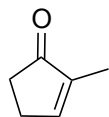
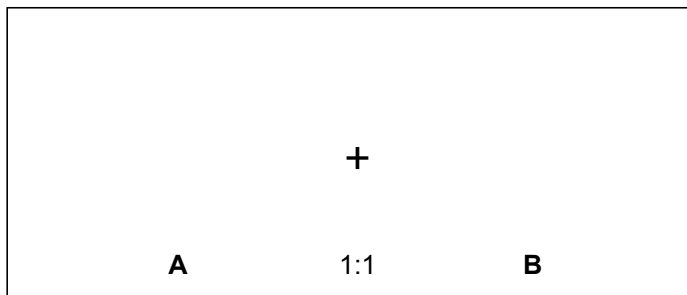


## Total Synthesis of Hyperforin

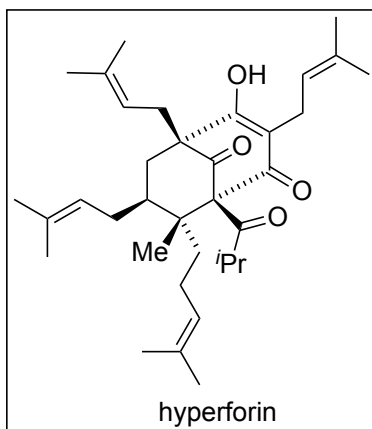
Ting, C. P.; Maimone, T. *J. Am. Chem. Soc.* **2015**, *137*, 10516



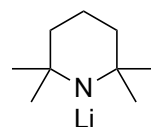
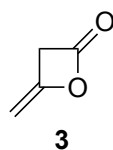
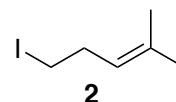
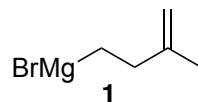
1 – 5



6 – 10



- 1) **1**, CuBr·DMS, LiCl, TMSCl
- 2) MeLi·LiI *then* **2**, HMPA *then* TsOH, Δ
- 3) LDA, prenyl bromide
- 4) LTMP, **3**
- 5) TMSCHN<sub>2</sub>, MeOH, Toluene



Lithium tetramethyl piperidine (LTMP)

- 6) PhI(OAc)<sub>2</sub>, KOH, MeOH
- 7) LTMP, TsCl
- 8) LTMP, *i*-PrCOCN,
- 9) *i*-PrMgBr·LiCl, LDA, Li(2-Th)CuCN, *then* prenyl bromide
- 10) LiCl, DMSO, Δ

What are the two major types of cuprates?

*Hint:* in step 2 there is also an isomerization

Propose a mechanism for step 4

What is the pK<sub>a</sub> of LTMP?

Only one isomer is taken forward. The other can be recycled, how could this be done (2 steps)

Propose a mechanism for step 6

*Hint:* Step 7 is a chlorination

Suggest a reason that LDA was added in step 9.