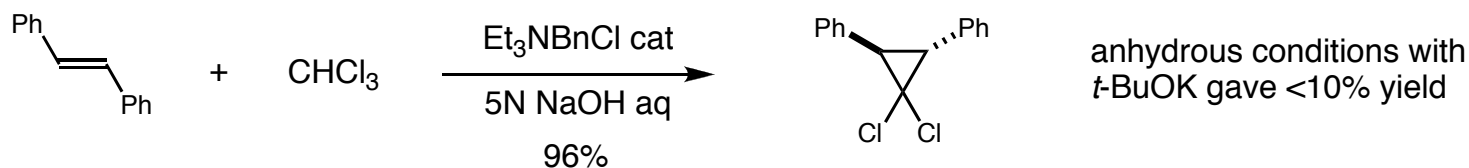


- Other PTC applications in organometallic chemistry includes reductions, hydrogenations and Heck reactions

Practical Applications of PTC

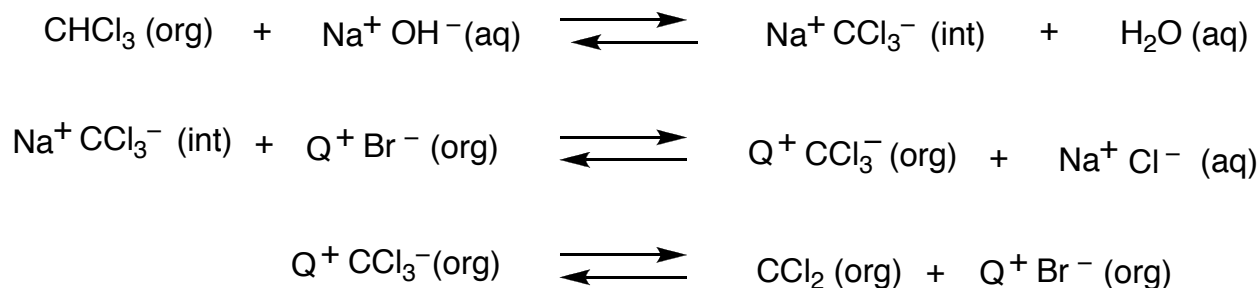
■ Generation and reactions of carbenes

- PTC in which dichlorocarbene (DCC) is generated by treatment of chloroform with concentrated aqueous NaOH solution in the presence of a quaternary ammonium salt is very efficient.
- Numerous reports have shown that PTC assures substantially higher yields compared the the reactions carried in other base/solvent systems. Using PTC only negligible amounts of DCC is decomped by aqueous NaOH.



Encyclopedia of Catalysis Vol. 5 (Ed.: Horvath, I. T.), Wiley-Interscience, Hoboken, NJ, **2003**, 535.

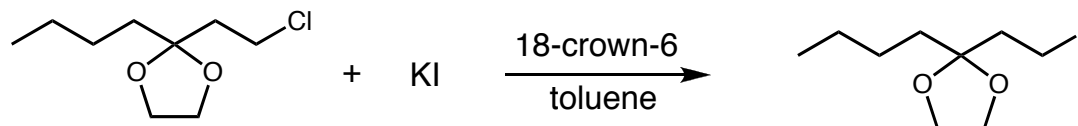
- Under PTC, the carbene is formed in the organic phase, away from the base and the water which minimizes hydrolysis.



- Under anhydrous conditions the carbene and the organic base share the same environment which increase the probability of side reactions.

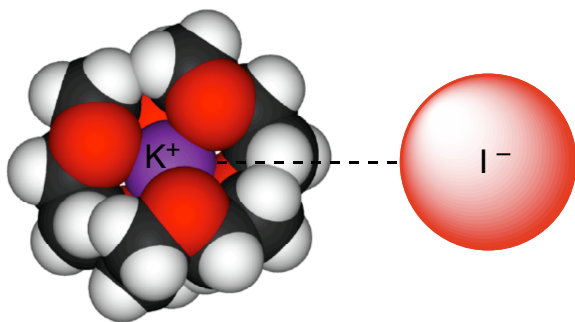
Practical Applications of PTC

■ Solid-liquid PTC



Royer, J., Husson, H. -P., *J. Org. Chem.* **1985**, 50, 670

- Crown ethers are capable of dissolving salts from the solid phase
- In many solid-liquid PTC, small amounts of water play an important role in the catalytic process



Coordination of the crown ether onto the potassium reduces the energy of the potassium/iodide pair. This leads to an increase in the nucleophilicity of the iodide

■ PTC has shown to be very powerful in reactions involving charged species. Other examples includes:

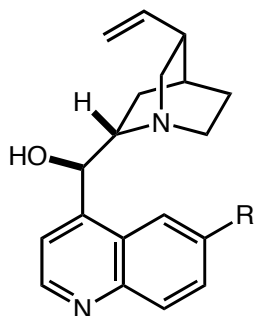
- Reductions
- Oxidations
- Eliminations

Asymmetric PTC

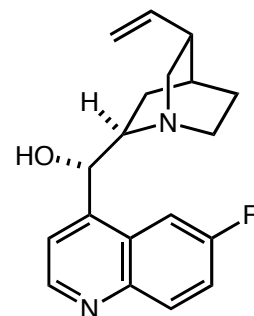
Chiral quaternary Ammonium Salts Catalysts for Asymmetric Transformations

■ Chiral quaternary ammonium salt derived from cinchona alkaloids are the most widely used catalyst for asymmetric PTC

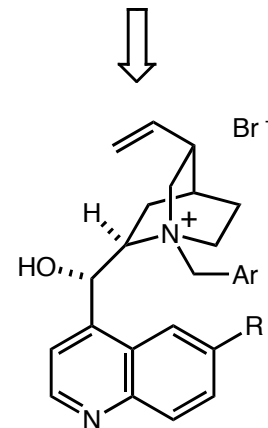
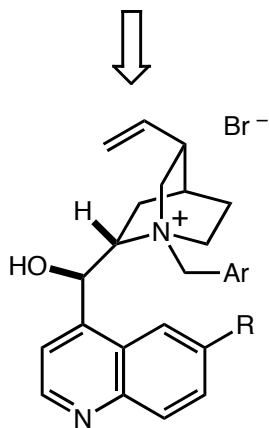
● Cinchona alkaloids are a family of natural products that can be isolated from cinchona trees. The following four are the most abundant and can be isolated from the bark of the tree:



R = OMe [(-)-quinine], \$2.74/g
R = H [(-)-cinchonidine], \$0.64/g



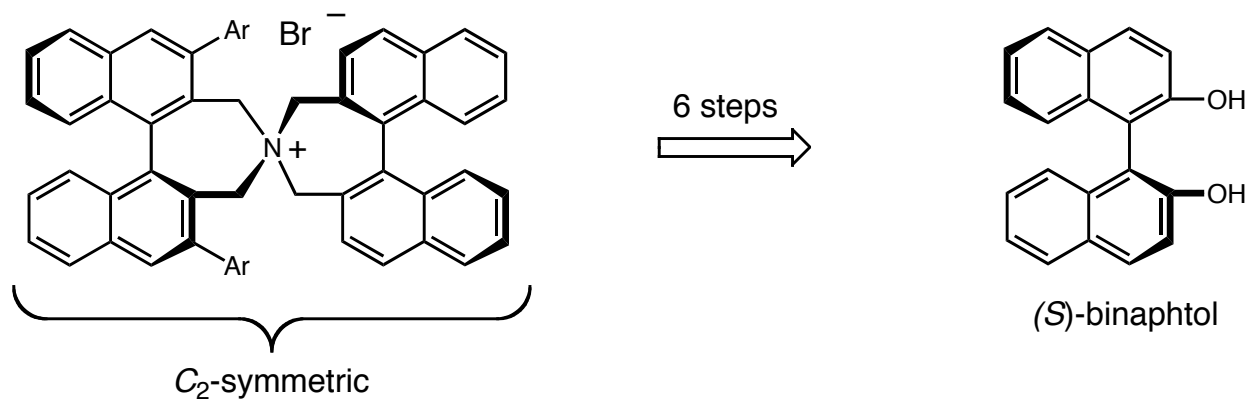
R = OMe [(+)-quinidine], \$5.06/g
R = H [(+)-cinchonine], \$0.76/g



Asymmetric PTC

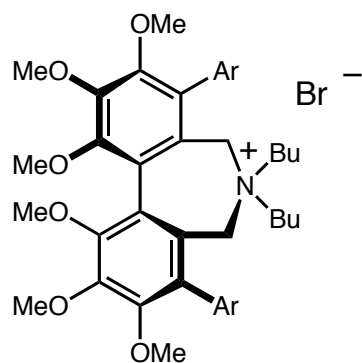
Chiral quaternary Ammonium Salts Catalysts for Asymmetric Transformations

■ Maruoka's spirobinaphthyl quaternary ammonium salts

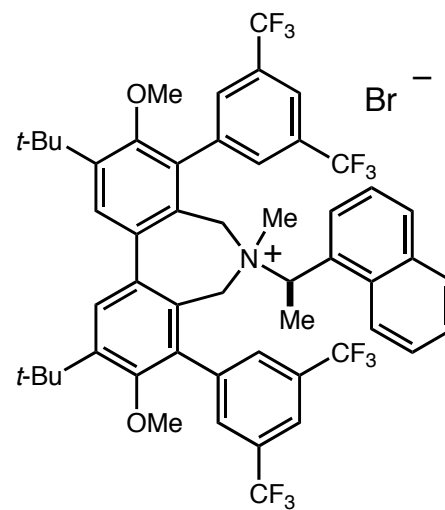


Ooi, T.; Kameda, M.; Maruoka, K. *J. Am. Chem. Soc.* **1999**, *121*, 6519

■ Quaternary ammonium salt with structural similarities have also display efficiency in some transformations



Maruoka, K. *et. al Tett. Lett.* **2005**, *46*, 8555

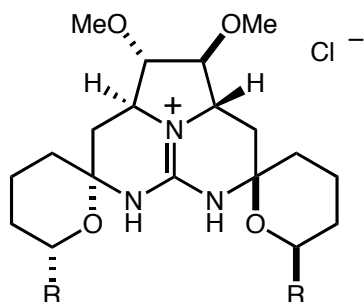


Lygo, B. *et. al Tett. Lett.* **2003**, *44*, 5629

Asymmetric PTC

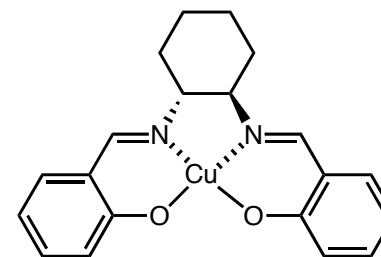
PTC Catalysts for Asymmetric Transformations

- Various PTC catalysts possessing no quartery ammonium moiety have been used successfully



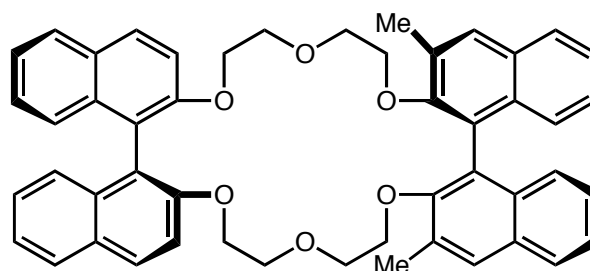
Guanidines

Nagasawa, K. *et al. Angew. Chem. Int. Ed.* **2002**, 41, 2832



Chiral copper-salen complex

Belokon, Y. N. *et al. Tetrahedron Asymmetry* **1998**, 9, 851



Chiral crown ethers

Sogah, G. D. Y.; Cram, D. J. *J. Chem. Soc. Chem. Comm.* **1981**, 625

Asymmetric PTC

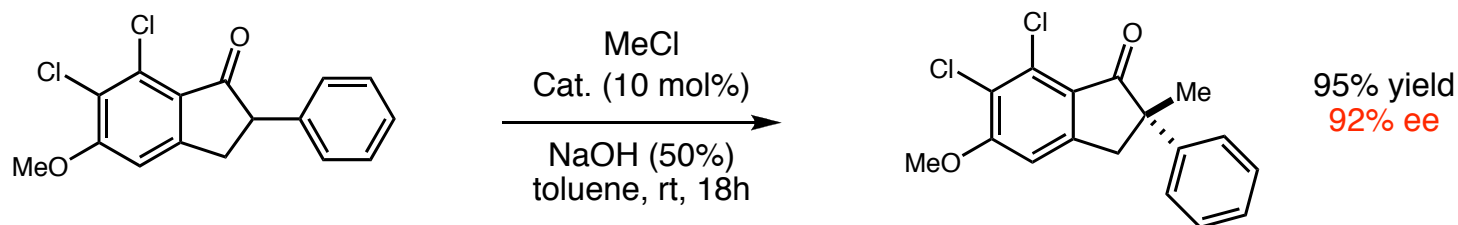
■ Several reactions have been done using chiral quaternary ammonium salts as asymmetric phase transfer catalysts

■ These reactions includes:

- 1) Alkylations
- 2) Michael Additions
- 3) Aldol and related condensations
- 4) Darzen Reactions
- 5) Epoxidations

Asymmetric PTC Enantioselective Alkylation

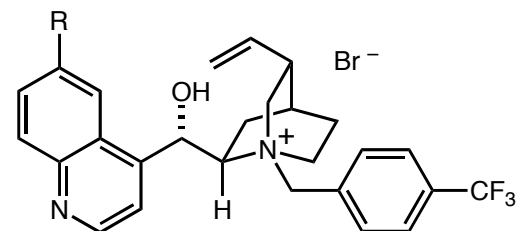
■ First Example: Enantioselective methylation of phenylindanone derivatives (Merck Process Research)



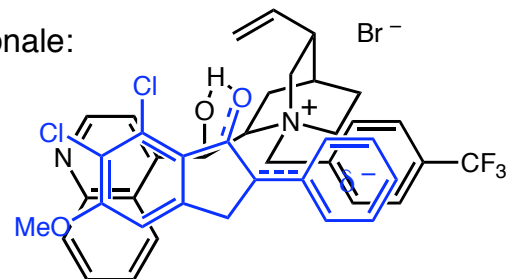
● Conclusion of mechanistic and kinetic studies:

- Step 1: Enolate Anion Formation.
Rxn proceeds best in 50% NaOH
- Step 2: Anion extraction into organic phase.
Catalyst could be working as a dimer
- Step 3: Chiral methylation in organic phase.
Less polar solvents affords High ee's

Catalyst:



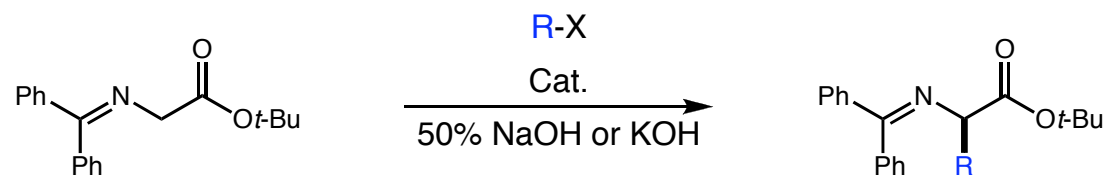
Rationale:



Asymmetric PTC

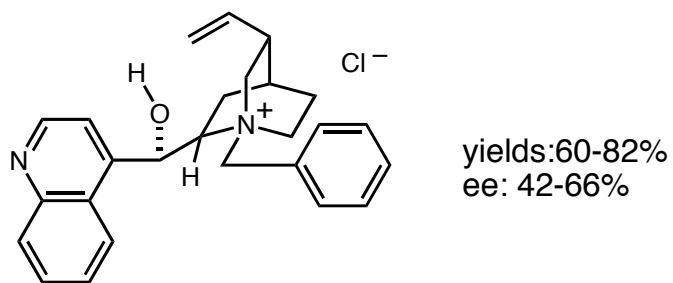
Enantioselective Alkylation

Application to the synthesis of amino acids



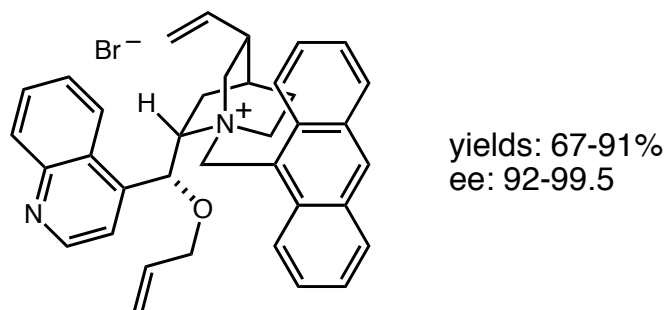
O'Donnell:

O'Donnell *et al.* *J. Am. Chem. Soc.*, **1989**, *111*, 2353

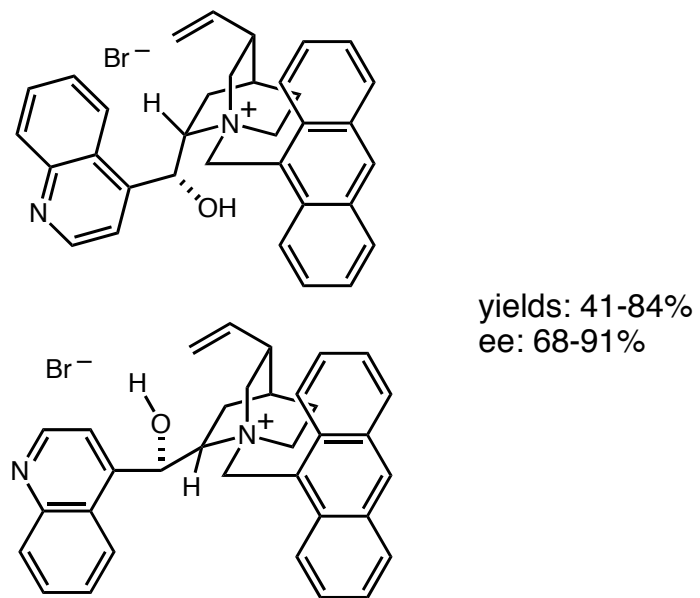


Corey:

Corey *et al.* *J. Am. Chem. Soc.*, **1997**, *119*, 12414



Lygo



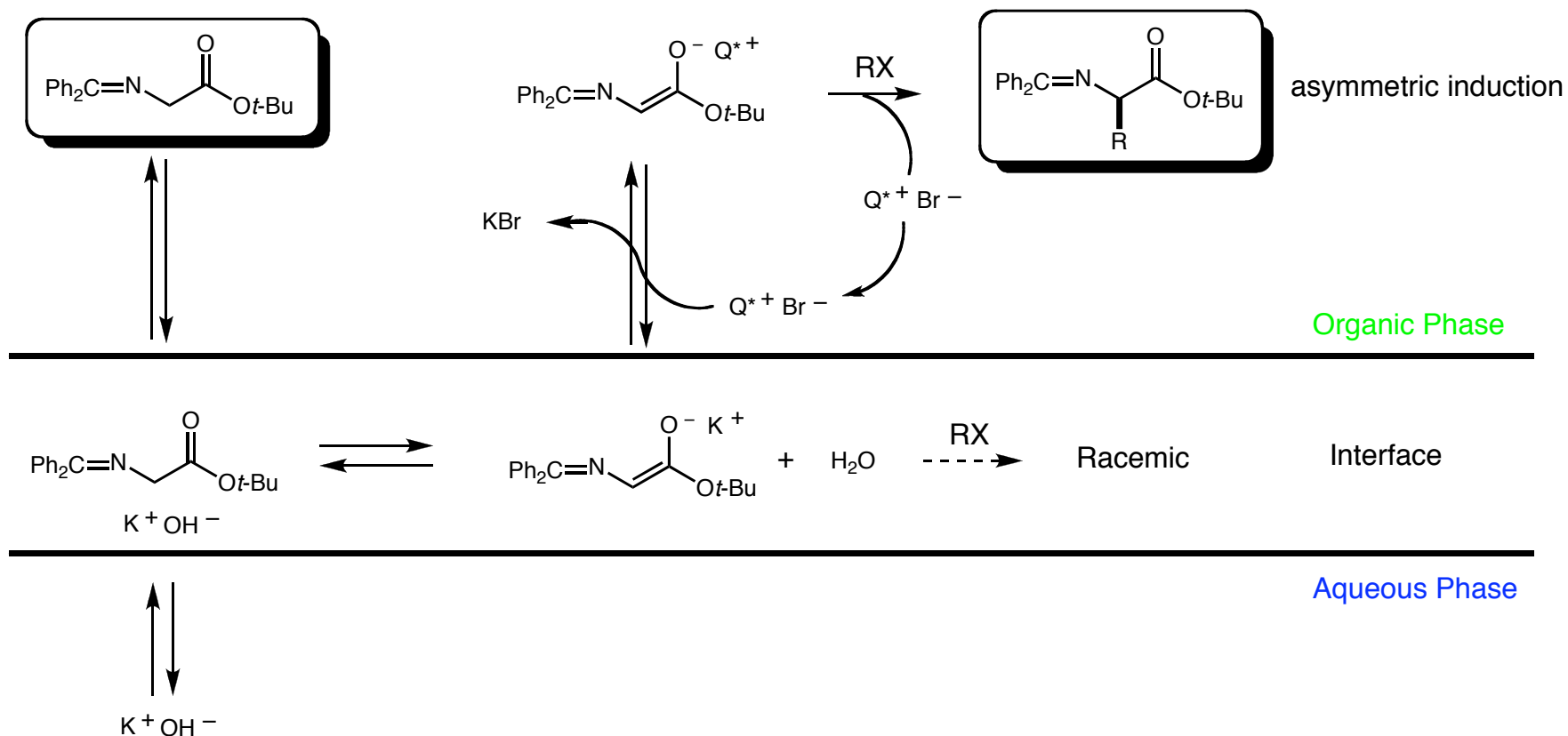
Lygo *et al.* *Acc. Chem. Res.* **2004**, *37*, 518

Lygo *et al.* *Tett. Lett.* **1999**, *40*, 1389

Lygo, B.; Andrews, B. *Tett. Lett.* **1999**, *40*, 1385

Asymmetric PTC Enantioselective Alkylation

- General mechanism for the enantioselective alkylation of a glycine Schiff base:

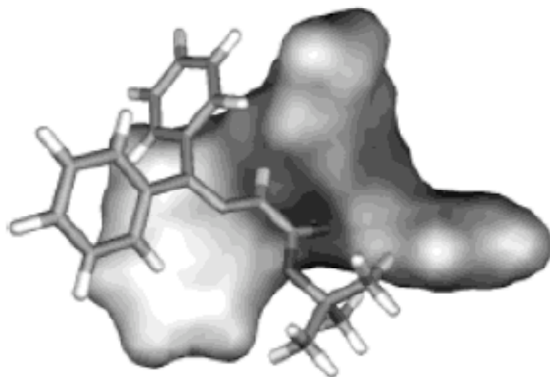


- Mechanistic and kinetic studies have shown that the process occurs following these steps:

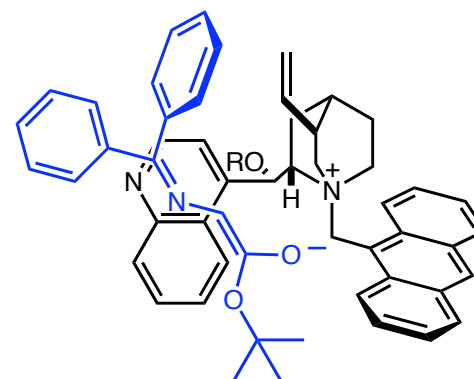
- 1) Deprotonation of the substrate at the interface
- 2) Ion exchange to form the catalyst/substrate ion pair
- 3) Alkylation in the organic phase

Asymmetric PTC Enantioselective Alkylation

■ Stereochemical rationale:

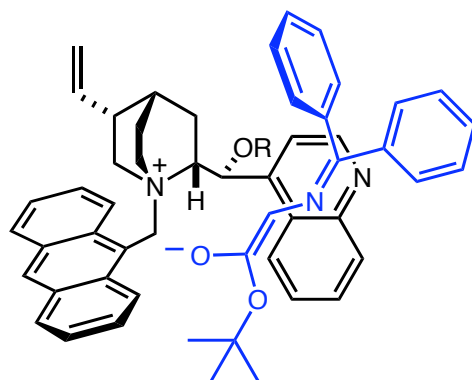


≡



cinchonidine derived

- Molecular modeling of the cinchonidine/substrate ion pair shows that the Re-face of the enolate carbon is blocked by the quinoline ring of the catalyst.



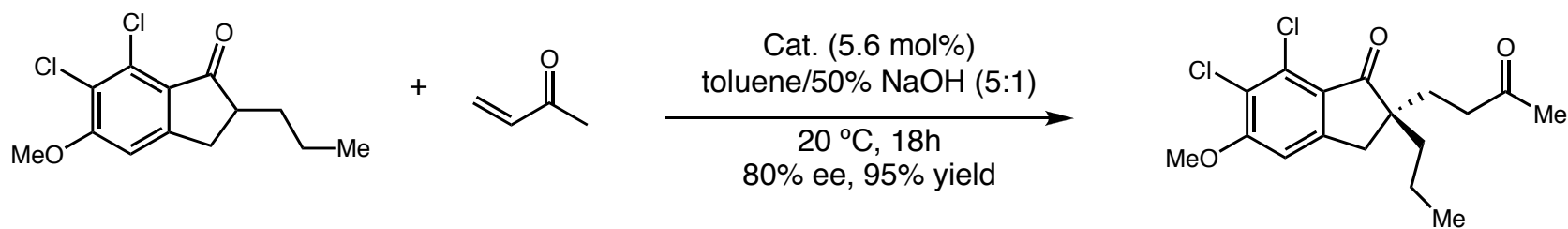
cinchonine derived

- The cinchonine derived catalyst is believed to produce the same kind of interactions

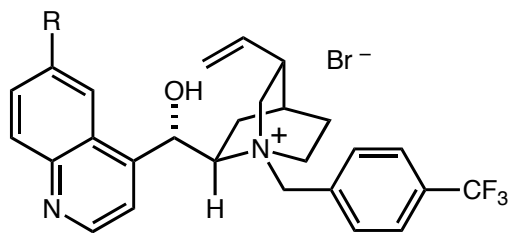
Asymmetric PTC

Enantioselective Michael Additions

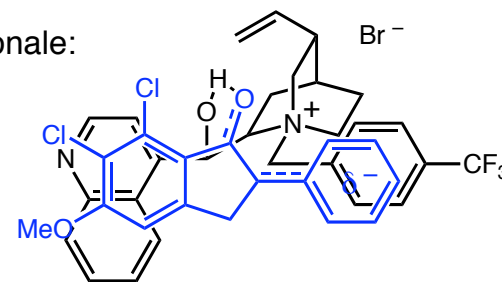
■ Early work by Merck Process showed success in the asymmetric PTC addition of indanone derivatives to methyl vinyl ketone (MVK)



Catalyst:



Rationale:

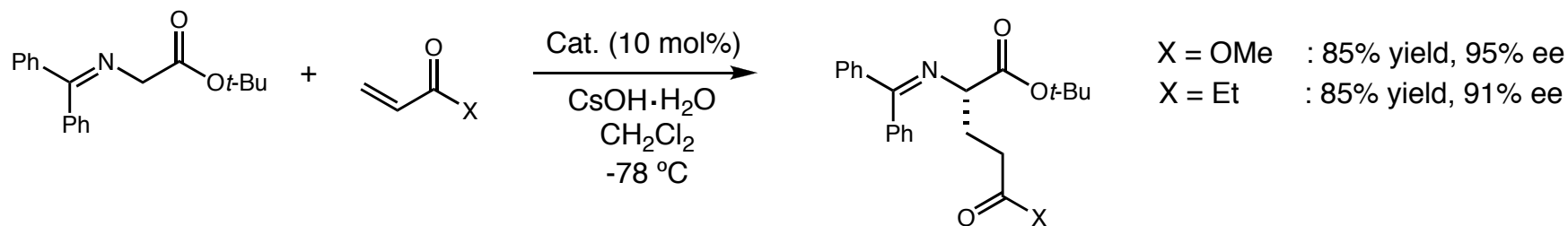


● Same stereochemical rationale as in the alkylation

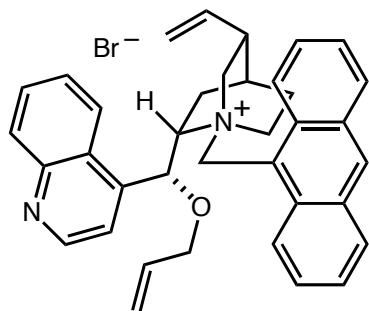
Asymmetric PTC

Enantioselective Michael Additions

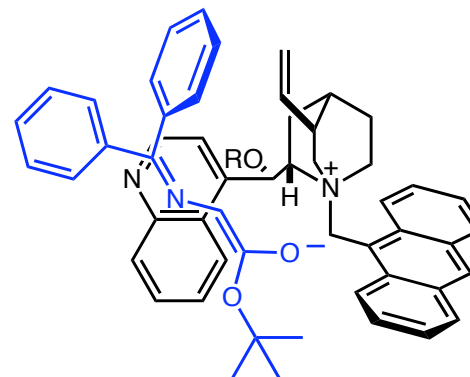
Enantioselective Michael addition of glycinate Schiff base



Catalyst:



Rationale:

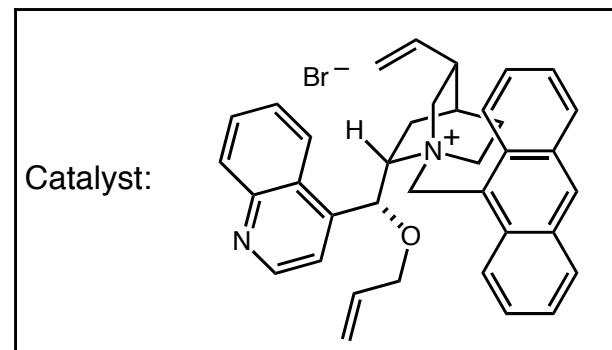
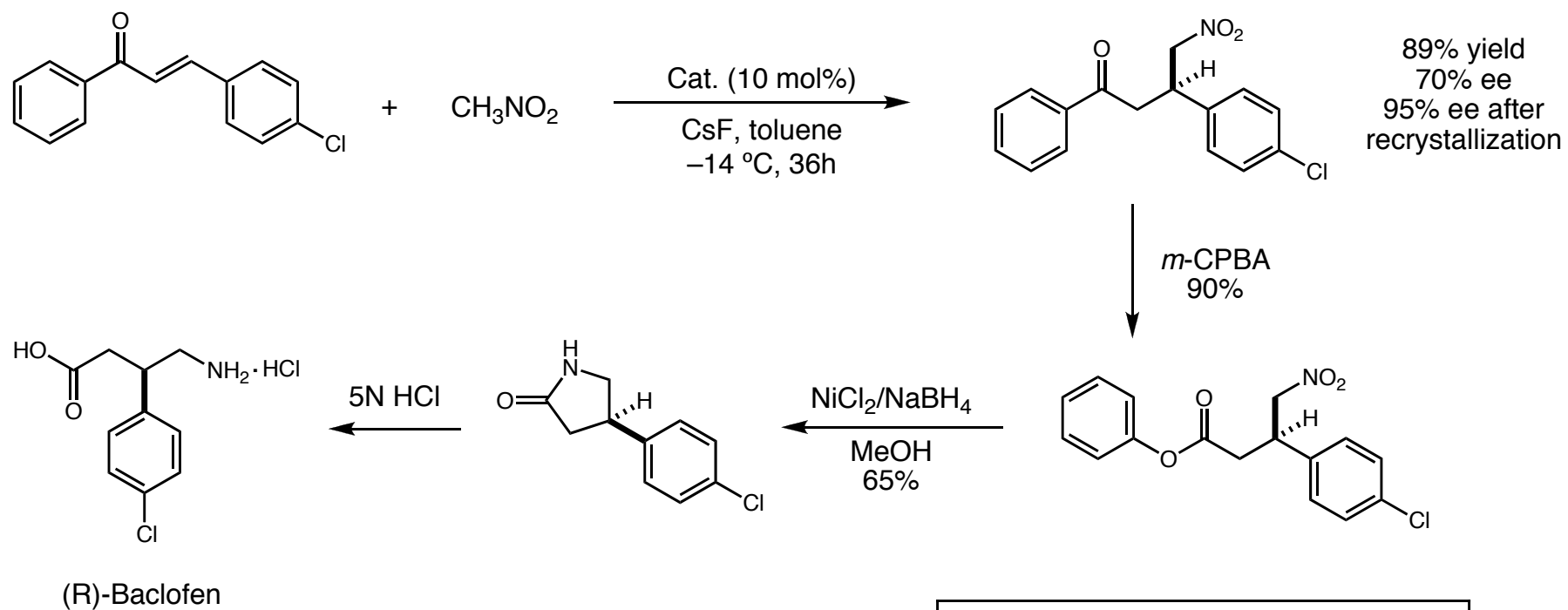


- Same stereochemical rationale as in the alkylation

Asymmetric PTC

Enantioselective Michael Additions

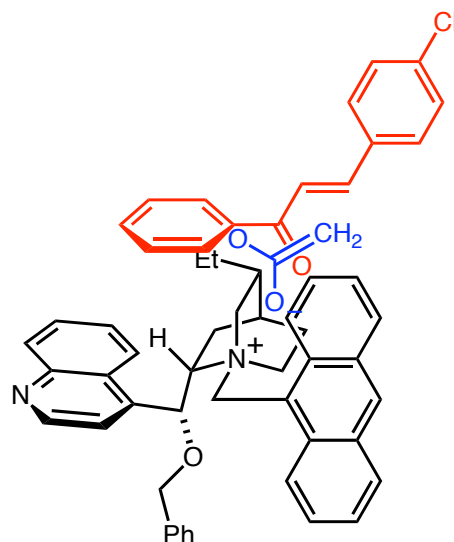
Synthesis of (R)-Baclofen



Asymmetric PTC

Enantioselective Michael Additions

■ Stereochemical rationale

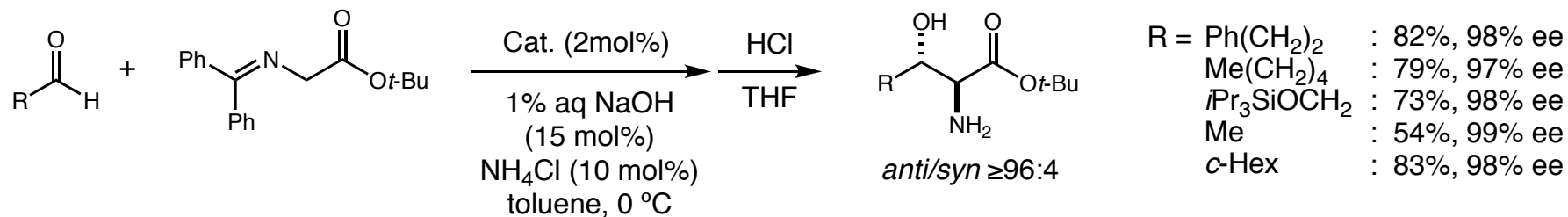


- The carbonyl oxygen of the enone is positioned so that close ion pairing with the N^+ of the catalyst can occur in the Michael transition state. The anthracenyl subunit is shielding one face for enantiocontrol

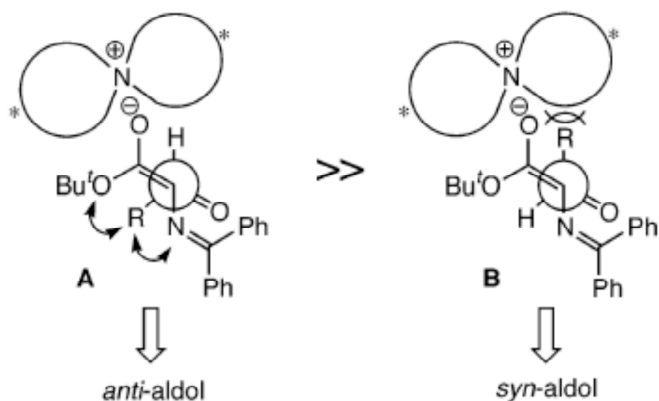
Asymmetric PTC

Enantioselective Direct Aldol Reactions

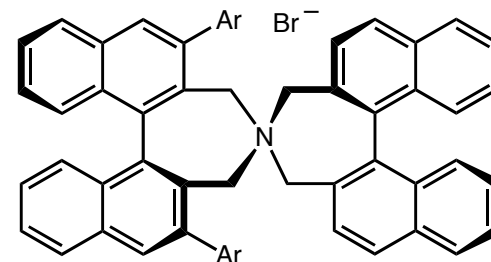
■ Maruoka's chiral N-spiroammonium salts are the most effective catalysts for asymmetric direct aldol reactions



Diastereoselective rationale:



Catalyst:

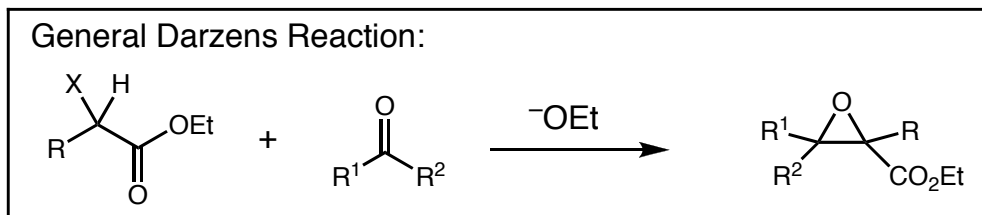


–Huge steric repulsion caused by the catalyst overwhelms the gauche interactions between the substituent (R) and both the imino moiety and the *tert*-butoxy group

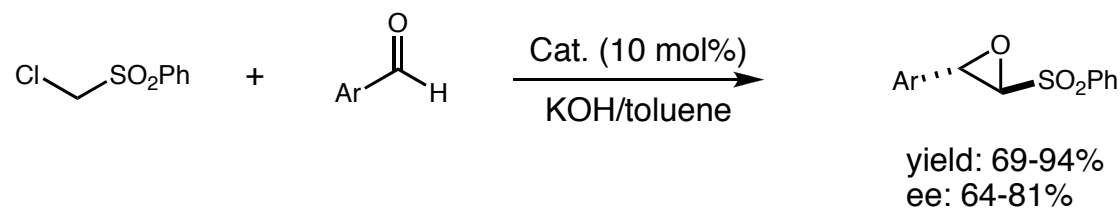
Maruoka *et al.* *Angew. Chem. Int. Ed.* **2002**, 41, 4542
 Maruoka *et al.* *J. Am. Chem. Soc.* **2004**, 126, 9685

Asymmetric PTC

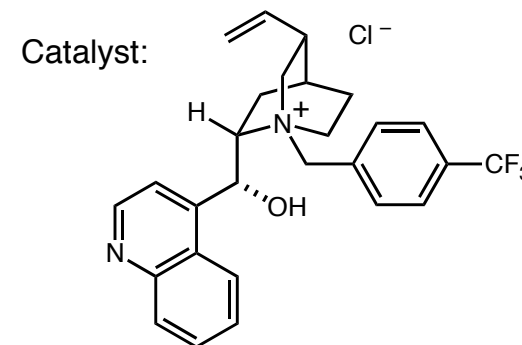
Enantioselective Darzens Reactions



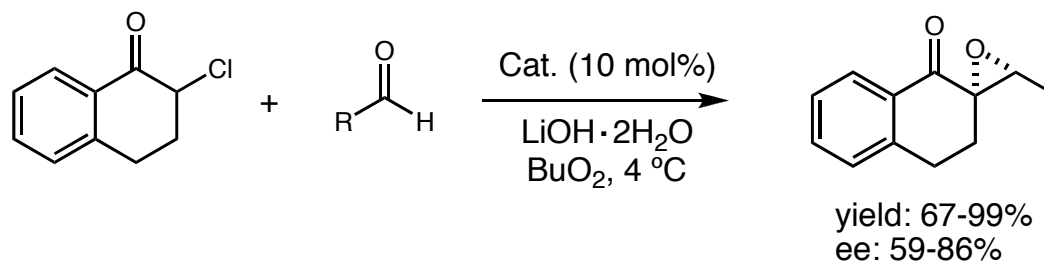
Asymmetric Darzens reactions of chloromethyl phenylsulfone



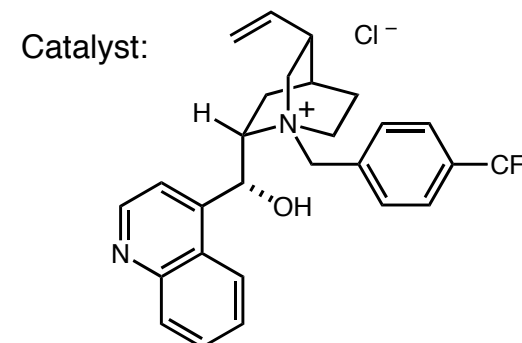
Arai, Shiori *et al. Tett. Lett.* **1998**, 39, 8299



Asymmetric Darzens reaction of with an α -chloro ketone.

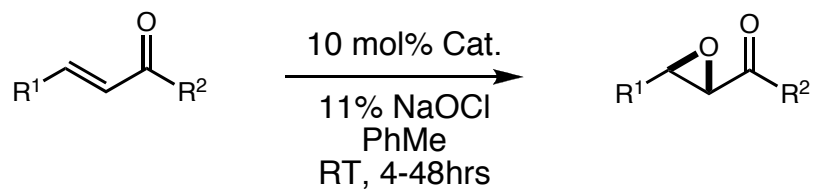


Arai, Shiori *et al. Tett. Lett.* **1999**, 55, 6375

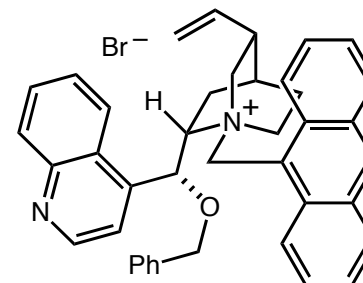


Asymmetric PTC Enantioselective Epoxidations

■ PTC is an efficient way to access chiral epoxides



Catalyst:



$R^1 = n\text{-hexyl}$

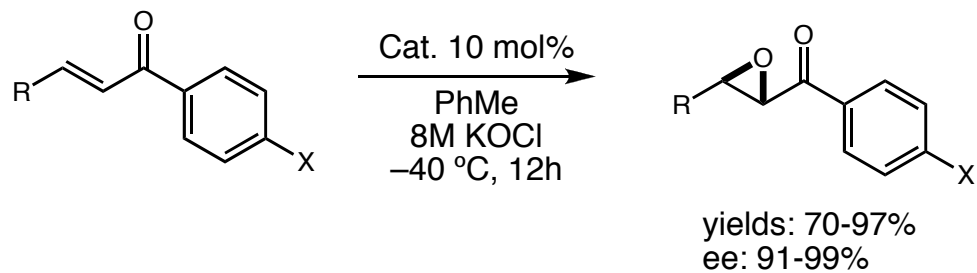
R^2	%ee	%Yield
	77	92
	90	79
	84	94
	81	93

$R^2 = \text{phenyl}$

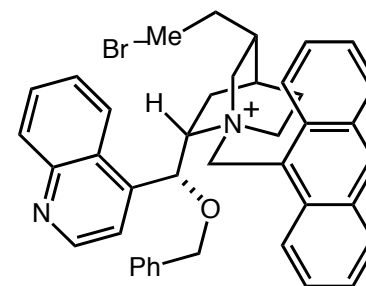
R^2	%ee	%Yield
	86	90
	83	85
	85	82
	85	40

Asymmetric PTC Enantioselective Epoxidations

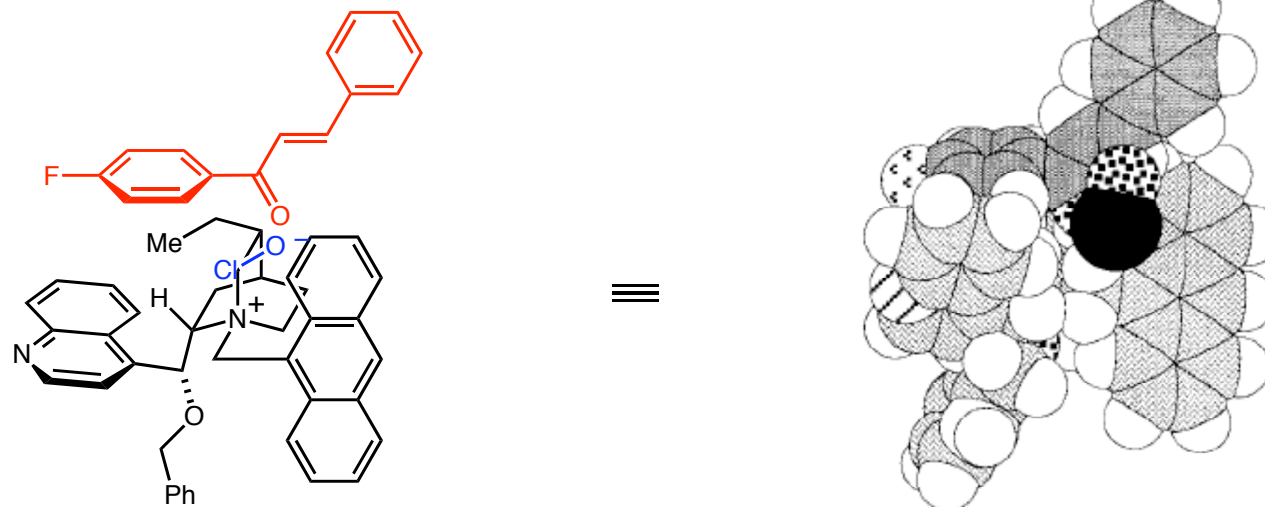
Corey's PTC chiral epoxidation:



Catalyst:



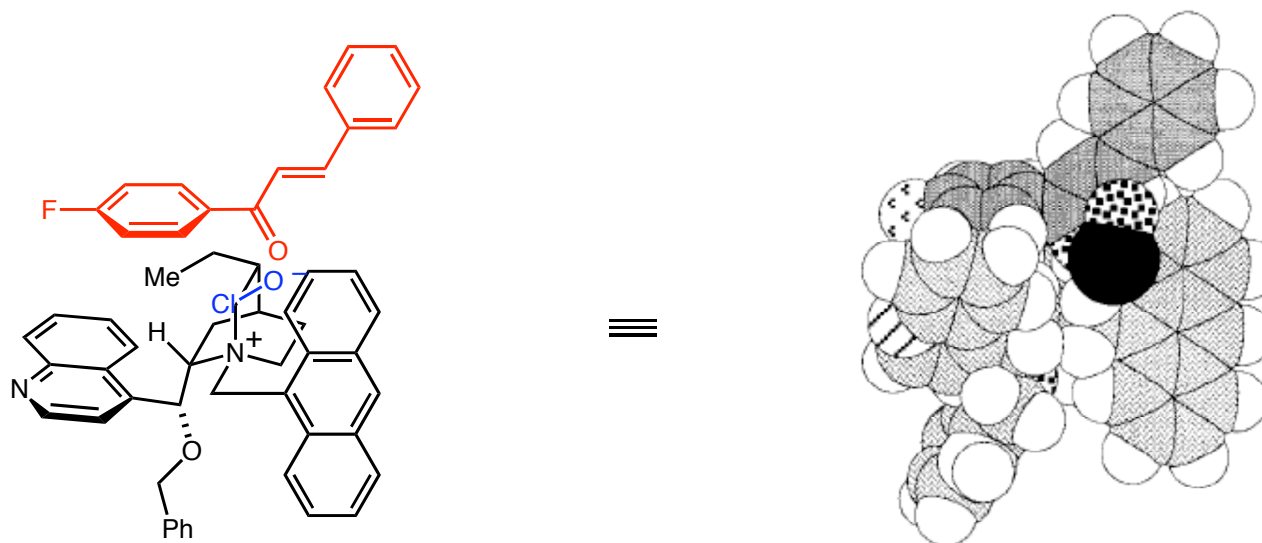
Stereochemical rationale:



Asymmetric PTC

Enantioselective Epoxidations

■ Stereochemical rationale

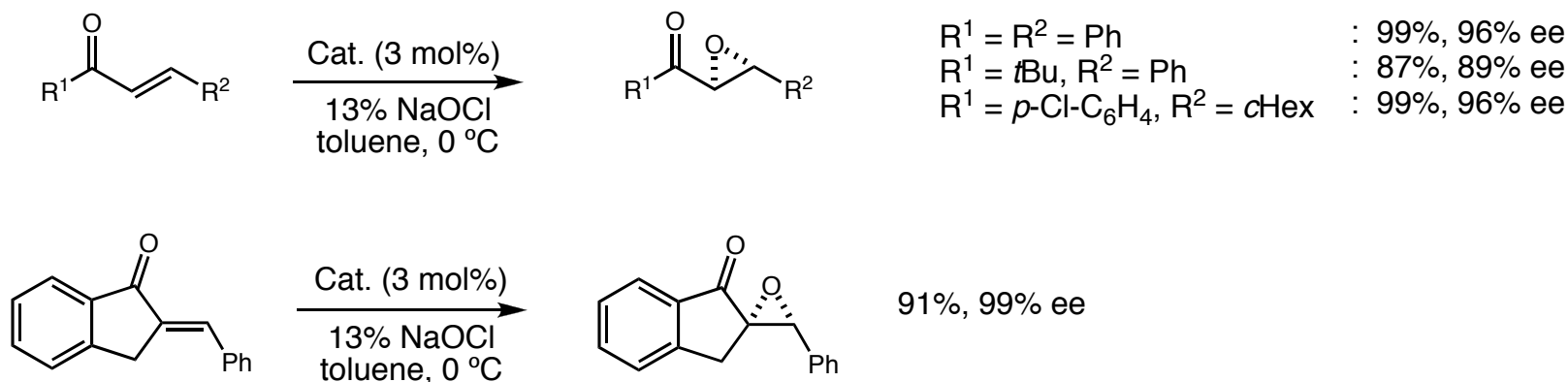


- The hypochlorite ion is contact ion-paired with the only accessible face of the charged nitrogen.
- The enone is situated with the phenyl ring containing the halogen between the ethyl group and the quinuclidine ring. The carbonyl oxygen is as close to the charged nitrogen as possible.
- In this arrangement, the hypochlorite ion oxygen is ready for nucleophilic attack at the β -carbon

Asymmetric PTC

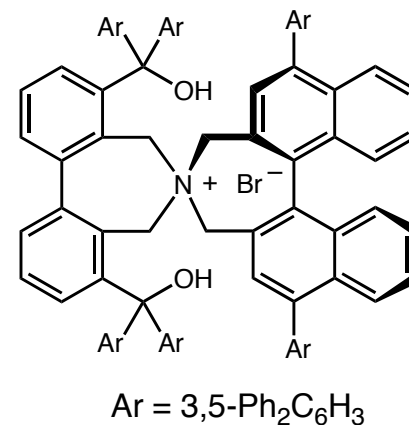
Enantioselective Epoxidations

■ Maruoka's PTC enantioselective epoxidation



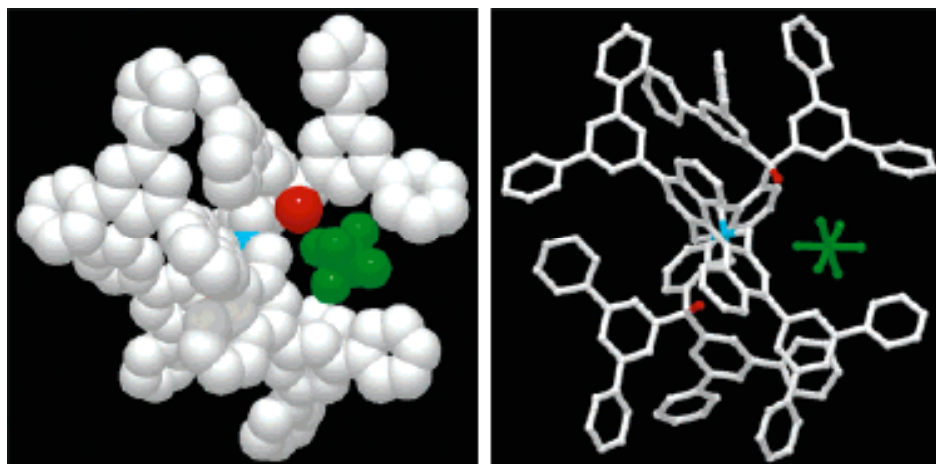
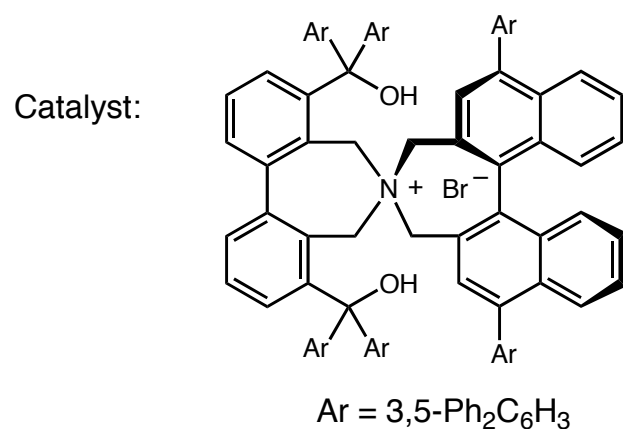
- Maruoka's chiral N-spiroammonium salt catalyst is also believed to act as H-bond donor to the enone carbonyl group

Catalyst:



Asymmetric PTC Enantioselective Epoxidations

■ Single-crystal X-ray diffraction analysis gives insight to the mechanism:



– X-ray structure of the catalyst-PF₆ complex

- Biphenyl and binaphthyl subunits of the core *N*-spiro structure are nearly perpendicular which creates an attractive chiral reaction cavity around the central nitrogen.
- The anion is located inside the cavity being surrounded by the radially spread 3,5-diphenylphenyl groups and the hydroxy moiety (red) is situated above the the nitrogen and sticks to the anion.
- Hypochlorite ions would be correctly position before the reaction and the expected hydrogen-bonding interactions would bring the enone inside the cavity to provide an ideal proximity to the hypochlorite anion resulting in efficient bond formation with rigorous enantiofacial differentiation

Conclusion

■ There are a number advantages that PTC offers over homogeneous alternatives:

- The reactions are relatively easy to perform and are highly scalable.
- PTC is "green chemistry", for this reason industrial applications are expanding
- Usually involves inexpensive reagents (NaOH, KOH, K₂CO₃ etc. instead of NaH, KHMDS *t*-BuOK, etc.)