Arenophile-Mediated Strategies for Dearomatative Functionalization of Simple Arenes

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Background and Strategy

- Bioactive compounds bearing functionalized acyclic motifs
  - oseltamivir (Tamiflu®) [antiviral]
  - morphine [analgesic]
  - serotonin (Zolof®) [antidepressant]
- Strategies for dearomatization functionalization
  - Develop dearomatization methods using simple and non-activated arenes
  - Site-selective introduction of functionalities to the parent arene with concomitant loss of aromaticity

Arenophile-mediated Dearomatized Reduction

- Dearomatization of mononuclear arenes and arene-philic modifications
  - MTAD visible light; for A: cycloreversion (NH2 or OH; then CuCl2)
  - MTAD visible light; for B: fragmentation (1. NH3 or KOH; then BzCl

Strategies for dearomatization

-的发展 dearomatization methods using simple and non-activated arenes
- Site-selective introduction of functionalities to the parent arene with concomitant loss of aromaticity

Palladium-Catalyzed Syn-1,4-Amino-functionalizations

- Syn-1,4-carboamination with Li-enolates
  - MTAD visible light, EtCN; then: ketone or ester, LDA [Pd(2.5-5.0 mol%) EtCN/THF]
- Derivatization

Synthesis of Idarubicinone via Global Functionalization of Tetracene

1. CoTPP (cat.) (PhO)2SiO2 17% 2. [Rh(0)cat.] PPh3, O2 then: MesO2Si, 42% 3. MTAD visible light, Ph(CH3)2Br (5 mol%) dbq (5 mol%) HbCat; then: AOP, 55% (gram scale) 31.18 4. 1BuOK, MesO2SiO2 79% 2. MH, Pd(OAc)2O2, 70% 3. 1BuOK, MesO2SiO2, 79%

Synthesis of Sertraline from naphthalene

1. H2 (1 atm) Rh/C, A 98% 2. Br, Ph2PCH2Ph; KOH, A 51% 3. MTAD, CH2Cl2 visible light, Pd(dba)2 (5 mol%) (S)-DIFLUORPHOS

Reaction Set-ups

- LED lights used
- Small-scale reactions in test tubes (~0.5 mmol)
- Large-scale reactions in glass bottle (up to 20 mmol scale)

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