

SCI/YCP Introduction to Physical Organic Chemistry

Jeallott's Hill Research Centre

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Outline of Day

- **Session 1** - *General Introduction: Physical Organic Chemistry (POC) for Synthetic Organic Chemists (SOC)*
- **Session 2** - *Introduction to Kinetics I*
- **Session 3** - *Introduction to Kinetics II*
- *Break*
- **Session 4** - *Techniques for Data Collection.*

Outline of Day

- **Session 5** - *Reaction Design (for 1st Order Kinetics).*
- *Lunch*
- **Session 6** - *What does it mean?*
- **Session 7** - *Taking POC for SOC further.*
- *Break*
- **Session 8** - *Case study*

General Introduction

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Introduction and Aims of Day

- Demystify Physical Organic Chemistry and particularly Reaction Kinetics Analysis for the practicing chemist.
- Provide a baseline knowledge of Kinetic theory.
- Provide “hints and tips” to ease practical work.
- Encourage people to address chemistry problems by using kinetics analysis to guide development work.

What is Physical Organic Chemistry?

- Glib Response:
 - That subject I hated at university but now find really useful in doing my job! Why didn't I pay more attention?
- A collection of equations and models that explain observed chemical behaviour accurately.

Formal Definition

- The study of:
 1. Molecular Structure & Thermodynamics
 2. Kinetics, Reactivity & Mechanisms
- These are inter-related – awareness of both is required to generate full picture of chemical understanding.

Today's Focus

- The study of:
 1. Molecular Structure & Thermodynamics
 2. Kinetics, Reactivity & Mechanisms

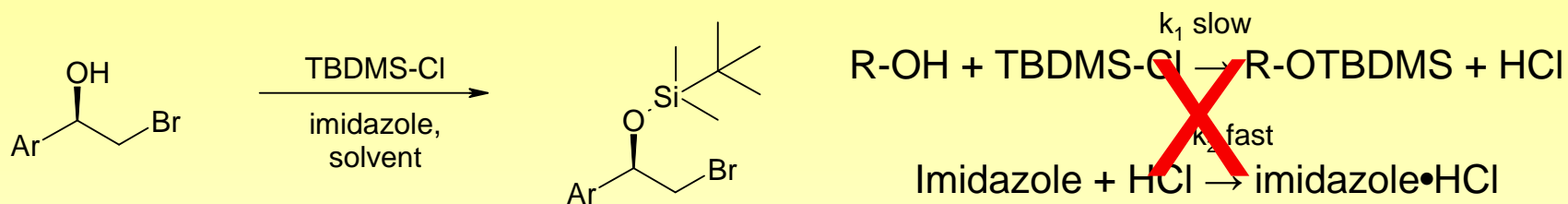
Today's Focus

- As practitioners, we are interested in chemical **reactions**.
- Study of kinetics and mechanism gives us understanding of the **reactions**.
- Structure and thermodynamics impacts the result of the reaction and the kinetics so we need **awareness** of these but the understanding of the actual **kinetic transformation** is critical to identifying improvement opportunities.

Why is it worth it?

- The “Safety Net”
 - Too easy to assume we “know” a mechanism.
 - Physical Organic Chemistry is our check to ensure that our intuition matches the reality of what is actually happening.
- Understanding
 - Trying to understand the Physical Organic Chemistry of our reactions is the quickest way to achieve true *understanding* of our chemistry.

Reactions are Complicated



- Expectation is that RDS will be silylation of alcohol by $\text{S}_{\text{N}}2\text{Si}$ mechanism.
- Imidazole should not impact RDS (if enough is present).
- This holds for solvent = CH_2Cl_2 .
- This does NOT hold for solvent = EtOAc.
 - Imidazole is clearly involved in the RDS.

Understanding

- We live in a world where technology allows hundreds of reactions to be run in parallel.
- Huge amounts of data can be generated.
- Understanding still needs to be generated from knowledge.
 - This is a human activity.

Understanding

- Thermodynamics tells us “*why*” reactions proceed to products.
- Kinetics tells us “*how*” reactants form products and explain ratios.
- Knowing the “*how*” and “*why*” provides more understanding compared to just asking “*what*”.

Benefits/Objectives of Day

- Academia
 - Facilitates fundamental understanding of reaction mechanism enabling better design of methodologies.
- Pharmaceutical/ Fine chemical industry
 - Allows robustness to be understood from scale-independent experiments.
 - Rapid assessment of relationship of side-reactions and hence purity control.