



SC

CHIM3430 Chimie organique avancée

[22.5h]

Langue d'enseignement : français

Niveau : cours de 3ème cycle

Objectifs (en terme de compétences)

Enseignement de troisième cycle à périodicité bisannuelle visant à approfondir les connaissances des étudiants en chimie organique. L'enseignement traitera de stratégies récentes pour l'obtention de cibles particulières et de méthodologies générales assurant le contrôle de la sélectivité (chémo-, régo-, stéréo- et énantiosélectivité) en synthèse

Objet de l'activité (principaux thèmes à aborder)

Le contenu de cet enseignement diffèrera d'année en année ; il abordera notamment les aspects suivants :- les nouveaux réactifs, les nouvelles réactions et les nouvelles stratégies en synthèse totale ;- l'utilisation des métaux de transition en synthèse organique ;- les développements récents en chimie radicalaire, en photochimie et en chimie hétérocyclique ;- la synthèse asymétrique ;- la chimie supramoléculaire ;- la chimie organique des dérivés du bore, du silicium et du phosphore.

Résumé : Contenu et Méthodes

Enseignants : St. Nolan (Univ. New Orleans, USA) (11 h)

R.J.K. Taylor (Univ. York, UK) (11,5 h)

Contenu du cours :

1ère partie: R.J.K. TAYLOR

Our research involves the development of new methods for organic synthesis, mainly in the areas of organometallic, organosulfur and oxidation chemistry, and their application to the preparation of bioactive natural products and potential drug candidates.

i. The synthesis of natural products and related compounds of biological interest. Major achievements include the syntheses of rocaglamide, (+)-leukotriene B₄, (-)-aranarosin, colabomycin D and (+)-manumycin A. Current targets are the tricholomenyns, the diepoxins, the preussomerins, the oxazolomycins, the oximidines, the salicylihalamides, the lobatamides the sphingomyelinase inhibitor scyphostatin, the HIV-integrase inhibitor integrastatin, and ajudazol A.

ii. The study of all aspects of the Ramberg-Bäcklund reaction (RBR) for alkene synthesis. Our mechanistic studies have been fundamental resulting in the first isolation of episulfone intermediates from Ramberg-Bäcklund reactions and thus providing absolute confirmation of the mechanism. In addition, we have developed new variants of the RBR, such as the epoxy-RBR and tandem conjugate addition-RBR, and developed novel procedures for the generation and reaction of episulfone α -anions.

A major research effort has involved synthetic applications of the RBR. Current studies include the preparation of carbocyclic nucleosides, bioactive spirocyclic β -amino acids, C-glycosylated amino acids and C-disaccharides. A major current initiative involves the development of RBR methodology to allow the direct preparation of unprotected C-glycosides using RBR methodology.

iii. The development of novel stereoselective routes for polyene synthesis. Major discoveries involve the design of stereoselective routes to conjugated dienes by organolithium addition to pyrylium salts (for *Z,E*-dienal synthesis) and double acetylene carbocupration (for *Z,Z*-diene synthesis). This methodology provided the cornerstone for new synthetic routes to leukotriene and pheromones, and the organocuprate chemistry has been widely used by others.

Current research involves the use of palladium-catalysed cross-coupling and other organometallic procedures for stereoselective polyene and enamide synthesis, and in addition we are developing new catalysts for the Stille coupling reaction of benzylic halides which give high chemoselectivity (e.g. to allow organotin reagents to couple to benzylic halides in preference to aryl halides).

iv. The design of new organometallic procedures for carbon-carbon bond formation based on organometallic reagents containing copper, lithium, phosphorus, titanium and zirconium, and the application of this methodology to natural product synthesis. This research, which is largely curiosity-driven, utilises the selectivity provided by different metals to tune reactivity to a required application. Highlights include new tandem carbolithiation procedures for cyclopentane synthesis and the development of hydroboration-Suzuki coupling procedures, and the preparation of highly functionalised organolithium reagents, for the preparation of novel amino acids.

v. The development of telescoped organic procedures which enable two, three or more conventional reactions to be carried out in a single process, thus reducing the number of operations and improving the overall yields. To date, most attention has been concentrated on telescoped oxidation processes (TOP) involving the initial manganese dioxide oxidation of alcohols followed by in situ elaboration. Thus, oxidation-Wittig trapping, oxidation-imation. and oxidation-oxime formation processes have been developed. The highlight in this area is the TOP method for the conversion of alcohols into amines in which oxidation and reduction (as well as imine formation) are achieved in a one-pot process. In addition, TOP procedures for the direct conversion of alcohols into nitriles, esters and amides have also been achieved. These processes have attracted considerable attention from industry, and are increasingly being adopted by other academic groups.

Current research involves the design of TOP procedures for the synthesis of heterocycles such as quinoxalines, pyrazines, piperazines, triazines and pyridines.

2ème partie: St. NOLAN

" Ligand Effects in Homogeneous Catalysis "

- Palladium and Nickel mediated cross coupling with emphasis on C-C and C-N bond formation
- Cationic palladium complexes and their chemistry
- Olefin Metathesis-there's a lot of material there...
- Copper mediated catalysis
- The use of N-heterocyclic carbenes in nucleophilic catalysis