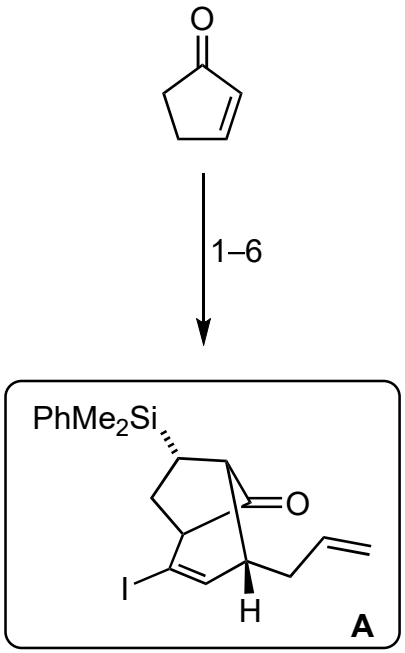
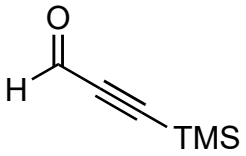
Total Synthesis of Chalcitrin

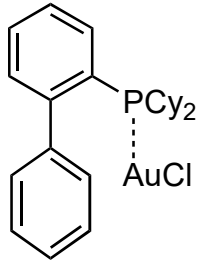
M. Yang, F. Yin, H. Fujino, S. A. Synder, *J. Am. Chem. Soc.* **2019**, *141*, 4515–4520.



1) $PhMe_2SiLi$, MeLi, CuCN, *then* **1**
2) MOMBr, DIPEA
3) $AgNO_3$, NIS
4) KHMDS, TIPSCl
5) **2**, AgOTf
6) allylTMS, $SnCl_4$

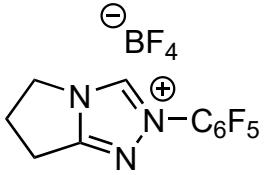


1



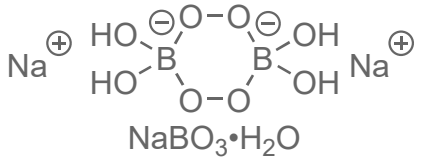
2

7) $(Sia)_2BH$, *then* $NaBO_3•H_2O$
8) DMP
9) **3**, NEt_3

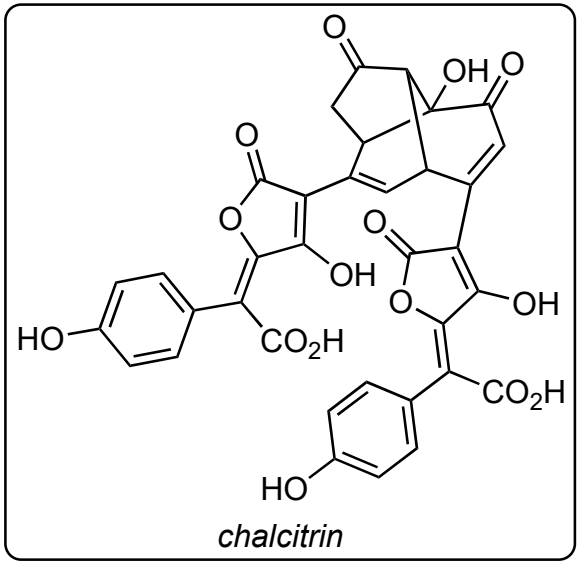


3

1) Hint: No methyl addition.
5) Name of the reaction?
Conia–ene
6) Who developed this? The reaction is more known with carbonyls instead of allylic halides, ethers, and acetates.
Hosomi–Sakurai
7) Who developed this chemistry (nobel prize 1979)? Structure of $NaBO_3•H_2O$?
Herbert C. Brown
9) Mechanism? Name of the reaction?
see below; Acyloin/Benzoin addition

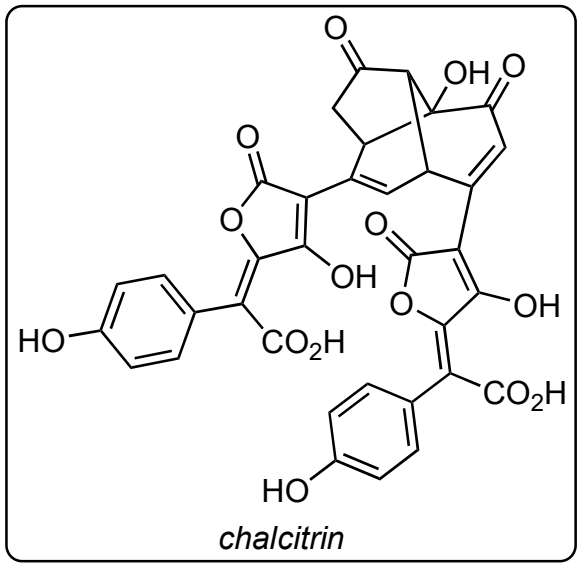


$NaBO_3•H_2O$



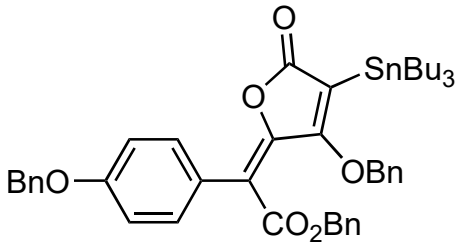
chalcitrin

10–17



chalcitrin

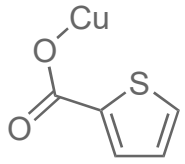
10) BF_3, AcOH
11) CSA, $CH(OMe)_3$, MeOH, *then* H_2O_2, KF, $NaHCO_3$
12) DMP
13) *t*-BuOOH, PIDA, Cs_2CO_3
14) LiOH
15) $(COBr)_2$, DMF
16) $Pd(PPh_3)_4$, CuTC, **4**
17) BBr_3



4

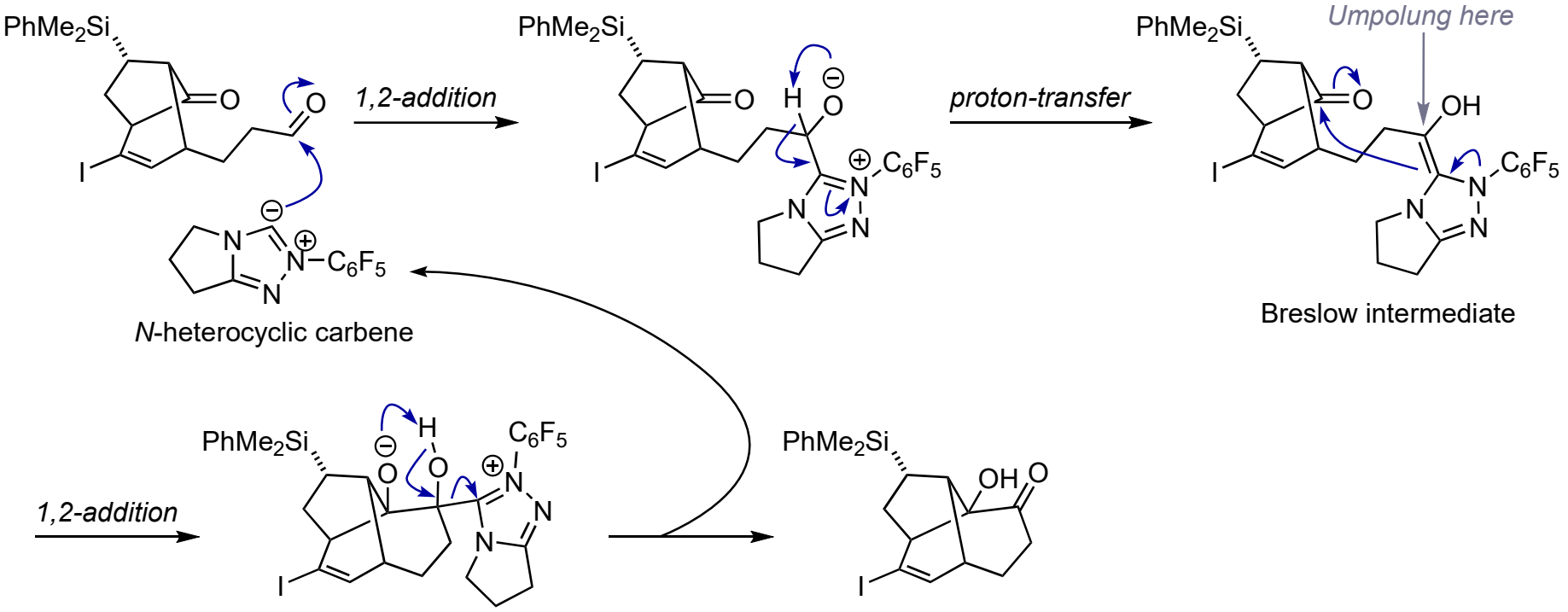
10–11) Name of the reaction?
Tamao–Fleming oxidation
11) Hint: An enol ether is formed in the first part of reaction 11.
13) Mechanism?
see below
16) Name of the reaction?
Structure of CuTC? What is the role of copper(I) here?
Stille coupling; Cu(I) is accerlerating the Stille coupling due to increased transmetalation rates; different mechanisms could explain this, see also: *J. Org. Chem.* **1994**, *59*, 5905–5911.

NMR hint for compounds with readily protonated/deprotonated species: Only when synthetic chalcitrin was titrated in DMSO-d_6 with NaDMSO-d_5 did its NMR data match that of the natural.



CuTC

Mechanism of step 9:



Proposed mechanism of step 13:
Org. Lett. **2010**, *12*, 2128–2131.