Enantioselective Synthesis of (-)-Halenaquinone

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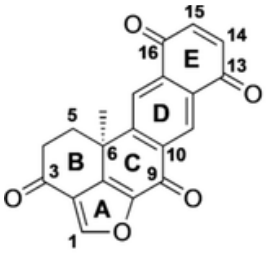
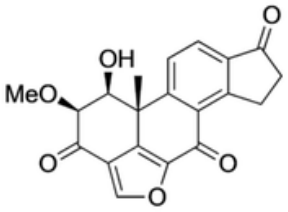
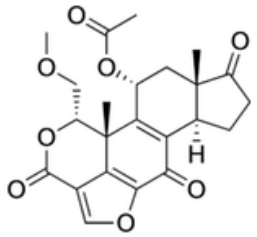


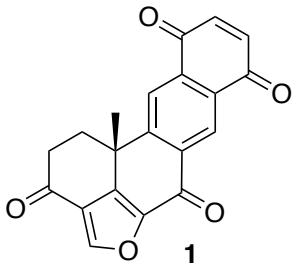
(+)-halenaquinone (**1**)



viridin (**2**)



wortmannin (**3**)



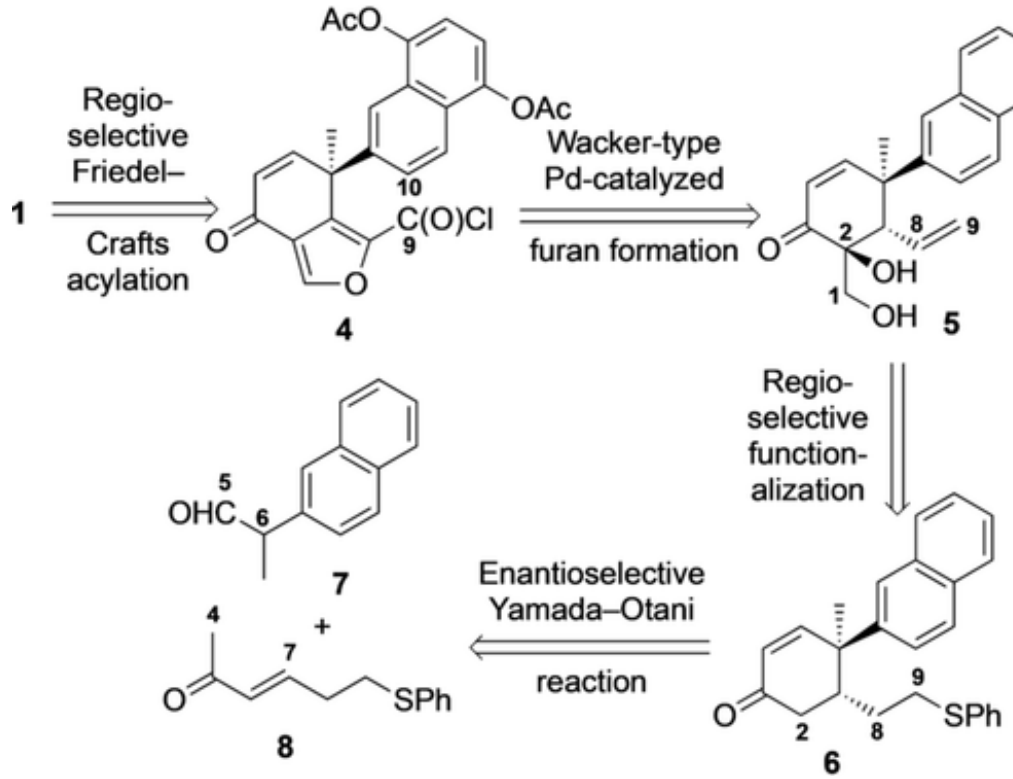
-(-) Halenaquinone

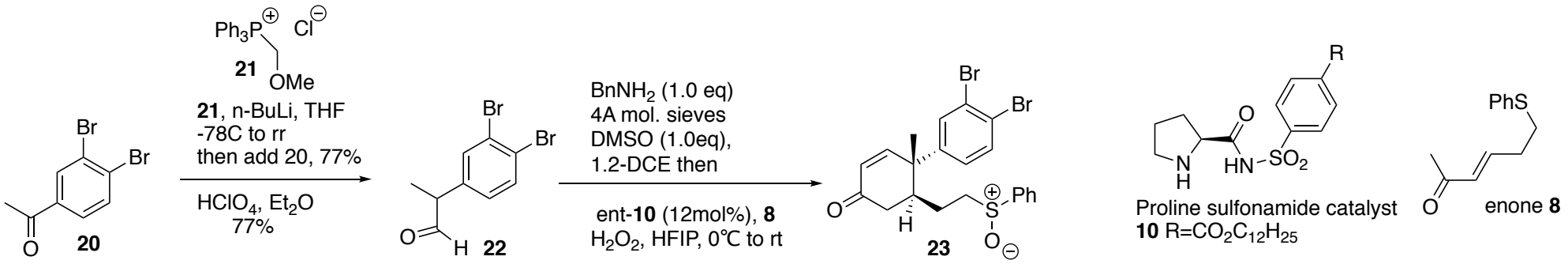
- (+)-Halenaquinone was isolated by Scheuer and Clardy in 1983 from the Marine sponge Xestospongia exigua and showed antibiotic ability.
- Two of the major challenges present within halenaquinone are the construction of the C6 all-carbon quaternary stereocenter and the all-fused tricyclic ABC core with a reactive furan ring. (see Figure 1).
- A efficient 14 step scalable, enantioselective total synthesis of (-)-Halenaquinone.

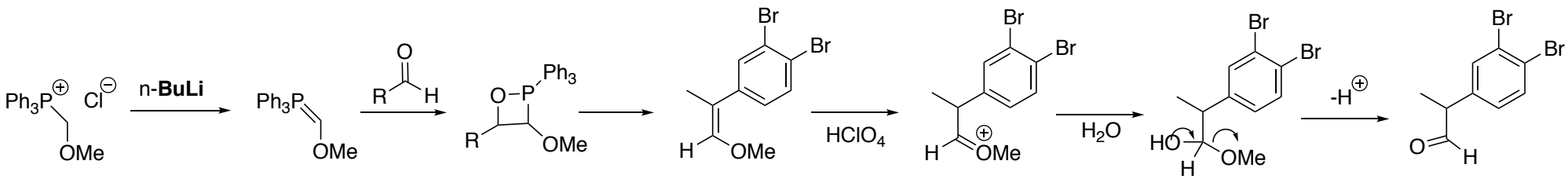
Liu Research Group

Julia Liu

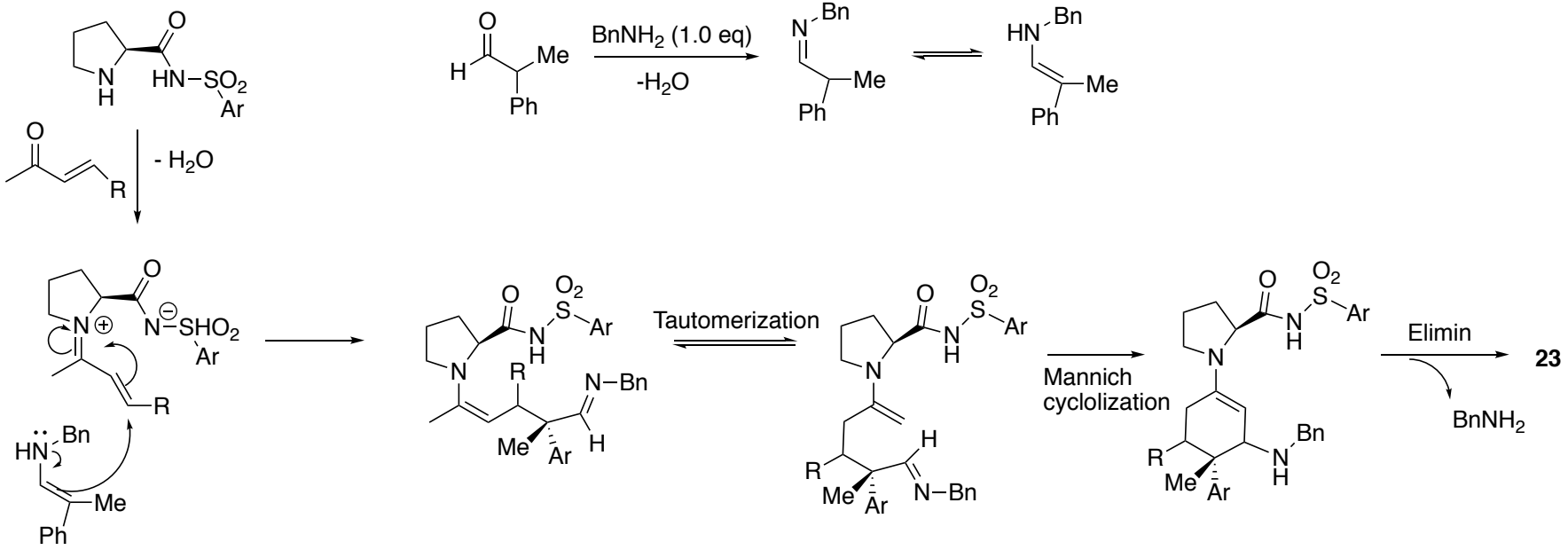
Retrosynthetic analysis

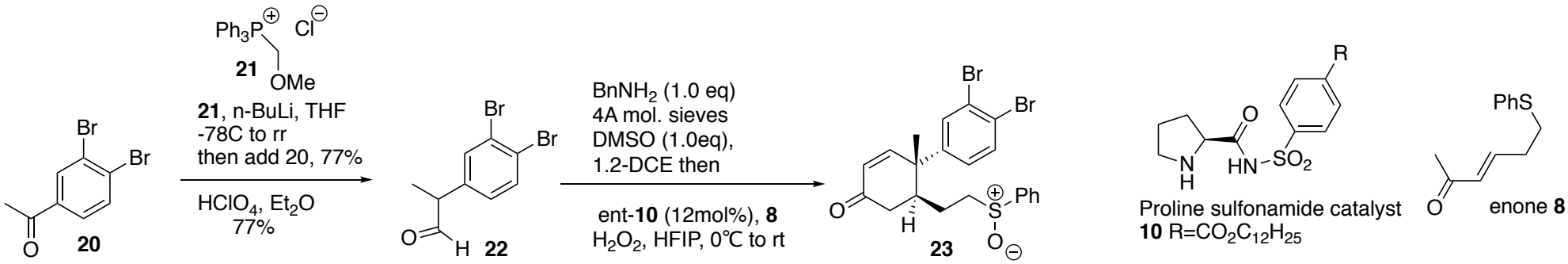


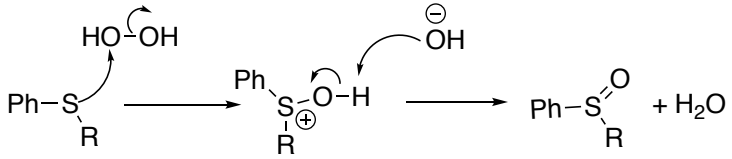


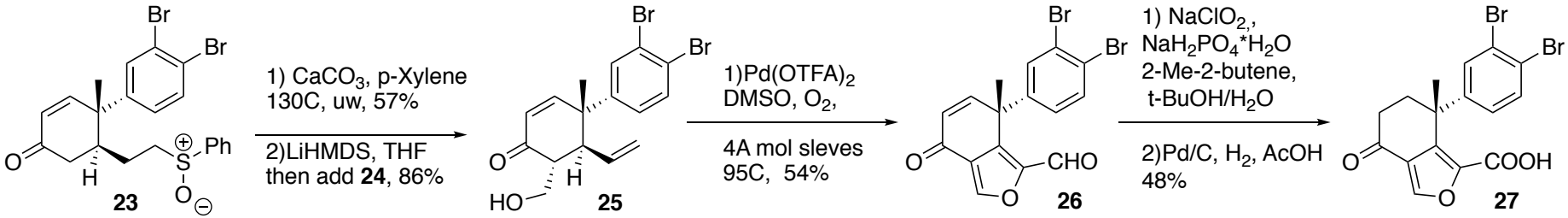


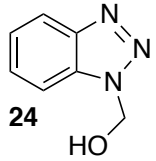
22 to **23 Yamada-Otani reaction**



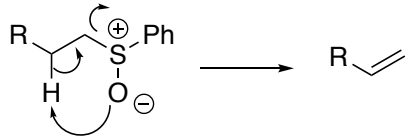

Ph3P Cl
21
OMe
21, n-BuLi, THF
-78C to rr
then add 20, 77%
HClO4, Et2O
77%
20
22
BnNH2 (1.0 eq)
4A mol. sieves
DMSO (1.0eq),
1.2-DCE then
ent-10 (12mol%), 8
H2O2, HFIP, 0℃ to rt
23
Proline sulfonamide catalyst
10 R=CO2C12H25
enone 8

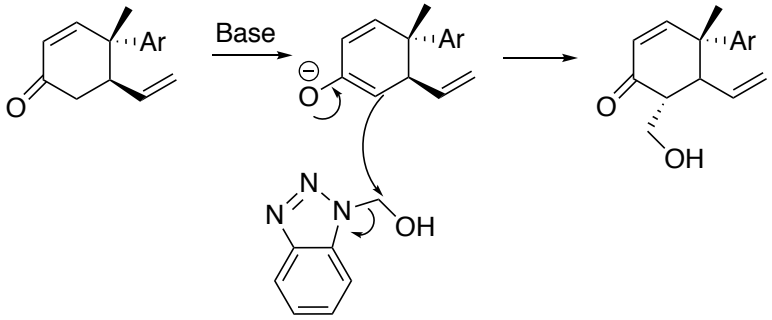

HO OH
Ph S R
OH
Ph S O H R
Ph S O R
+ H2O

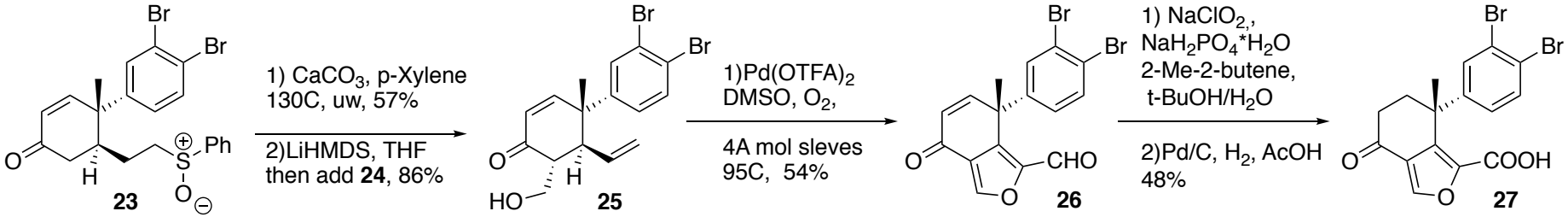

Br
Br
O
H
S
Ph
O
23
1) CaCO3, p-Xylene
130C, uw, 57%
2)LiHMDS, THF
then add 24, 86%
HO
25
1)Pd(OTFA)2
DMSO, O2,
4A mol sleves
95C, 54%
CHO
26
1) NaClO2,
NaH2PO4*H2O
2-Me-2-butene,
t-BuOH/H2O
2)Pd/C, H2, AcOH
48%
COOH
27


N
N
N
HO
24

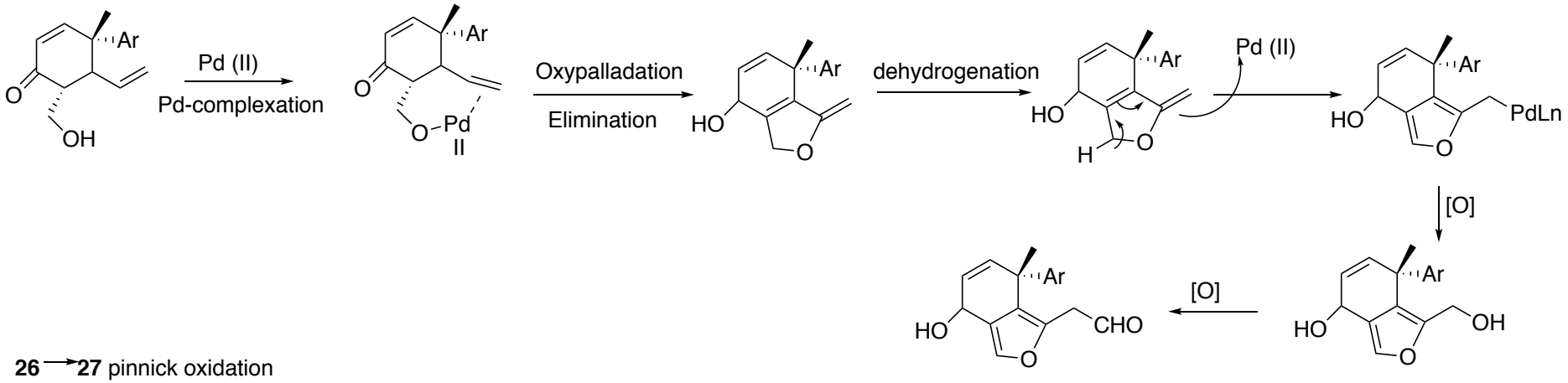
23 → **25**


R
Ph
S
H
O
R

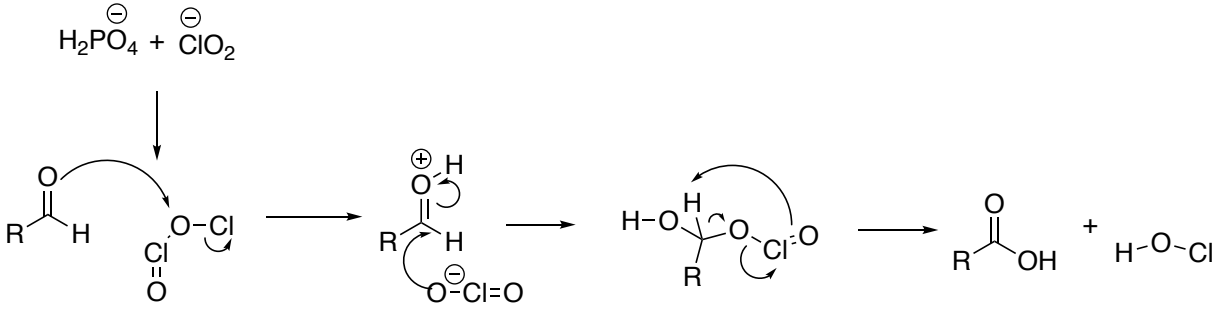

Ar
Base
O
Ar
N
N
OH
O
Ar
OH

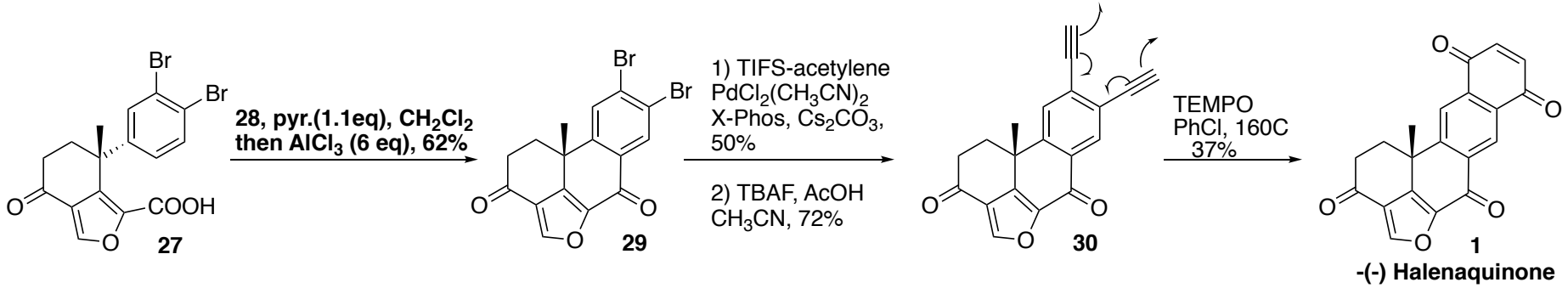


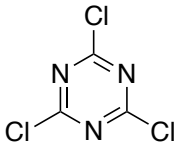
25 → **26** furanyl aldehyde synthesis



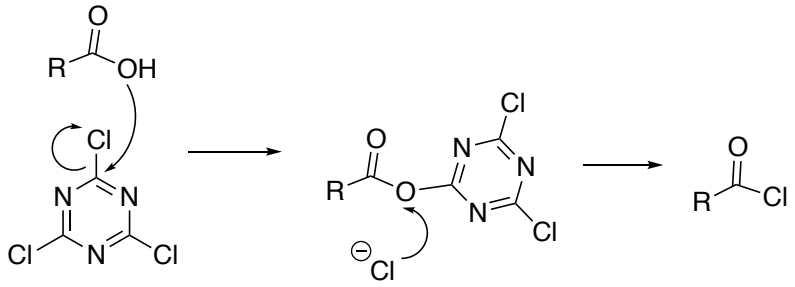
26 → **27** pinnick oxidation

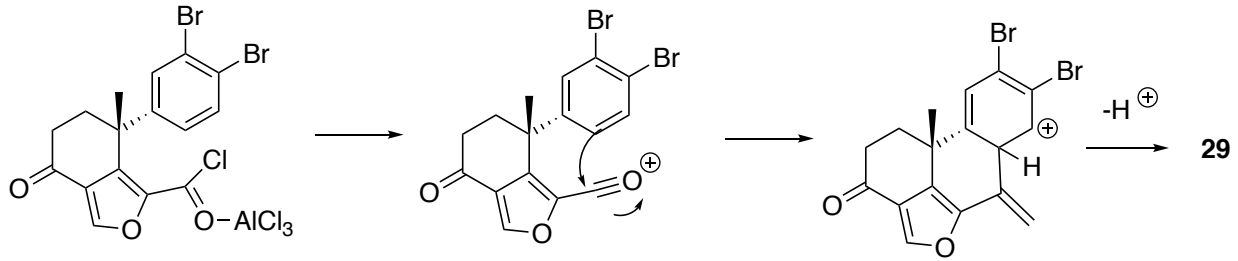


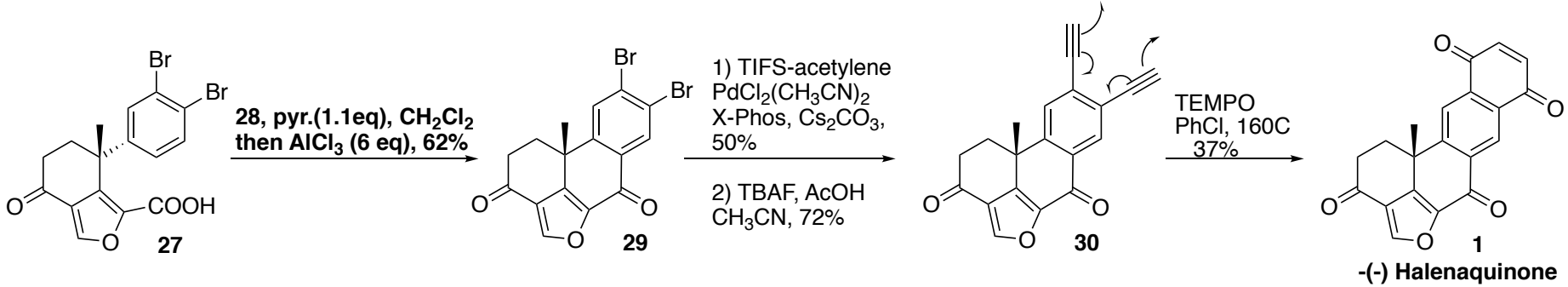


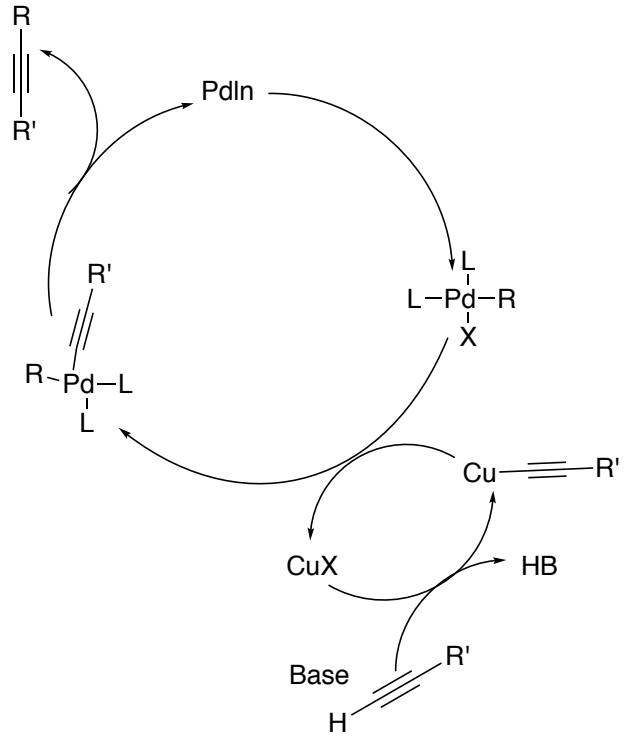


27 → **29** Freidel-Crafts acylation









30 → **PDT** Bergman cyclization