Writing Reasonable Organic Reaction Mechanisms

A Short Course

Purpose and Audience

The purpose of this course is to teach a chemist how to draw a reasonable mechanism for an organic transformation, given the starting materials, reaction conditions, and products. An ability to discern what mechanism is likely to be operating in any particular organic reaction is essential for understanding and remembering new reactions and for identifying why a particular reaction gives an unexpected product instead of the expected one. The course pays particular attention to those transformations that are widely used in the pharmaceutical and contract synthesis industries, with special emphasis on polar and organometallic reactions.

The course targets B.S. and M.S. chemists who have had no formal training in drawing reaction mechanisms. Dr. Grossman has taught the course at several pharmaceutical company sites and at American Chemical Society national meetings.

Students will benefit from this course because afterwards, they will better be able to:

- look at an organic transformation and understand how it is occurring
- formulate mechanistic hypotheses themselves, rather than relying on others to tell them what is happening
- choose appropriate reaction conditions for reactions they are executing
- identify unexpected by-products from a reaction by rationalizing how they might arise
- decide how to modify reaction conditions if their reactions don't work as well as they want

About the Instructor

Robert B. Grossman, Professor of Chemistry at the University of Kentucky, received his principal training in synthetic organic chemistry from world leaders at Princeton University and Massachusetts Institute of Technology. Dr. Grossman is the author of close to 50 papers and articles concerned with the development of new synthetic methods and the total synthesis and biosynthesis of natural products. He is also the author of *The Art of Writing Reasonable Organic Reaction Mechanisms*, on which this course is based, and the cocreator of ACE Organic, a Web-based organic chemistry homework program.

Topics covered

Basic Concepts

Conventions and first steps

Polar mechanisms: nucleophiles, electrophiles, leaving groups; acids, bases, the pK_a rule

Free-radical mechanisms: chain and nonchain

Pericyclic and transition-metal-mediated and -catalyzed mechanisms

Polar Mechanisms under Basic Conditions

Substitution and elimination at C(sp^3) via S_N2, E2, and E1cb

Addition to C(sp^2), including carbonyl additions and conjugate additions

Substitution at C(sp^2), including carboxylic acid derivatives and aromatic compounds

Substitution and elimination at C(sp^3) via other mechanisms, including carbene generation and chemistry

Polar Mechanisms under Acidic Conditions

Formation and typical reactions of carbocations
Substitution and elimination at C(sp^3) via S_N1, E1, and S_N2
Electrophilic addition to alkenes
Electrophilic aromatic substitution, including Bischler–Napieralski and Pictet–Spengler reactions
Nucleophilic addition to and substitution at electrophilic □ bonds

Pericyclic Mechanisms

Identifying and naming the four major types
1,3-Dipolar cycloadditions
Sigmatropic rearrangements, including Claisen rearrangements and the Fischer indole synthesis
"Sigmatropic rearrangements" that aren't
Heteroene reactions

Transition-Metal-Mediated and -Catalyzed Mechanisms

Conventions
Fundamental mechanistic steps or organometallic compounds
Addition reactions, including hydrogenation, hydroformylation, epoxidation, and dihydroxylation
Substitution reactions catalyzed by Pd and other metals, including hydrogenolysis, Heck reaction, cross-couplings (Suzuki, Buchwald–Hartwig, etc.), and Trost–Tsuji reaction
Rearrangements and eliminations, especially alkene and alkyne metathesis reactions

Logistical matters

Attendees are expected to obtain a copy of *The Art of Writing Reasonable Organic Reaction Mechanisms*. Dr. Grossman can arrange for a 33% discount from the list price of $54.95. No other course materials are required. The text contains a large number of mechanism problems for students to exercise the knowledge they have gained in the course, and solutions are available for free on the Web. An additional small fee provides access to the mechanism problems in ACE Organic, where students can get feedback about their proposed mechanisms.

The course is taught for two full days (8 am to 5 pm). The fee is $10,000 plus Dr. Grossman's expenses.