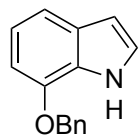


Total Synthesis of (+)-Haplophytine

Hirofumi Ueda, Hitoshi Sato, Koji Matsumoto, Kenji Sugimoto, Tohru Fukuyama, Hideotoshi Tokuyama

Angew. Chem. Int. Ed. **2009**, *48*, 7600



1-9

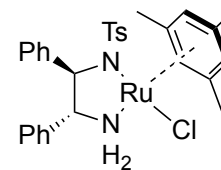


10-14

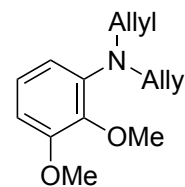


- 1) POCl₃, DMF
- 2) MeNO₂, NH₄OAc, reflux
- 3) LAH, THF
- 4) succinic anhydride
- 5) SOCl₂, MeOH
- 6) H₂, Pd/C, DCM/MeOH
- 7) MsCl, Et₃N, DCM
- 8) POCl₃, DCM, reflux
- 9) **1** (cat.), HCO₂H/Et₃N, DMF

- 10) CbzCl, DIPEA, DCM
- 11) NIS, DCM
- 12) AgOTf, **2**, DCM
- 13) LiOH, MeOH/H₂O
- 14) SOCl₂, DMF, *then* DIPEA



1



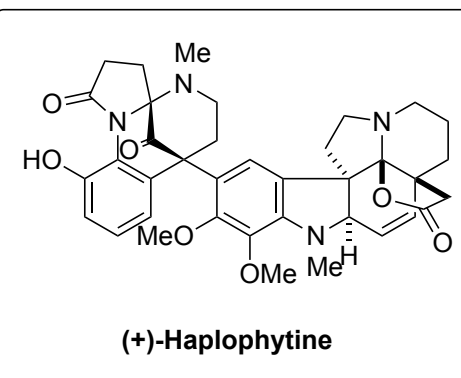
2

1) Name Reaction?

8) Name Reaction?
Mechanism?

9) Who developed this catalyst?

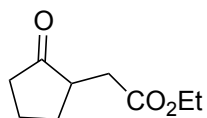
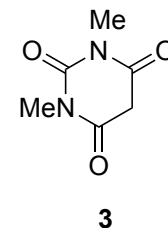
11-12) Mechanism?



15-19



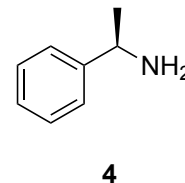
- 15) Pd(PPh₃)₄, **3**
- 16) FmocCl, NaHCO₃, 1,4-dioxane/
H₂O
- 17) *m*CPBA, NaHCO₃, DCM, rt
- 18) piperidine, DMF, rt
- 19) *i*-AmylONO, 6M HCl/MeOH/MeCN
then SnCl₂
hint: reductant for diazonium salt



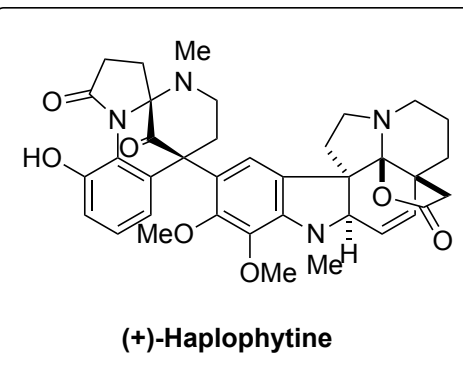
20-28



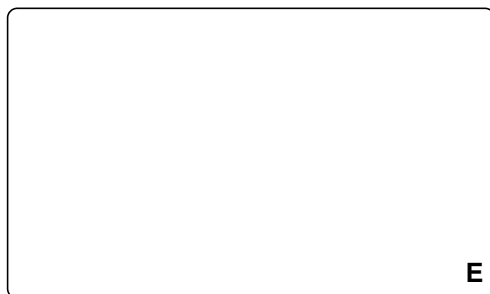
- 20) **4**, benzene, reflux
- 21) ethyl thioacrylate, THF, *then*
AcOH, EtOH/H₂O
- 22) NaBH₄, CeCl₃·7H₂O
- 23) MsCl, Et₃N, Me₃N·HCl
- 24) IZn(CH₂)₃NPhth, [PdCl₂(PPh₃)₂]
(10 mol%)
- 25) TMSO(CH₂)₂OTMS, TMSOTf,
DCM
- 26) LiCl, Li₂CO₃, 4Å MS, DMPU/
HMPA (*hint*: elimination)
- 27) MeHNH₂, EtOH, reflux
- 28) NsCl, Et₃N, DCM



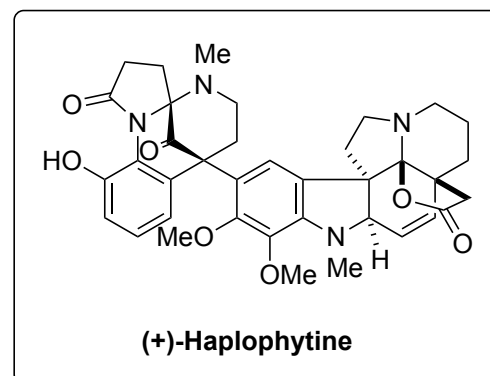
- 24) Name Reaction?
- 25) Who developed this
reaction?



29-34



35-42



- 29) O₃, DCM/EtOH, *then* NaBH₄
- 30) MsCl, DCM/pyridine
- 31) PCC, celite, DCM
- 32) CsCO₃, 3 Å MS, MeCN, 70°C
hint: ring formation
- 33) 1M HCl, THF
- 34) PhSH, Cs₂CO₃, MeCN, *then*
evaporation
then silica gel, DCM, reflux *then*
TMSCHN₂

34) Mechanism?

- 35) **D**, 50% aq. H₂SO₄
- 36) PTSA, *t*-BuOH, 80°C
- 37) benzeneseleninic anhydride
- 38) BBr₃, Me₅-Benzene
- 39) HCHO (37%), NaBH₃CN, AcOH
- 40) 1M NaOH, MeOH, 60°C
- 41) K₃[Fe(CN)₆], NaHCO₃,
t-BuOH/H₂O

36) Name Reaction?