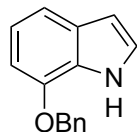


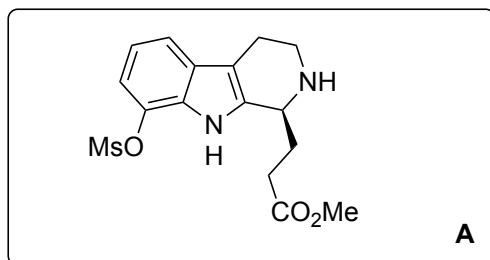
# Total Synthesis of (+)-Haplophytine

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

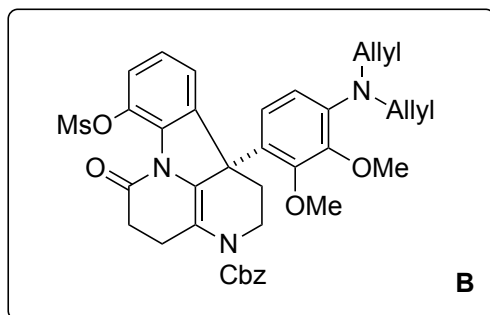
*Angew. Chem. Int. Ed.* **2009**, *48*, 7600



1-9

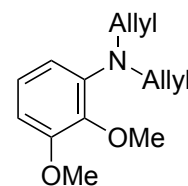
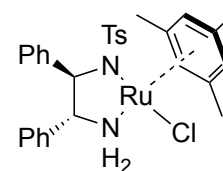


10-14



- 1) POCl<sub>3</sub>, DMF
- 2) MeNO<sub>2</sub>, NH<sub>4</sub>OAc, reflux
- 3) LAH, THF
- 4) succinic anhydride
- 5) SOCl<sub>2</sub>, MeOH
- 6) H<sub>2</sub>, Pd/C, DCM/MeOH
- 7) MsCl, Et<sub>3</sub>N, DCM
- 8) POCl<sub>3</sub>, DCM, reflux
- 9) **1** (cat.), HCO<sub>2</sub>H/Et<sub>3</sub>N, DMF

- 10) CbzCl, DIPEA, DCM
- 11) NIS, DCM
- 12) AgOTf, **2**, DCM
- 13) LiOH, MeOH/H<sub>2</sub>O
- 14) SOCl<sub>2</sub>, DMF, *then* DIPEA

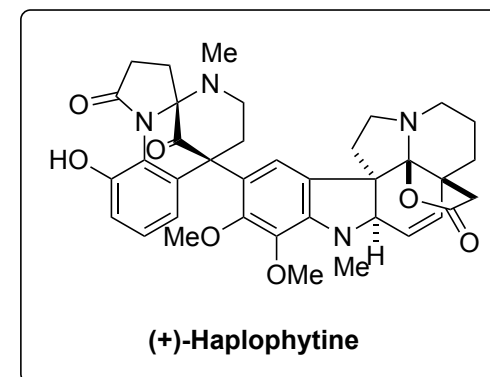


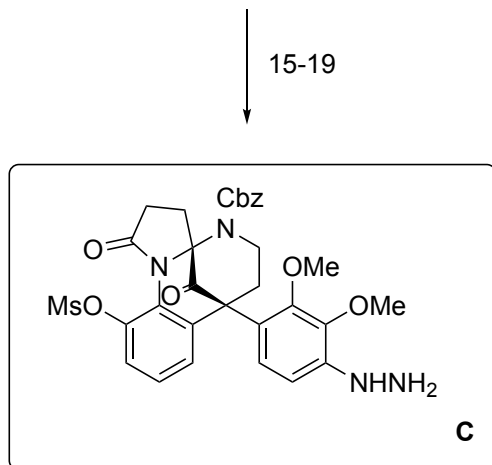
1) Name Reaction? Vilsmeier-Haack

8) Name Reaction? Bischler-Napieralski  
Mechanism? see below

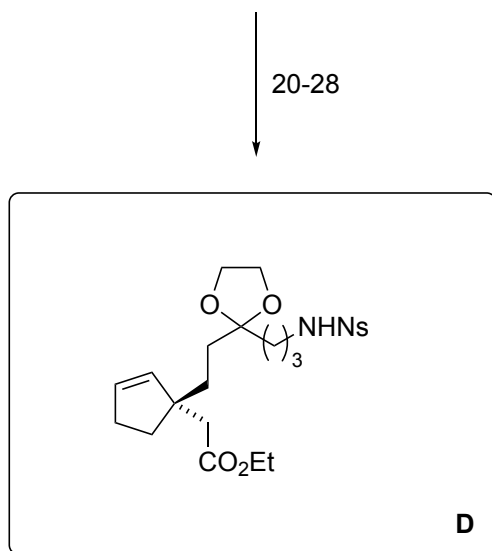
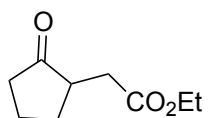
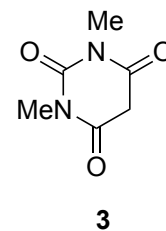
9) Who developed this catalyst? Noyori

11-12) Mechanism? see below

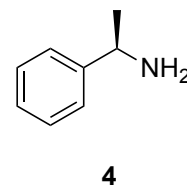




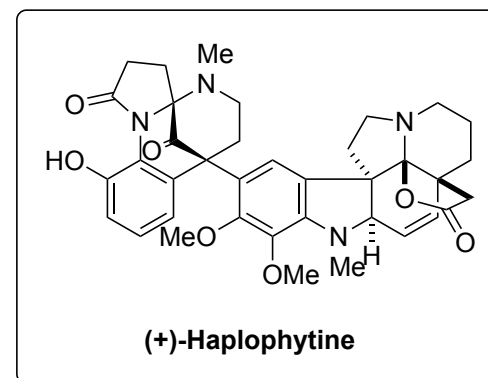
- 15) Pd(PPh<sub>3</sub>)<sub>4</sub>, **3**
- 16) FmocCl, NaHCO<sub>3</sub>, 1,4-dioxane/  
H<sub>2</sub>O
- 17) *m*CPBA, NaHCO<sub>3</sub>, DCM, rt
- 18) piperidine, DMF, rt
- 19) *i*-AmylONO, 6M HCl/MeOH/MeCN  
then SnCl<sub>2</sub>  
*hint*: reductant for diazonium salt



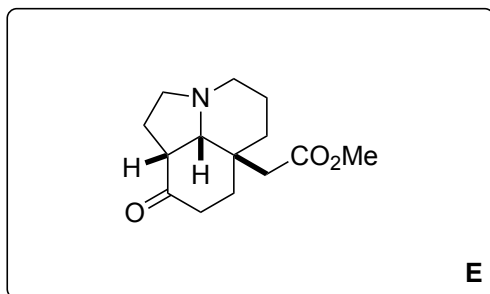
- 20) **4**, benzene, reflux
- 21) ethyl thioacrylate, THF, *then*  
AcOH, EtOH/H<sub>2</sub>O
- 22) NaBH<sub>4</sub>, CeCl<sub>3</sub>·7H<sub>2</sub>O
- 23) MsCl, Et<sub>3</sub>N, Me<sub>3</sub>N·HCl
- 24) IZn(CH<sub>2</sub>)<sub>3</sub>NPhth, [PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>]  
(10 mol%)
- 25) TMSO(CH<sub>2</sub>)<sub>2</sub>OTMS, TMSOTf,  
DCM
- 26) LiCl, Li<sub>2</sub>CO<sub>3</sub>, 4 Å MS, DMPU/  
HMPA (*hint*: elimination)
- 27) MeNHNH<sub>2</sub>, EtOH, reflux
- 28) NsCl, Et<sub>3</sub>N, DCM



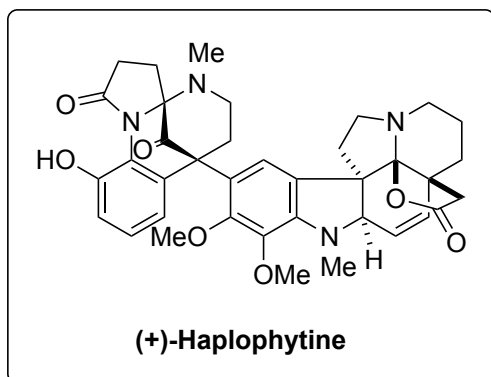
- 24) Name Reaction? Fukuyama Coupling
- 25) Who developed this Noyori  
reaction?



29-34



35-42



- 29)  $O_3$ , DCM/EtOH, *then*  $NaBH_4$
- 30) MsCl, DCM/pyridine
- 31) PCC, celite, DCM
- 32)  $CsCO_3$ , 3 Å MS, MeCN, 70°C  
*hint*: ring formation
- 33) 1 M HCl, THF
- 34) PhSH,  $Cs_2CO_3$ , MeCN, *then* evaporation  
*then* silica gel, DCM, reflux *then*  $TMSCHN_2$

34) Mechanism?  
see below

- 35) **D**, 50% aq.  $H_2SO_4$
- 36) PTSA, *t*-BuOH, 80°C
- 37) benzeneseleninic anhydride
- 38)  $BBr_3$ ,  $Me_5$ -Benzene
- 39) HCHO (37%),  $NaBH_3CN$ , AcOH
- 40) 1M NaOH, MeOH, 60°C
- 41)  $K_3[Fe(CN)_6]$ ,  $NaHCO_3$ ,  
*t*-BuOH/ $H_2O$

36) Name Reaction?  
Fischer Indole Synthesis

## Mechanisms

