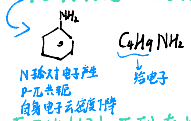
第14章 杂环化合物

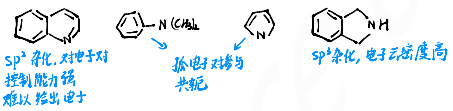
常见芳香杂环化合物的酸性、碱性和亲核性

碱性强弱取决于N上电子云密度，电子云密度越高，结合H^+能力越强，碱性越强

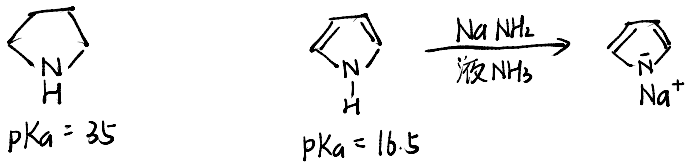
「Z14111」下列有机胺中碱性最弱的是



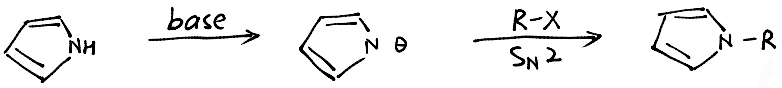
「Z14113」下列有机胺中碱性最强的是



吡咯的酸性、碱性和亲核性

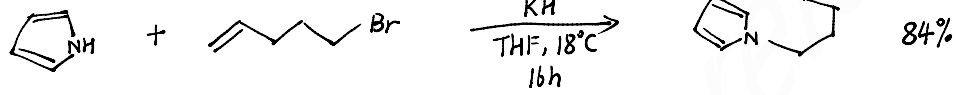


吡咯的N-烷基化和酰基化反应

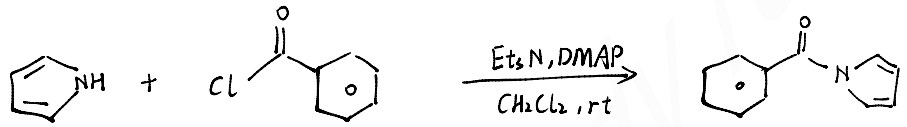


For example.

烷基化 1°

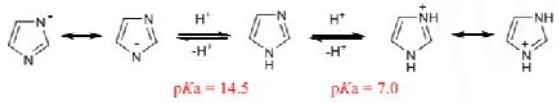


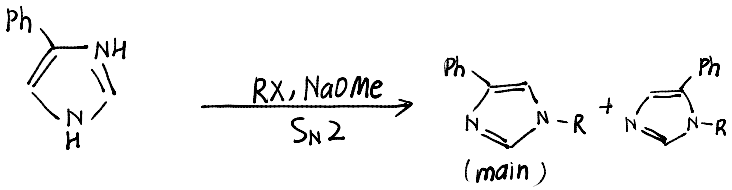
酰基化 2°



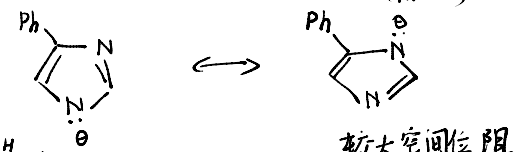
? 咪唑、噻唑和口恶唑的酸性、碱性和亲核性

咪唑具有弱酸性和弱碱性



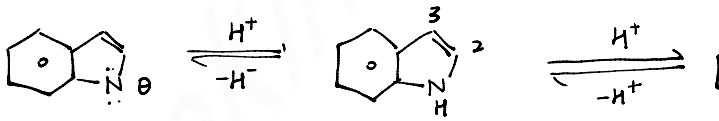


via

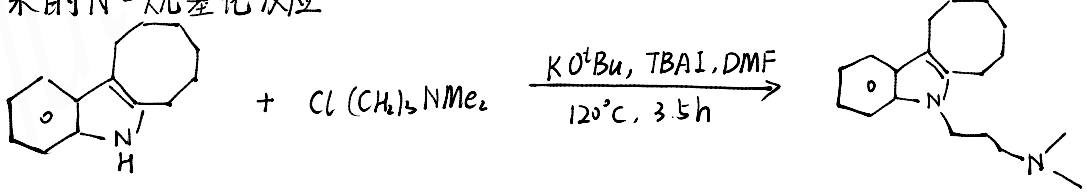


较大空间位阻

吲哚的碱性与酸性



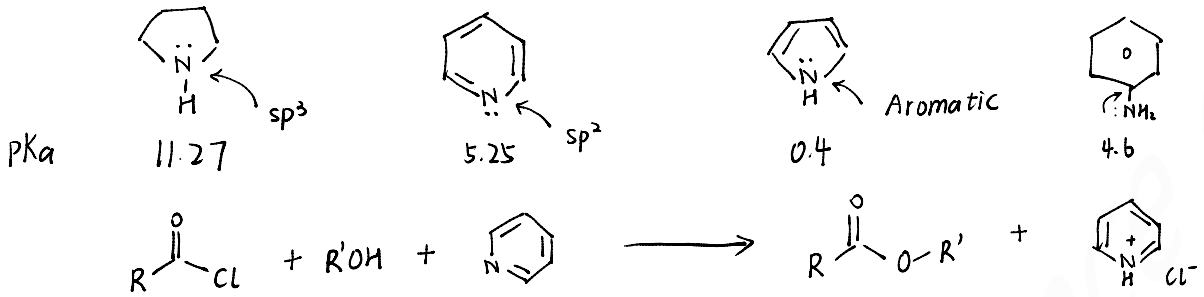
吲哚的N-烷基化反应



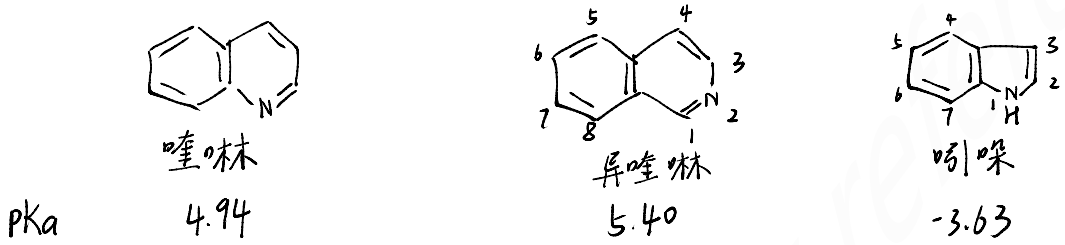
Iprindole

抗抑郁症药物

吡啶的碱性和亲核性

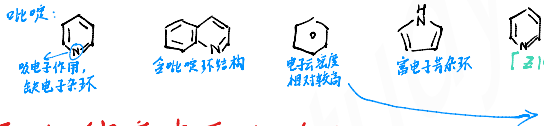


喹啉和异喹啉的碱性与亲核性

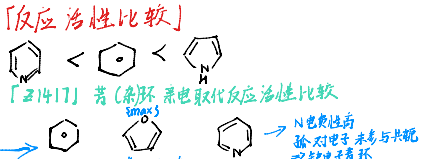


HOMO 轨道：Highest Occupied Molecular Orbital，体现给电子能力

「z1413」亲电取代活性

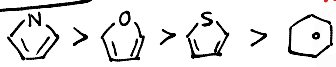


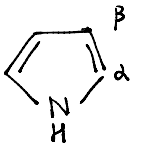
「反应活性比较」



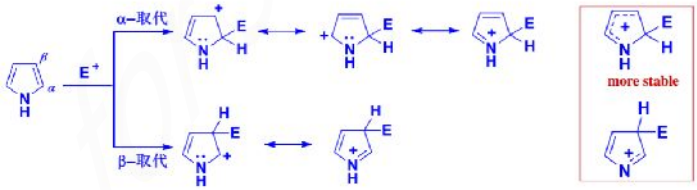
亲电取代反应

1) 吡咯 / 呋喃 / 噻吩的亲电取代反应

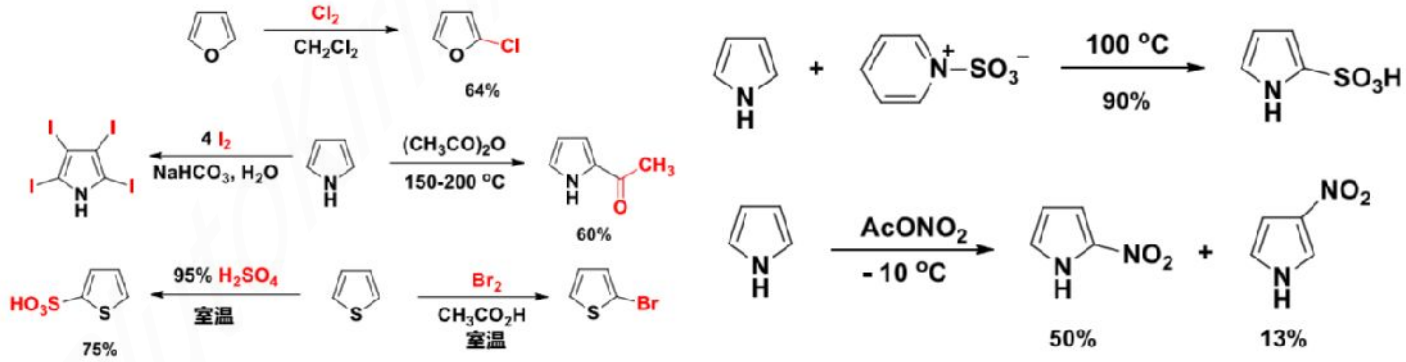
均比苯活泼，且  ；

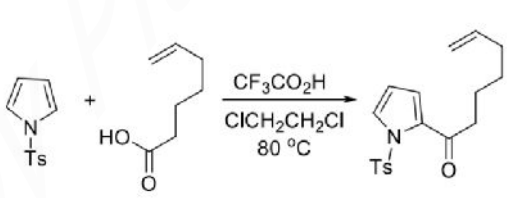


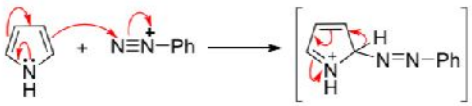
α-取代更稳定

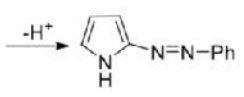


The examples are listed below:

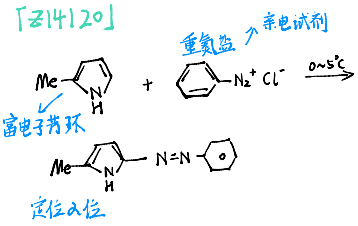




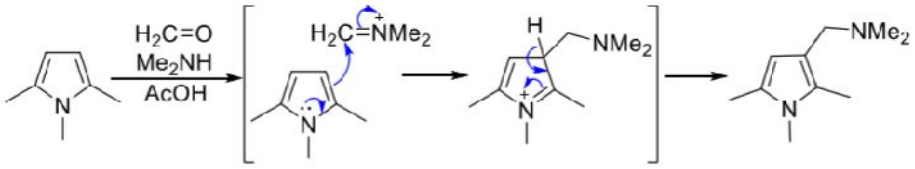




「z1412」

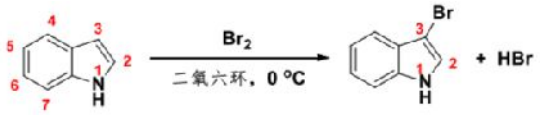


Mannich 反应



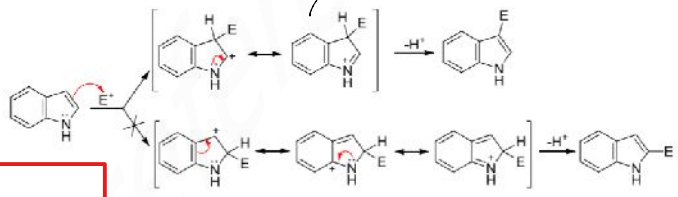
与酰胺 取代

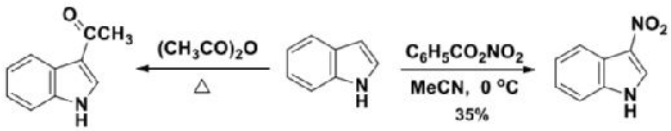
2) 吲哚的亲电取代反应



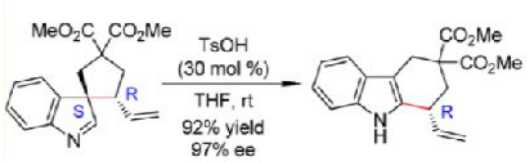
① 比苯活泼

② 优先 3-位取代 → 苯环结构保留，更稳定！

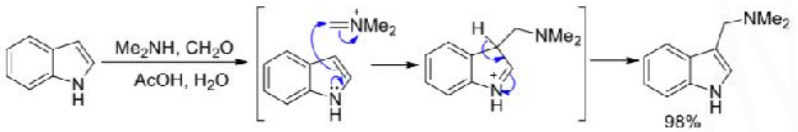




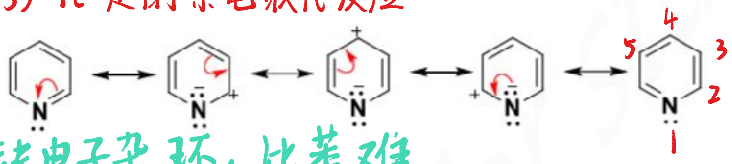
酸性条件下的1,2-迁移过程中迁移基团的构型保持



Mannich 反应

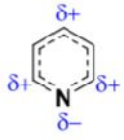


3) 吡啶的亲电取代反应

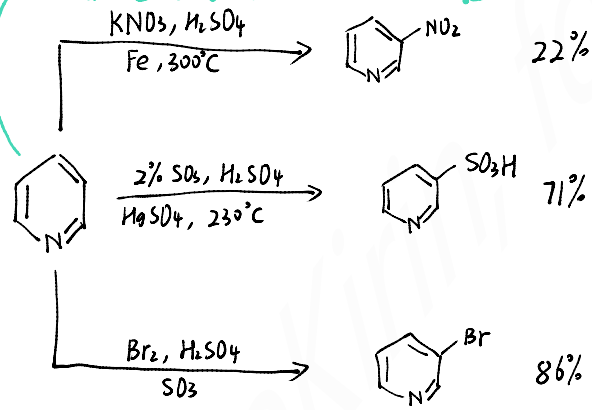


缺电子杂环，比苯难

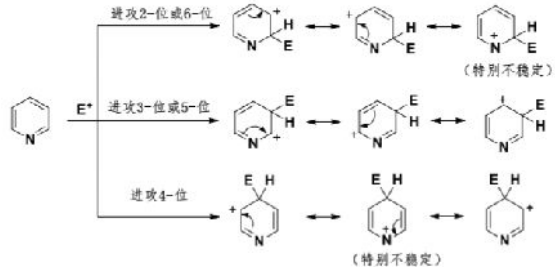
优先 3- 位取代 or 5 位



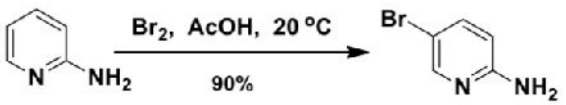
「Z1411」吡啶在 Br_2 / H_2SO_4 -SO_3 体系中进行溴代反应，其主要产物为

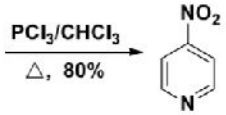


Reactivity:



Activating Pyridine Ring

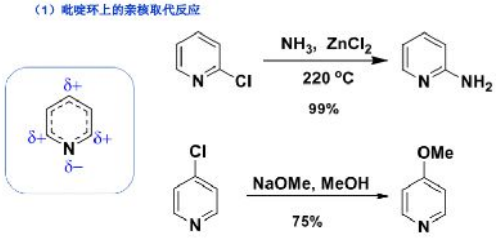


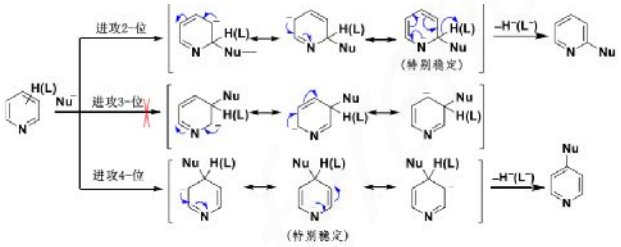


(4) 喹啉和异喹啉的亲电取代反应

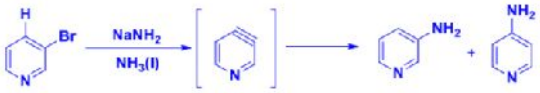
吡啶环亲核取代 ⟶ 加成-消除机理

（1）吡啶环上的亲核取代反应

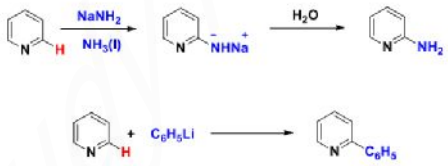




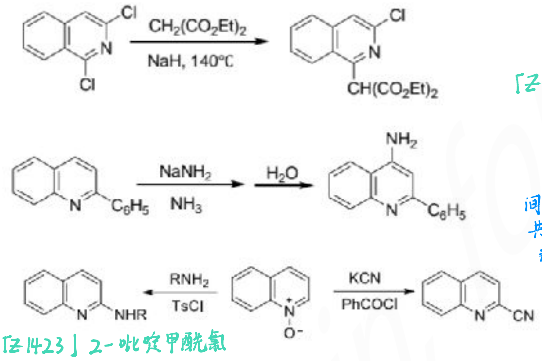
消除-加成机理（苄炔机理）



Chichibabin 反应



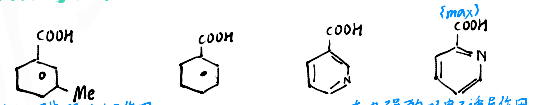
喹啉和异喹啉环亲核取代



「Z1423」2-吡啶甲酰氯

反应机理？

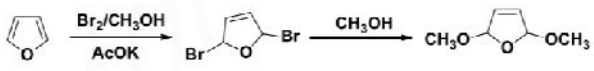
「Z1419」下列羧酸酸性最强的是



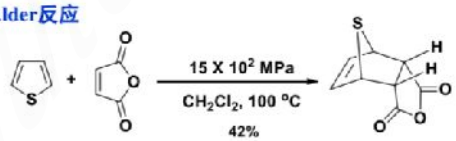
间位甲基弱给电子作用
共轭碱负电荷更集中
羧酸酸性下降

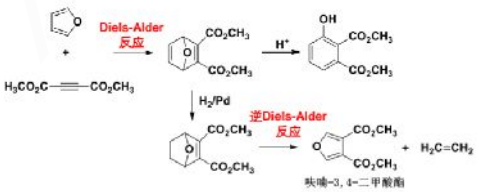
邻位N有更强的吸电子诱导作用，
共轭碱负电荷更分
酸性最强.

◆共轭加成反应

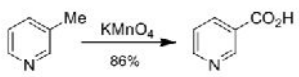


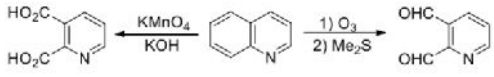
◆Diels-Alder反应



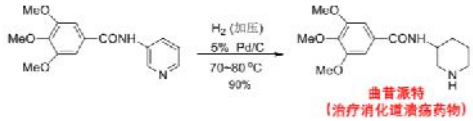


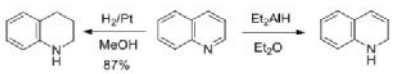
◆氧化反应





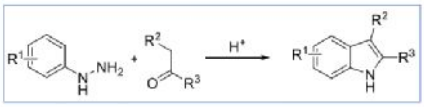
◆还原反应





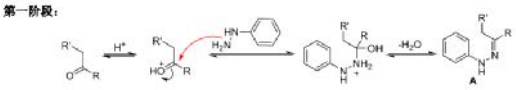
一些重要杂环化合物的经典合成方法

◆ Fischer吲哚合成法

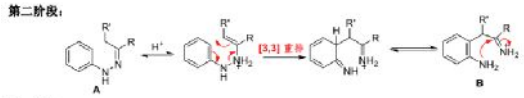


Catalysts: HCl, H_2SO_4, PPA, TsOH
BF_3 OEt_2, $ZnCl_2$, $FeCl_3$, $AlCl_3$

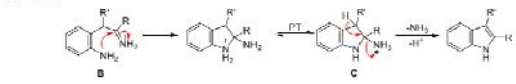
第一阶段：



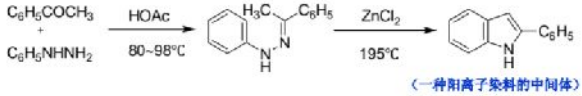
第二阶段：



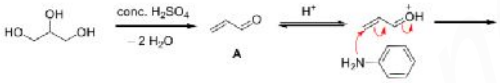
第三阶段：

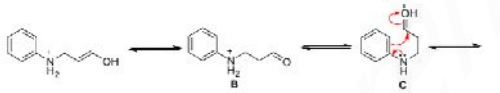


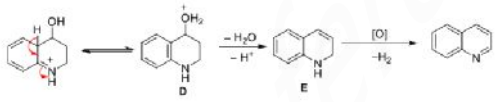
➢ 2-苯基吲哚的工业制备方法：

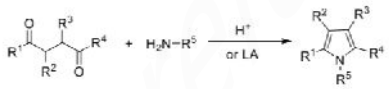


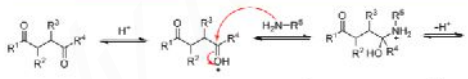
（一种阳离子染料的中间体）

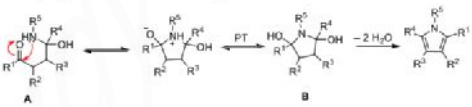










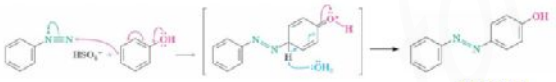


重氮盐的亲电取代反应

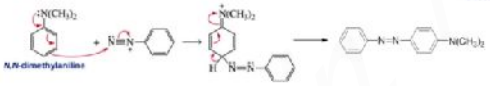
5. 重氮盐的亲电取代反应（偶联反应和偶氮化合物）

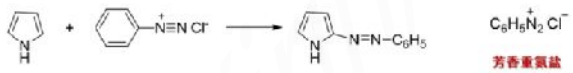
重氮盐作为亲电试剂，可在碱性条件下与带有强给电子基团的芳香族化合物（酚和芳胺—富电子芳香化合物）发生C—N键的偶联反应，生成偶氮化合物（azo compounds）：

芳香重氮盐　弱的亲电试剂　偶氮化合物

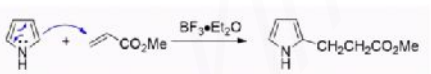


偶氮化合物



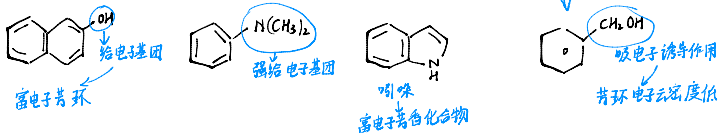


芳香重氮盐



可与富电子芳香化合物反应

[21411] 不可与芳基重氮盐反应生成偶氮化合物的为



第14章小结

◆ 吡咯/呋喃/噻吩/吡啶/吲哚/喹啉/异喹啉

◆ 酸性/碱性/亲核性

◆ 亲电取代反应：反应活性/区域选择性

◆ 经典杂环合成方法