Phase Transfer Catalysis

If a reagent in one phase can’t make a transfer into a second phase that contains the reactant, no reaction will occur!

S_N2 Reactions and Solvents

7 S_N2 reactions with alkyl halides often involve ionic nucleophiles since negatively charged nucleophiles react faster than the corresponding neutral nucleophile.

7 For example, ethyl chloride reacts much faster with sodium ethoxide than with ethanol.

\[
\text{CH}_3\text{CH}_2\text{Cl} + \text{CH}_3\text{CH}_2\text{O}^\text{Na}^- \rightarrow \text{fast} \rightarrow \text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3
\]

\[
\text{CH}_3\text{CH}_2\text{Cl} + \text{CH}_3\text{CH}_2\text{OH} \rightarrow \text{very slow} \rightarrow \text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3
\]
Solubility of Ionic Reagents

7 The problem with ionic nucleophiles in $S_N2$ reactions is the large difference in solubility of the alkyl halide and the ionic reagent.
7 In the case of ethoxide ion, we can use ethanol as a solvent. It dissolves both alkyl halide and the ionic sodium ethoxide.

\[
\text{CH}_3\text{CH}_2\text{Cl} + \text{CH}_3\text{CH}_2\text{O}^-\text{Na}^+ \xrightarrow{\text{fast ethanol}} \text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3
\]

Solubility Problems

7 However, for many ionic nucleophiles we cannot use the neutral form as solvent.
7 For example, in today’s reaction, 2-naphthol is a solid that melts above 100 °C – obviously not a reasonable solvent.
7 We also cannot use ethanol, since that would generate a second nucleophile (ethoxide anion) that could react with the halide.
Synthesis of 2-Allyl Naphthyl Ether

One solution is to use dipolar aprotic solvents (e.g. DMSO, DMF) that will dissolve both organics and salts.

Problems: Cost, toxicity, difficulty of removal

Phase transfer catalysts

What is needed is a way of getting the negatively charged nucleophile into the same phase as the organic electrophile.

Chemists at Conoco Oil Co. first showed that some quaternary ammonium salts that are soluble both in water and in organic solvents can catalyze reactions in non-polar organic solvents.

Na⁺X⁻ water soluble

H₄N⁺X⁻ water soluble

R₄N⁺X⁻ water and organic soluble
Phase transfer catalysts

The catalyst used today is benzyltributylammonium chloride. The alkyl side chains ‘hide’ the ionic character enough that these salts are soluble even in hexane.

\[ \text{Phase transfer catalysis} \]

The red boxes show the original location of the two reactants. The green box shows the quaternary ammonium salt that has brought the nucleophilic \( \text{ArO}^- \) into the organic phase.
Procedure

7 You will work with a partner for this lab
7 A reaction solution containing allyl bromide, 2-naphthol, and the catalyst in methylene chloride will be provided. You will place 2 mL in a conical reaction vial and spot a TLC plate with this mixture (only starting materials).
7 Reaction does not occur because only neutral naphthol is present.
7 You then add 2 mL of 3M NaOH.

Procedure

7 This generates a two-phase system that is stirred fast enough to mix the phases. The hydroxide ion will deprotonate naphthol to form the 2-naphtholate anion which will react with the allyl chloride.
7 You will stop stirring and remove a TLC sample of the organic layer at 10, 30, and 60 minutes.
7 Develop the TLC plate after taking the last sample.
Procedure

7 You will carefully remove the lower organic layer from the reaction vial **using the 1-mL syringe** provided in your bin,

7 Dry the solution over calcium chloride,

7 You will then take an 0.8 mL portion of this solution (measure using 1-mL syringe) and chromatograph it through a pre-prepared, silica-gel minicolumn prepared using a Pasteur pipet as the column.

Procedure

7 Any remaining 2-naphthol and the salts will be retained by the column while your product will pass through.

7 You will collect 5 fractions into pre-weighed vials and analyze each fraction by TLC to see which ones contain product.
Procedure

7 Evaporation of the methylene chloride from the fractions with product will give you your purified product. Calculate a yield (if it still contains CH₂Cl₂, your yield will be too high) and obtain an FTIR spectrum of your product.

7 Remember that your isolated product came from only 0.8 mL of your 2 mL total methylene chloride.

Cleanup

7 Dispose of all chemicals in waste bottles in hood.

7 Dispose of the mini-columns in container in hood.
Safety

7 Allyl bromide is a volatile lachrymator. An excess of this is used in the reaction and will be present until after chromatography. It should react with silica gel.

7 Evaporate solvents under the mini-hood at your station.

7 Wash hands before leaving lab.