



Introduction to Organic Synthesis – 2020-21

MOODLE: Introduzione alla sintesi organica 2020.

TEAMS:

<https://teams.microsoft.com/l/team/19%3a78fbc87902d24c628b75f07610f95119%40thread.tacv2/conversations?groupId=0a6dff3f-8331-4e3e-bbd4-1110d9e3fd9a&tenantId=a54b3635-128c-460f-b967-6ded8df82e75>

1. Introduction to retrosynthetic analysis: general concepts (disconnection, functional group interconversion, synthon, synthetic equivalent). Parameters of retrosynthetic analysis: carbon backbone and degree of structural complexity. Functional groups and molecular symmetry. Topological relationships between functional groups. Spatial correlations and control systems.

2. One-group C-X and C-C disconnections:

- Alcohols. Disconnection to carbonyl compound and carbanion. Disconnection to ester and carbanion. Reduction of carbonyl compound. Epoxide ring opening by carbanion equivalents. Maximum structural simplification.

- Olefins. Dehydration and regioselectivity. Full disconnection of the double bond, Wittig, Julia, Peterson and Horner – Wadsworth – Emmons olefinations. Metathesis with ruthenium and molybdenum carbenoid catalysts. Alkyne hydrogenation.

- Carbonyl compounds. α , β and γ -disconnections. Control in β disconnection: selective activation, enamines. Oxidation of alcohols. Alkyne hydration. α -disconnections of carboxylic acids and related compounds.

3. C-C bond formation by Pd(0) catalysts: Suzuki, Heck, Stille, Sonogashira, Hiyama and Kumada coupling reactions.

4. Two-groups disconnections: 1,1-difunctional compounds. 1,3-difunctional compounds (aldol addition and related reactions; 1,3-dicarbonyl derivatives – Claisen, Mannich, crotonic and Dieckmann reactions). 1,5-difunctional compounds (Michael and Knoevenagel additions). 1,2-difunctional compounds (olefin oxidation, pinacol reaction; α -hydroxyacids, α -aminoacids and α -hydroxyketones – illogical disconnections, reactivity inversion and synthetic equivalents of illogical intermediates; α -halogenocarbonyl compounds). 1,4-difunctional compounds (1,4-diketones and γ -hydroxyketones). 1,6-difunctional compounds.

5. Cycles: Robinson annelation to six-membered rings, asymmetric and organocatalyzed Robinson reactions: the Wieland – Misher ketone, its use in total synthesis (Danishefsky taxol synthesis: rings C and D). Nazarov cyclization to five-membered rings; Diels – Alder reaction to six-membered rings. Three-membered rings by intramolecular cyclization and insertion reactions. Four-membered rings by [2+2] cycloadditions. Polycyclic compounds.

6. Rearrangements and radical reactions for C-C bond synthesis. Claisen, Claisen – Cope and Carrol rearrangements. Pinacol and acyloin couplings.

Introductory textbook:

S. Warren P. Wyatt - **Organic Synthesis – the disconnection approach**, 2nd edition 2008, Wiley NY ISBN 978-0-470-71237-5

Reference textbook:

F.A. Carey – R.J. Sundberg – **Advanced Organic Chemistry Part B: Reactions and Synthesis**, 5th edition 2007, Springer NY. ISBN-3: 978-0-387-68350-8

Further readings:

E.J. Corey – **The Logic of Chemical Synthesis, multistep synthesis of carbogenic compounds** – Nobel Lecture 8 dic 1990. www.nobel.se

L. Cerruti – **Bella e potente – la chimica del '900 fra scienza e società**. Editori riuniti, Roma, 2003. ISBN13: 978-8-864-73166-7