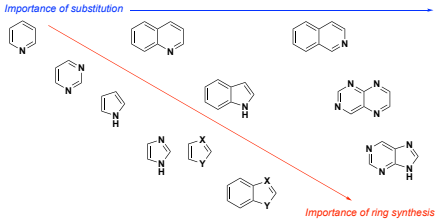
Lecture 4: Pyrroles



Basics of ring synthesis

- to synthesize or substitute, that is the question...
- ring synthesis is more logical when:
  - number of heteroatoms increases
  - number of fused rings increases
  - ring size goes from 6- to 5-membered

Pyrrole box of synthesis strategy:

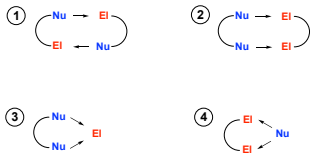
- Almost always make from scratch when:
  - 3 or more substituents
  - 3,4 disubstituted
  - polyalkylated



-Consider substitution when:
  - 2 and/or 5 substituted
  - 2,3 substituted
  - halogenated

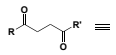


4 common cyclization reactions for any synthesis:

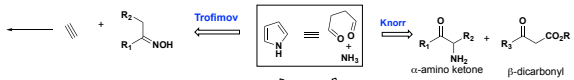


Nu = RN, O, S
El = carbonyl, imine, nitrile, halogen

POD#1



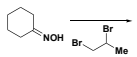
Pyrrole ring synthesis analysis:
(see Essentials I handout, PCC p. 285)

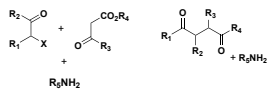


Hantzsch

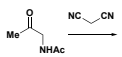
Paal-Knorr

Trofimov Pyrrole Synthesis Example:



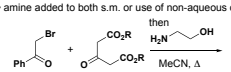


Gewald Synthesis:

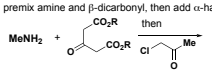


Hantzsch pyrrole synthesis details:

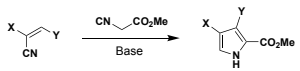
• amine added to both s.m. or use of non-aqueous conditions



• premix amine and β-dicarbonyl, then add α-haloketone

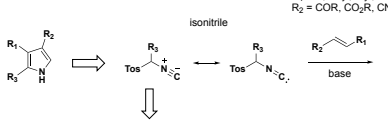


POD#2

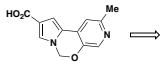


Van Leusen pyrrole synthesis

R_1 = H, alkyl, aryl, RCO, RO_2C
R_2 = COR, CO_2R, CN

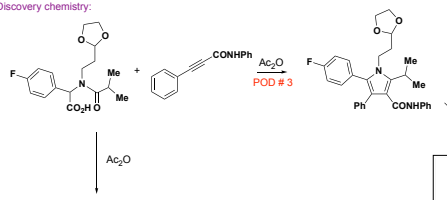


Consulting Corner:

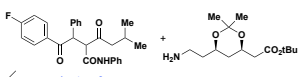


Synthesis of Lipitor[r]

Discovery chemistry:

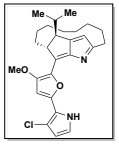


Process Chemistry:



Lecture 2

Synthesis of roseophilin



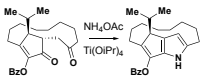
roseophilin

Fürstner:

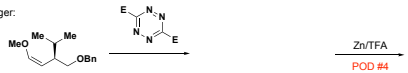


JACS, 1998, 2817

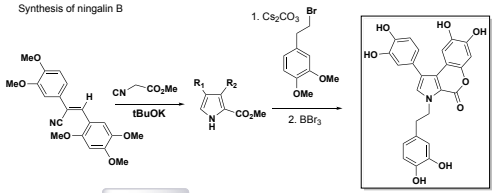
Tius:



Boger:



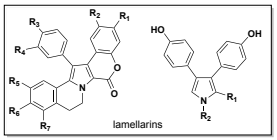
Synthesis of ningalin B



JOC, 2002, 9439

ningalin B

Synthesis of Lamellarins:



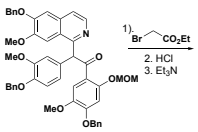
lamellarins

Fürstner: lamellarin O



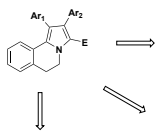
JOC, 1995, 6637

Iwao: lamellarin H and D



Tetrahedron, **1997,** 5951

POD #5



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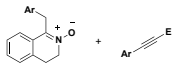
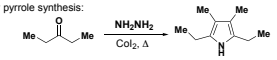
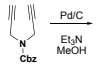


Miscellaneous methods for pyrrole sythesis:

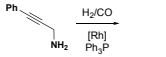
Piloty pyrrole synthesis:



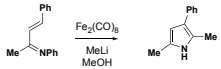
via:



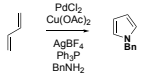
Synthesis **1989**, 262



Aust. J. Chem. **1992**, 1167

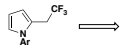


JCSPT1 **1990**, 761



JCSCC 1981, 59

Consulting Corner



Radiolabelling!
Stable label isotopes: ^{2}H, ^{13}C, ^{15}N
Radioactive isotopes: ^{3}H, ^{11}C, ^{14}C, ^{18}F

Labeled building blocks (* = radio label)
KC*N, C*O_2, Me*I, NaN*O_2, N*H_3, KF*, DCl, D_2O, D_2, H_2O*,

