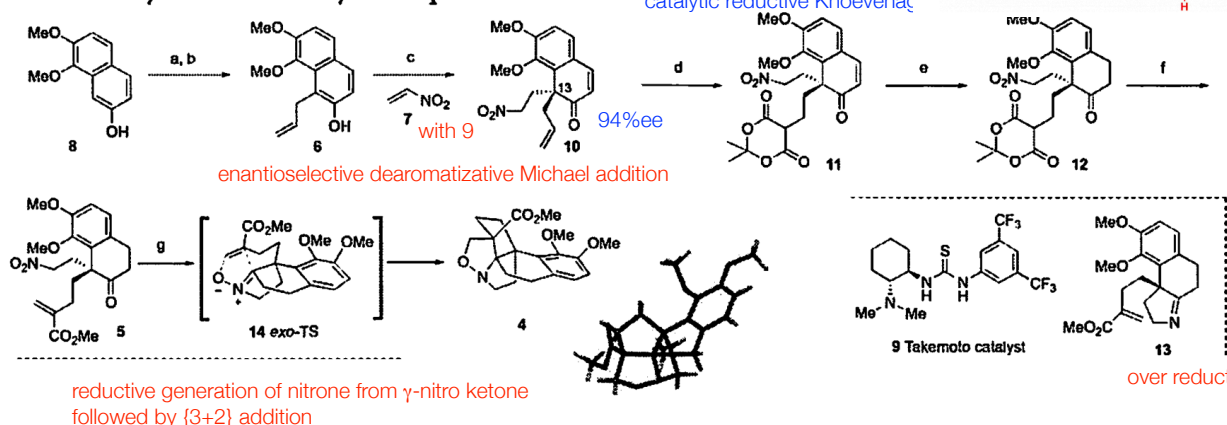


**Enantioselective Total Synthesis of (+)-Stephadiamine:** Baochao Yang, Guang Li, Qian Wang, and Jieping Zhu\*  
 Cite this: *J. Am. Chem. Soc.* 2023, 145, 9, 5001–5006

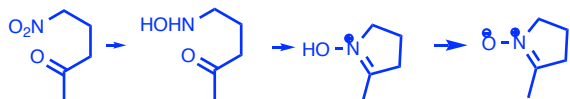
**Scheme 2. Synthesis of Pentacyclic Propellane 4<sup>a</sup>**



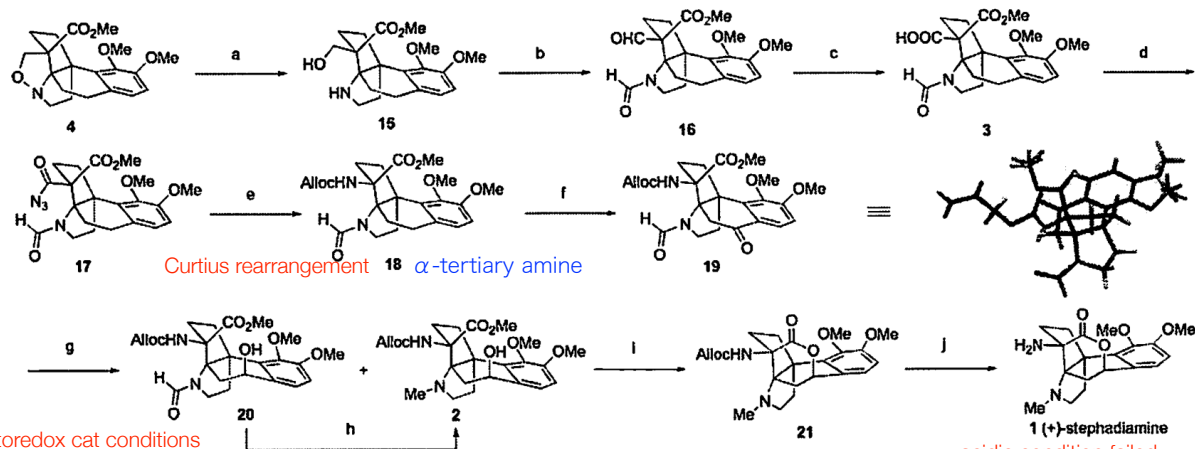
<sup>a</sup>Reagents and conditions: (a)  $\text{K}_2\text{CO}_3$ , allyl bromide, 82%. (b) 1,2-dichlorobenzene,  $180\text{ }^\circ\text{C}$ , 98%. (c) **6**, Takemoto catalyst (1*R*, 2*R*)-**9**, 3 Å MS, 66%, 94% ee. (d)  $\text{OsO}_4$ ,  $\text{NaIO}_4$ , 2,6-lutidine, dioxane/water

( $v/v = 3:1$ ), then Meldrum's acid, Hantzsch ester, *L*-proline, 72% over 2 steps. (e) *L*-Selectride, THF,  $-78\text{ }^\circ\text{C}$ , 78%. (f) Eschenmoser's salt, MeOH,  $65\text{ }^\circ\text{C}$ , 64%. (g)  $\text{Na}_2\text{S}_2\text{O}_4$ , MeOH/ $\text{H}_2\text{O}$ ,  $80\text{ }^\circ\text{C}$ , 63%.

optimized



**Scheme 3. Total Synthesis of (+)-Stephadiamine (1)<sup>a</sup>**



<sup>a</sup>Standard conditions: (a) Zn, AcOH,  $70\text{ }^\circ\text{C}$ , quantitative. (b)  $\text{HCO}_2\text{Et}$ ,  $70\text{ }^\circ\text{C}$ , sealed tube, then DMP, DCM, 84%. (c)  $\text{NaClO}_2$ ,  $\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$ , 2-methyl-2-butene, THF/ $\text{H}_2\text{O}$ /*t*BuOH,  $0\text{ }^\circ\text{C}$ . (d) DIPEA, DPCP, THF,  $0\text{ }^\circ\text{C}$ , then  $\text{NaN}_3$  in  $\text{H}_2\text{O}$ ,  $0\text{ }^\circ\text{C}$ , 82% over 2 steps. (e) allylic alcohol (*c* 0.06 M), 4 Å MS,  $80\text{ }^\circ\text{C}$ , 72%. (f)  $[\text{Ir}(\text{d}(\text{CF}_3)\text{ppy})_2:(5,5'\text{-dCF}_3\text{bpy})]\text{PF}_6$ ,  $\text{Cu}(\text{TFA})_2 \cdot (\text{MeCN})_2$ ,  $\text{K}_2\text{HPO}_4$ ,  $\text{H}_2\text{O}$ , MeCN, rt, air, blue LED, 83%. (g)  $\text{NaBH}_4$ ,  $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ , MeOH,  $-15\text{ }^\circ\text{C}$ , 20, 86%. (h)  $\text{NaBH}_4$ ,  $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ , TFA, THF,  $-15\text{ }^\circ\text{C}$ , 46%, 24% of recovered **20**. (i) NaH, THF,  $0\text{ }^\circ\text{C}$ , 93%. (j)  $\text{Pd}(\text{PPh}_3)_4$ , dimedone, THF, rt, 72%. DMP = Dess-Martin periodinane; DIPEA = *N,N*-diisopropylethylamine; DPCP = diphenyl chlorophosphate; dimedone = 5,5-dimethylcyclohexane-1,3-dione.

diverse oxidative conditions failed