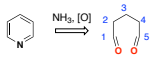
# *Lecture 7: Pyridines*

Pyridine ring synthesis analysis

Three ways to make pyridines:

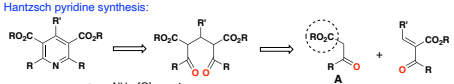
1. condensation
2. rearrangement
3. cycloaddition

1. condensation:

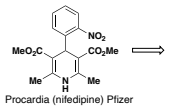



**See the PCC book's pyridine synthesis starburst (p.89) for a classification of the myriad approaches to the pyridine core but also to appreciate the utility and versatility of the 1,5-dicarbonyl approach in pyridine synthesis.**

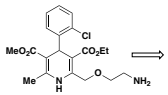
Hantzsch pyridine synthesis:




- If $CO_2R$ is replaced with CN: Guareschi–Thorpe synthesis (often for pyridones)
- If $CO_2R$ is replaced with *N*-pyridinium: Kröhnke synthesis (has one element of oxidation embedded in the s.m.)

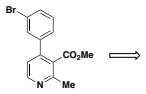



Procardia (nifedipine) Pfizer

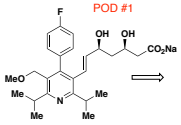



Norvasc (amlodipine)
Pfizer

**Consulting Corner**

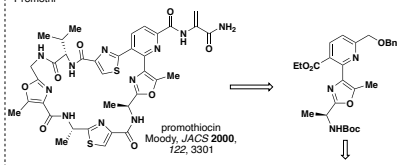



POD #1



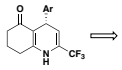

Lipobay and Baycol (cerivastatin)
Bayer (withdrawn in 2001)

Promothi

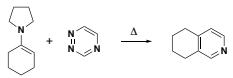



promothiocin
Moody, *JACS* **2000**, *122*, 3301



Boger pyridine synthesis



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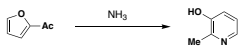
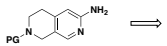


**Consulting Corner**



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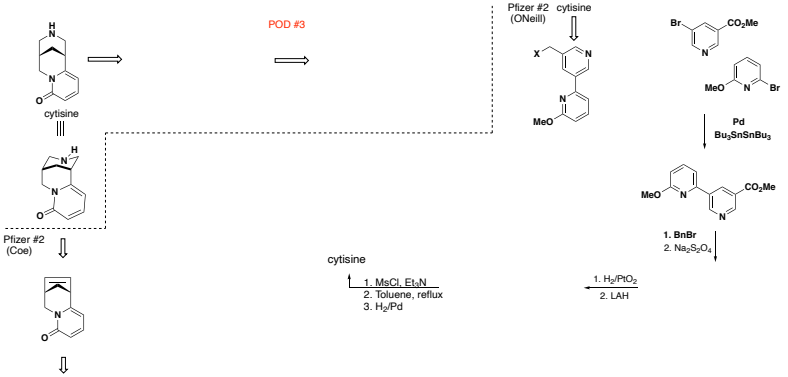

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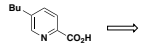


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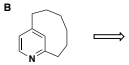


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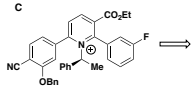


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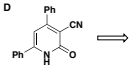


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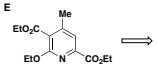


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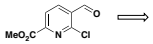
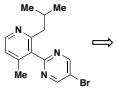
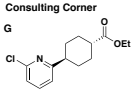



**Consulting Corner**




**Consulting Corner**

G

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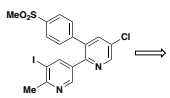
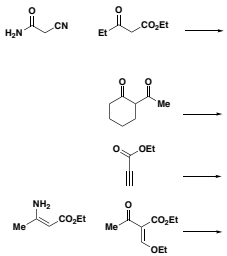



No metals allowed!

Guareschi Pyridine Scaffold



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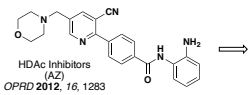

HDAc Inhibitors
(AZ)
*OPRD* **2012**, *16*, 1283

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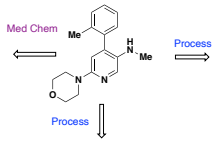
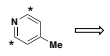
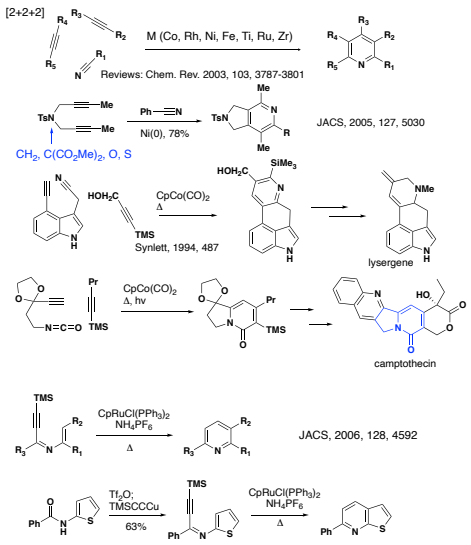
Med Chem vs Process

(Roche) POD #5




POD #6




[2+2+2]
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Reviews: Chem. Rev. 2003, 103, 3787-3801
Ni(0), 78%
JACS, 2005, 127, 5030
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CpCo(CO)2
Δ
Synlett, 1994, 487
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camptothecin
CpRuCl(PPh3)2
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Δ
JACS, 2006, 128, 4592
Tf2O;
TMSCCCu
63%