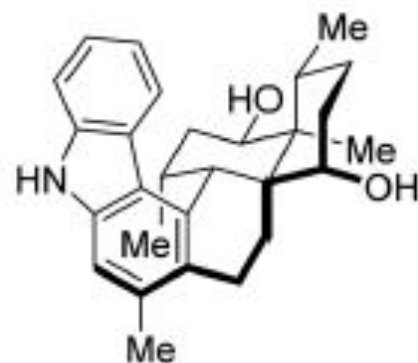


Total Syntheses of Aflavazole and 14-Hydroxyaflavinine

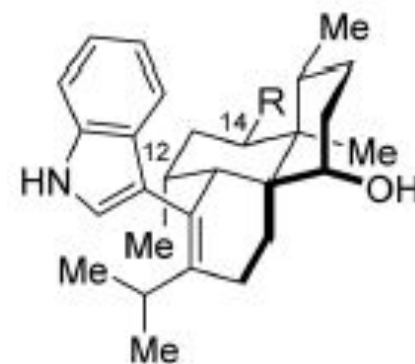
Hailong Li,[†] Qifeng Chen,[†] Zhaohong Lu, and Ang Li*^{ID}

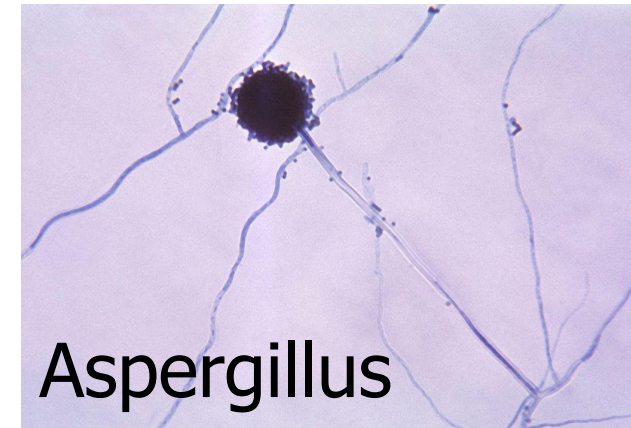
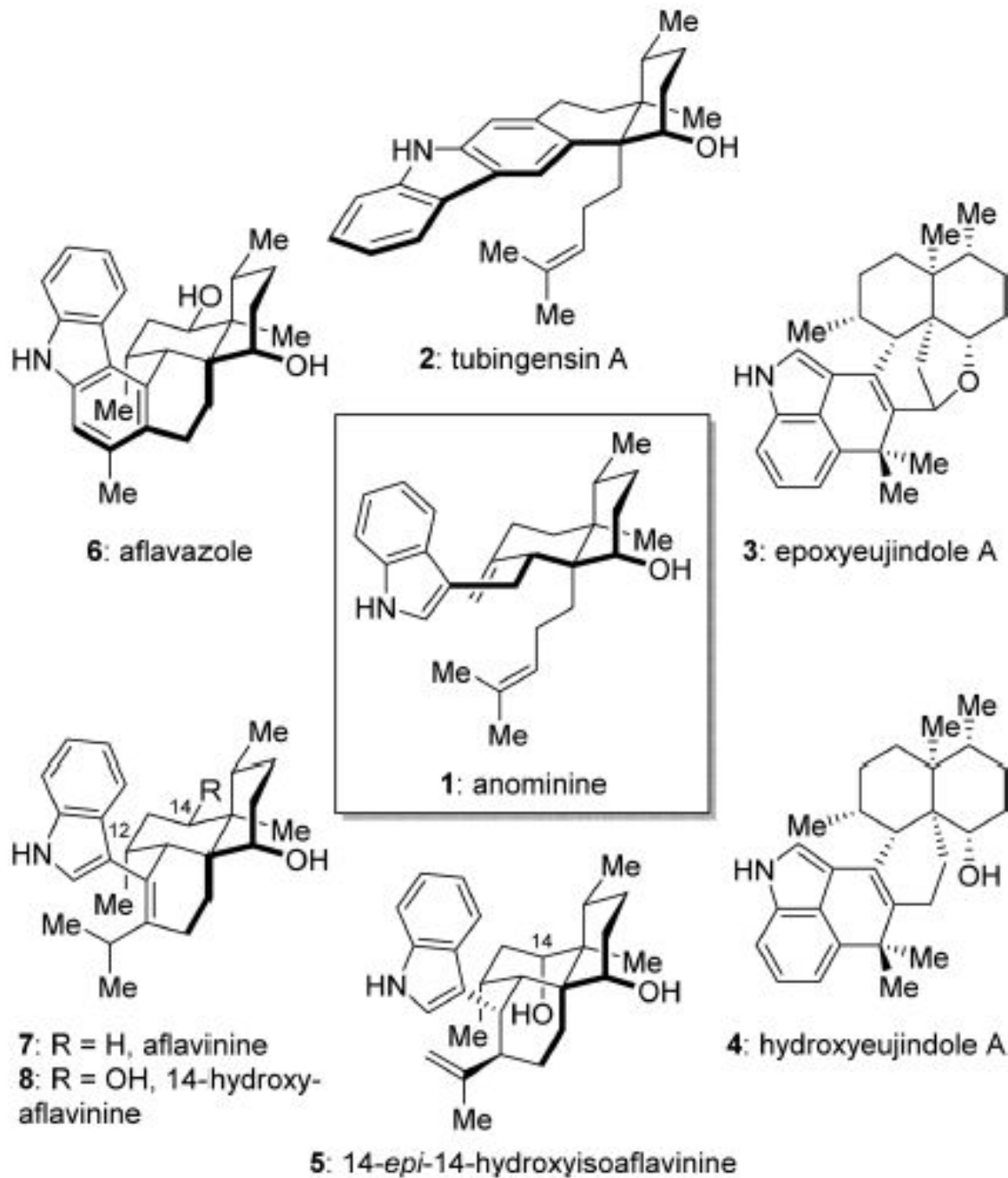
State Key Laboratory of Bioorganic and Natural Products Chemistry, Collaborative Innovation Center of Chemistry for Life Sciences, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, China

ABSTRACT: The first total syntheses of aflavazole (6) and 14-hydroxyaflavinine (8), two sterically congested indole diterpenoids, were accomplished. AlI_3 -promoted alkyne Prins cyclization was exploited to construct their key structural motifs. An electrocyclization–aromatization sequence assembled the pentasubstituted arene of 6, and a Stille–Migita coupling furnished the tetrasubstituted olefin of 8. The benzylic and allylic C–O bonds were reductively cleaved at the late stage of the syntheses, respectively.



6: aflavazole

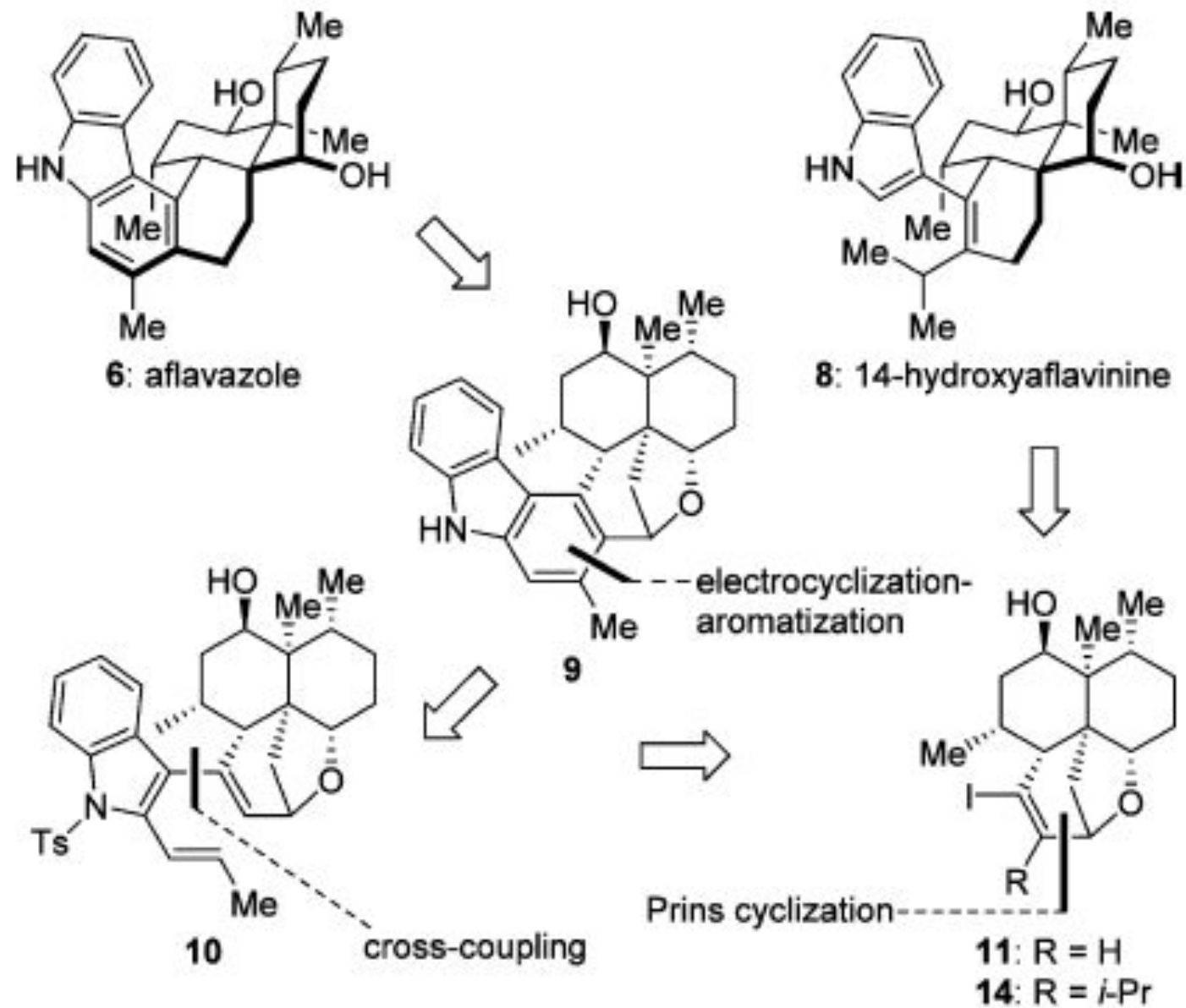




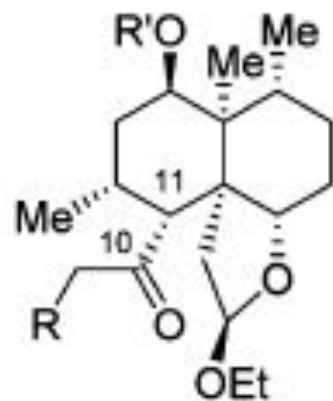
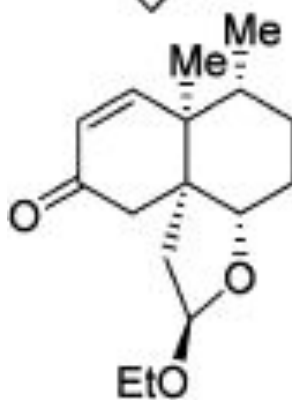
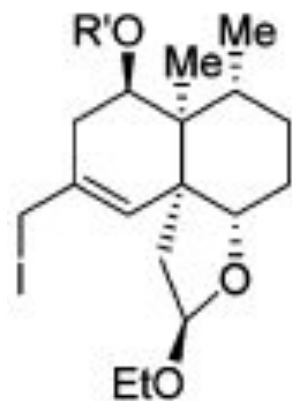
Aspergillus

promising biological properties

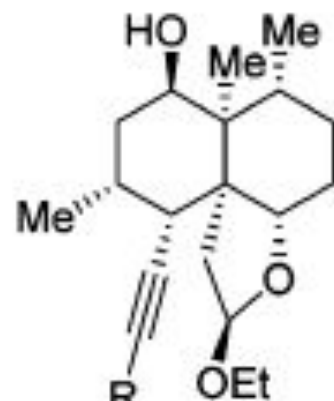
Ретросинтез



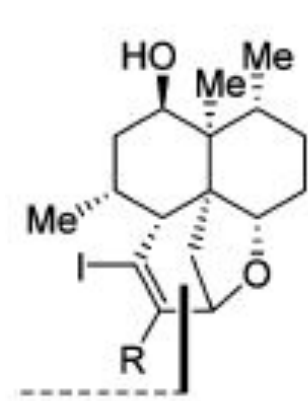
Ретросинтез



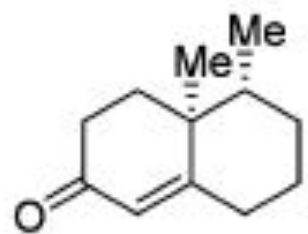
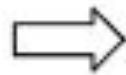
15: R = H
16: R = *i*-Pr



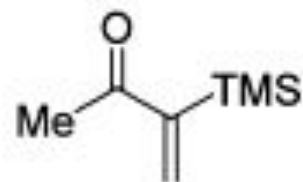
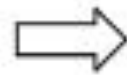
12: R = H
13: R = *i*-Pr



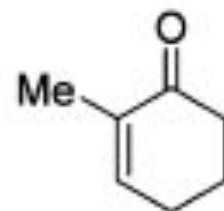
11: R = H
14: R = *i*-Pr



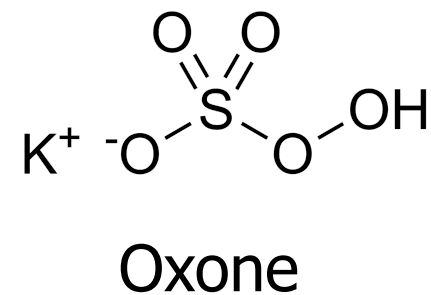
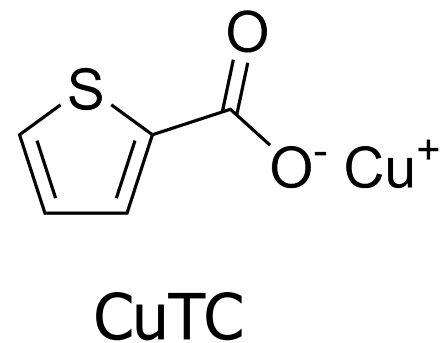
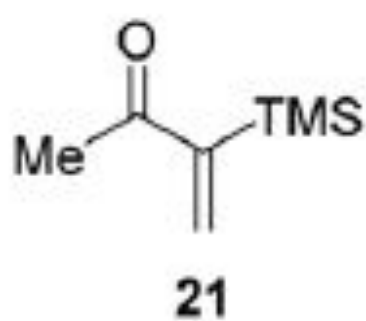
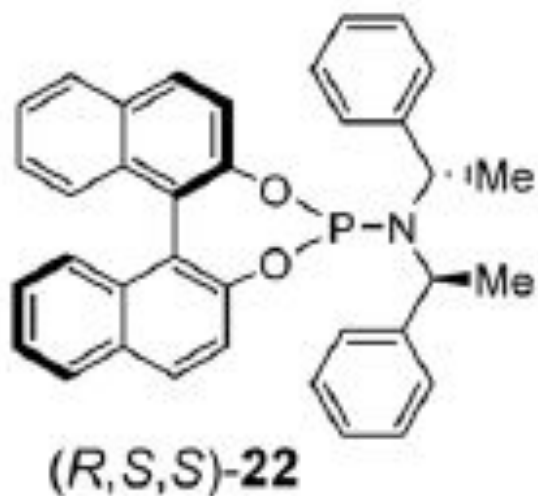
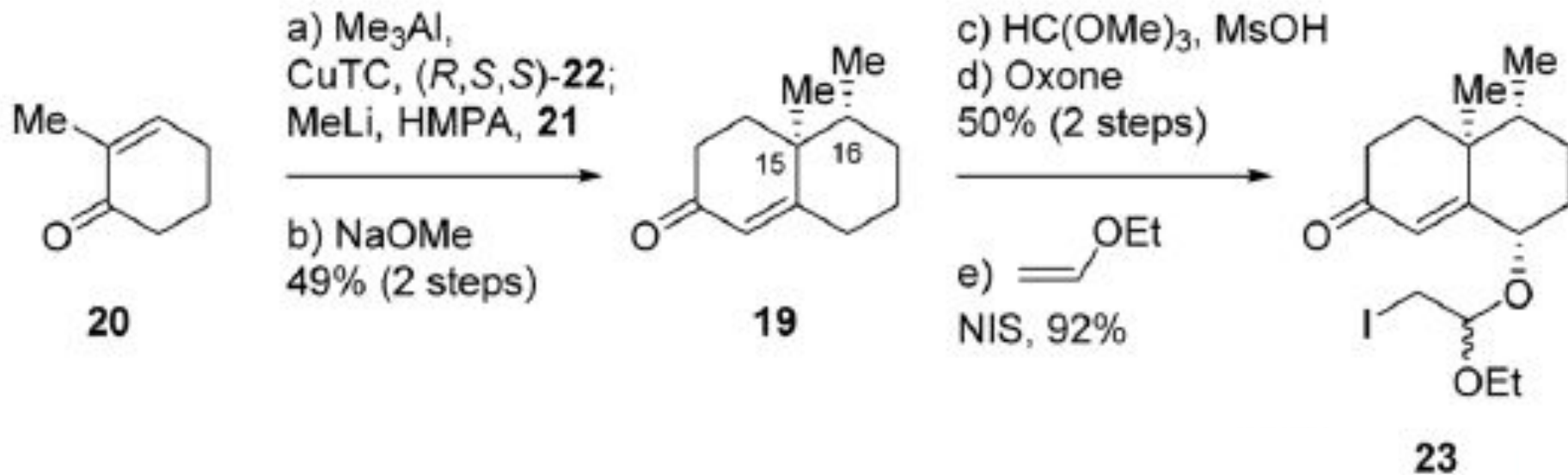
19

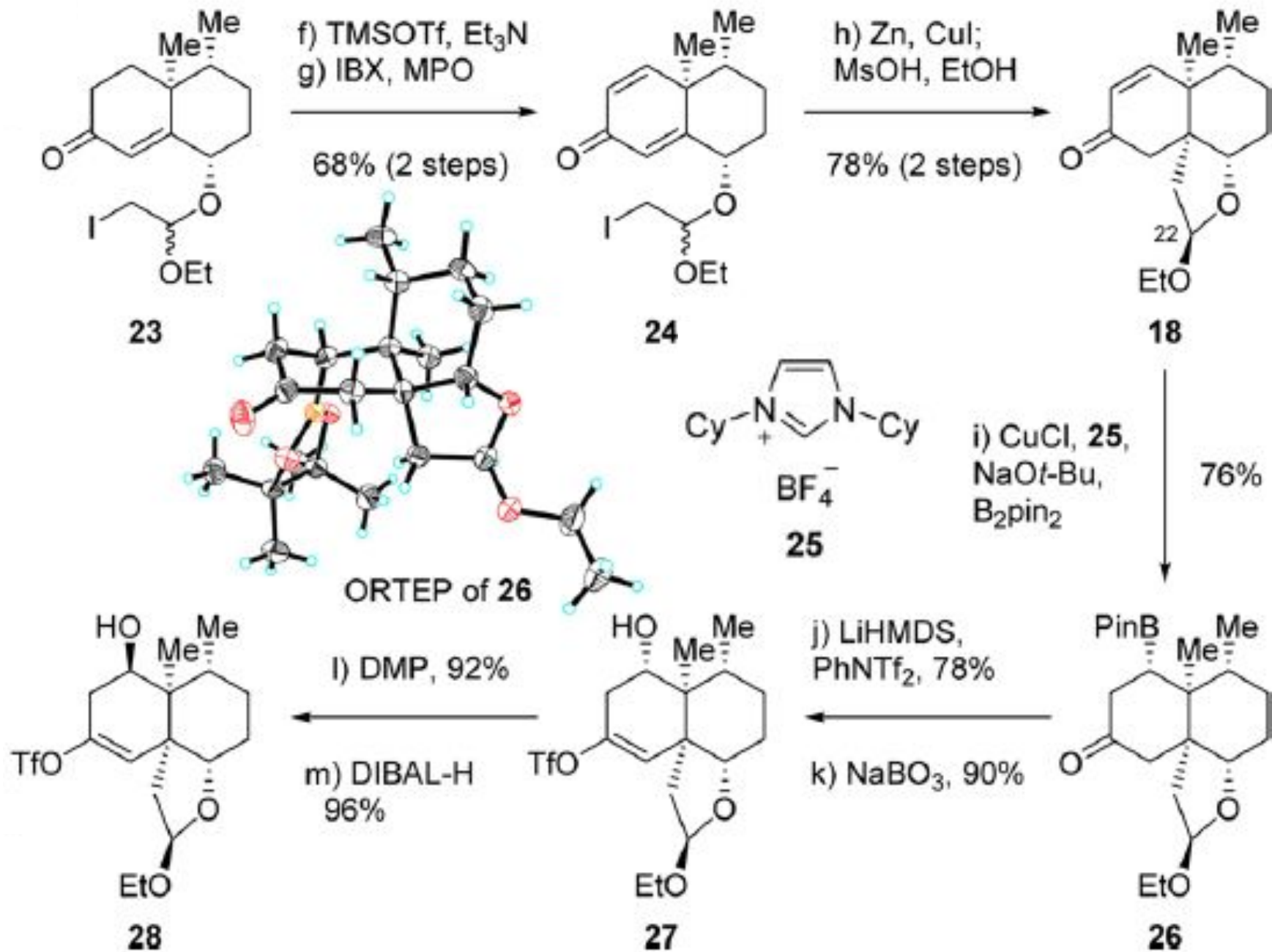
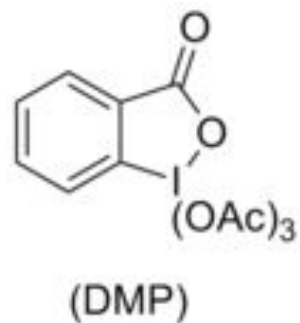
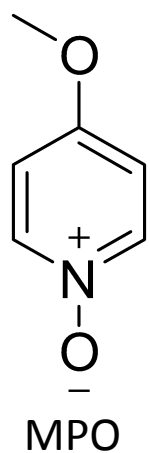
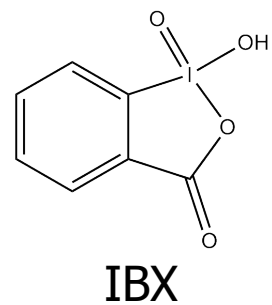


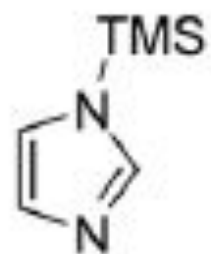
Me₃Al



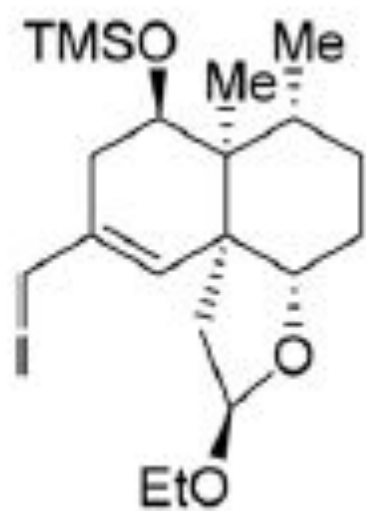
20







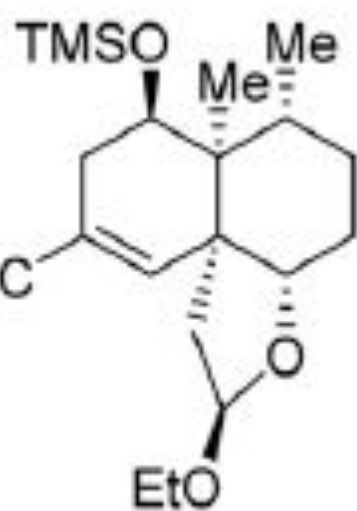
29



17

p) DIBAL-H, 96%

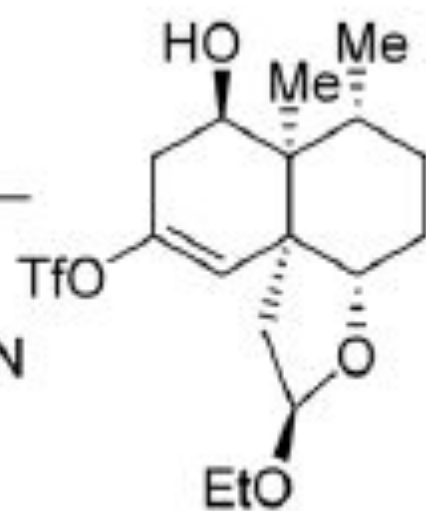
q) PPh₃, I₂,
imidazole, 98%



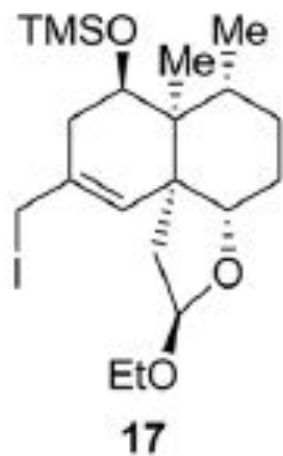
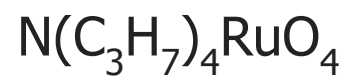
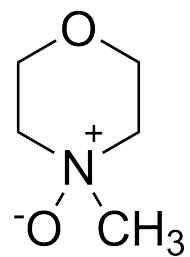
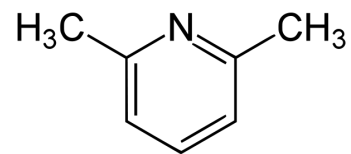
30

n) **29**, 95%

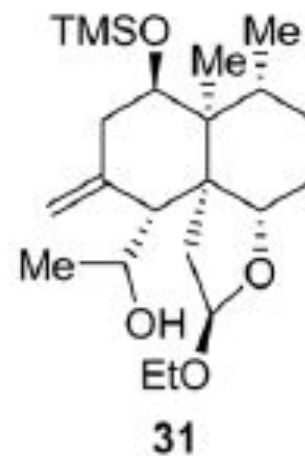
o) Pd(PPh₃)₄,
CO, MeOH, Et₃N
73%



28

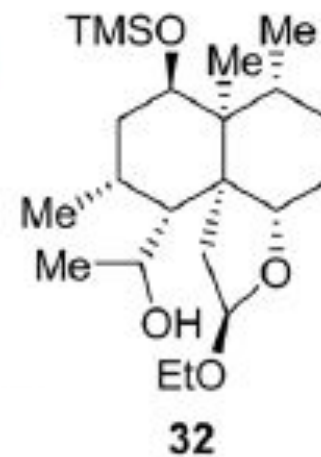


a) acetaldehyde,
CrCl₂, Lil, 4 Å MS,
2,6-lutidine



b) NaBH₄,
NiCl₂

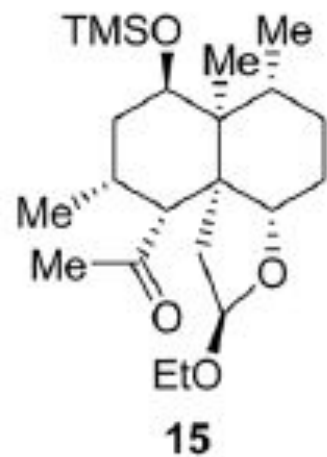
93%

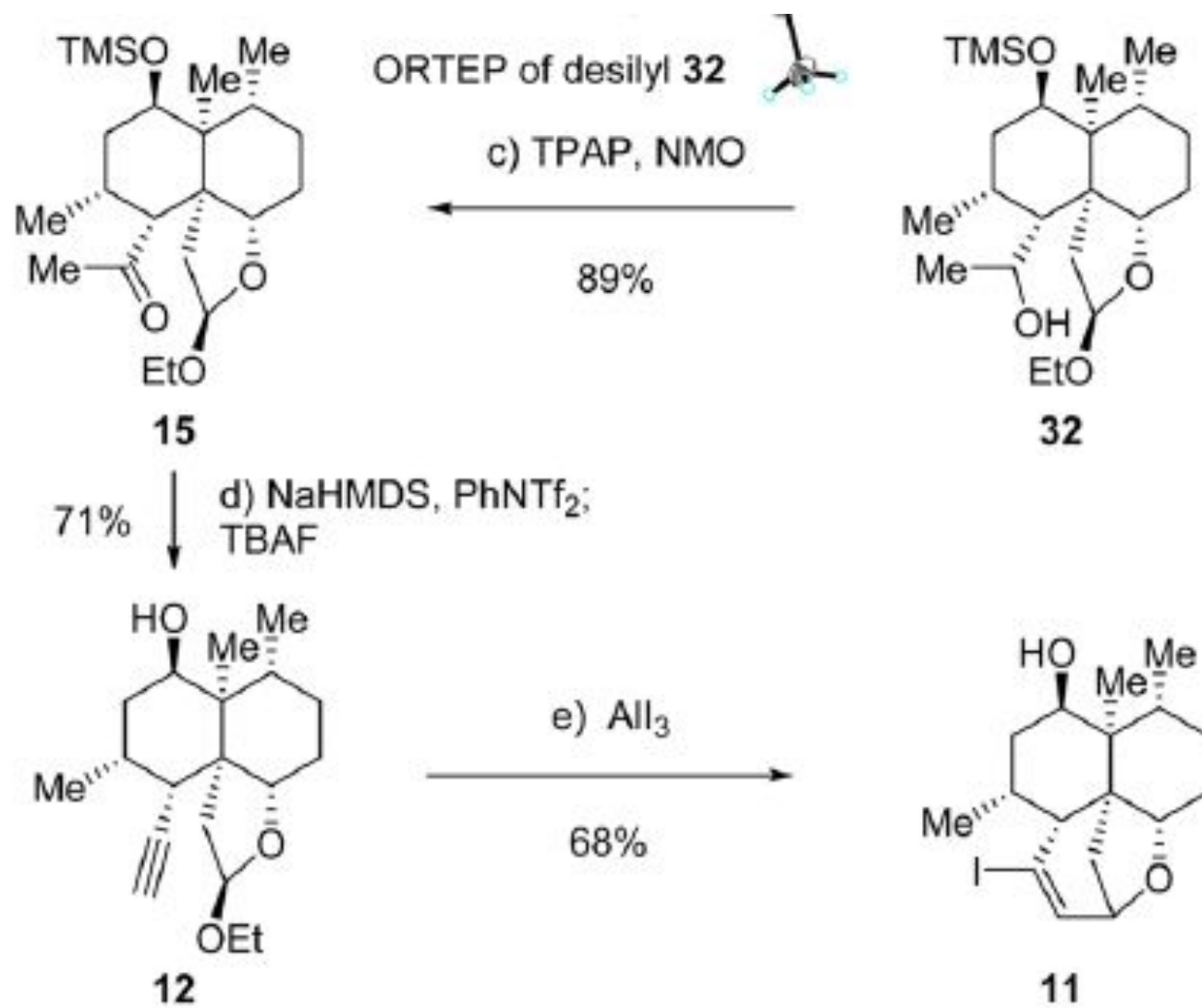


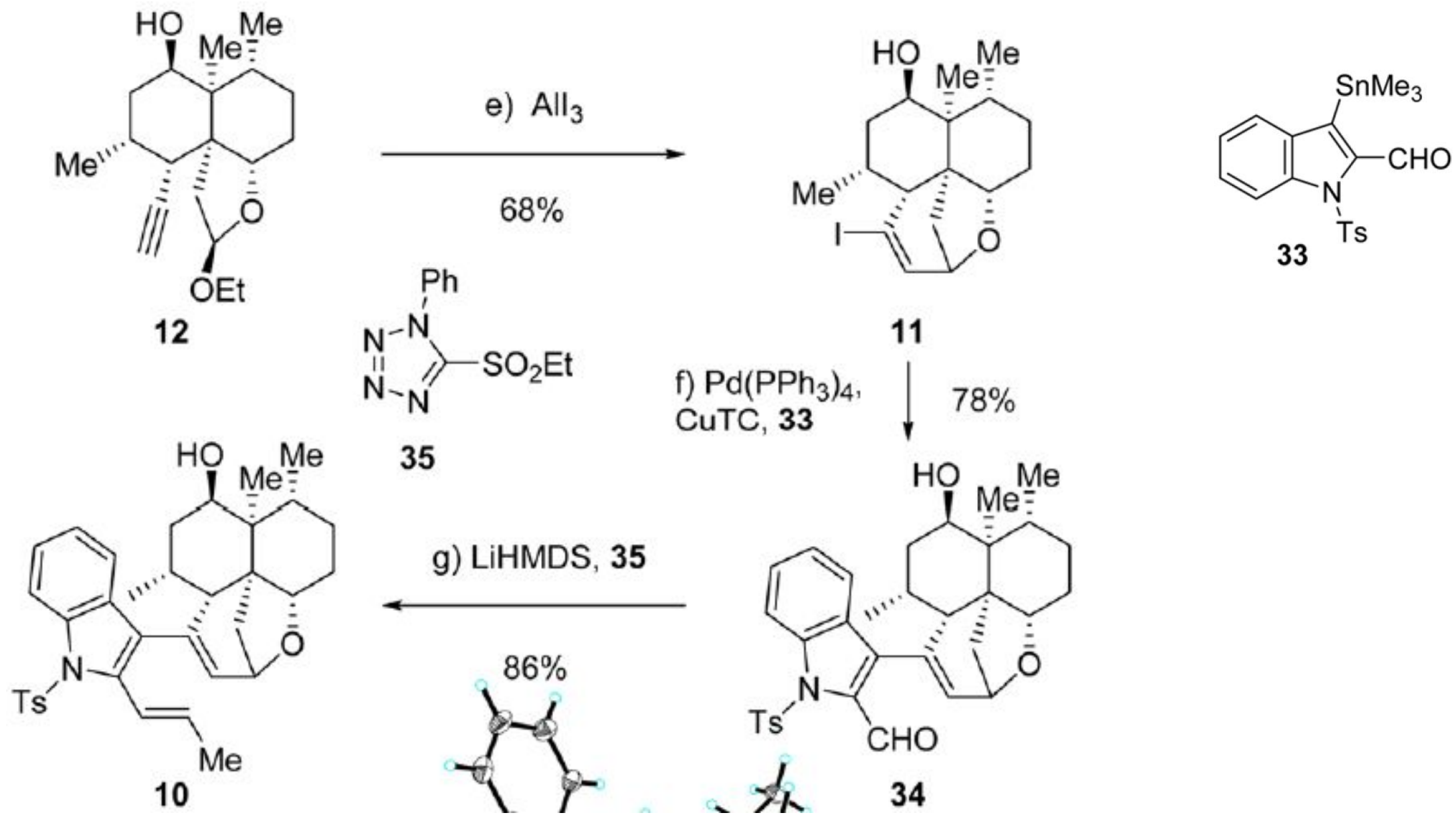
ORTEP of desilyl 32

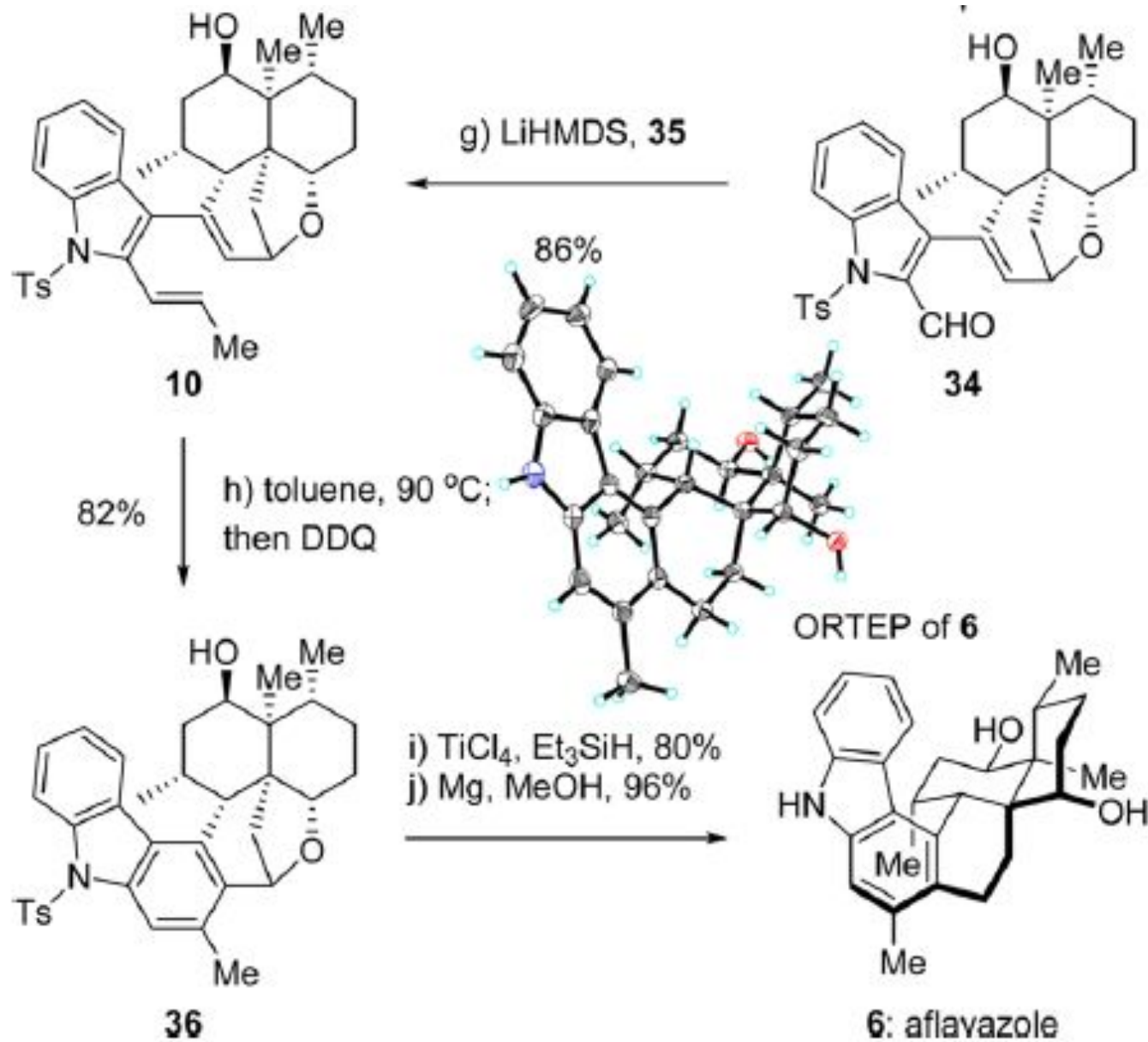
c) TPAP, NMO

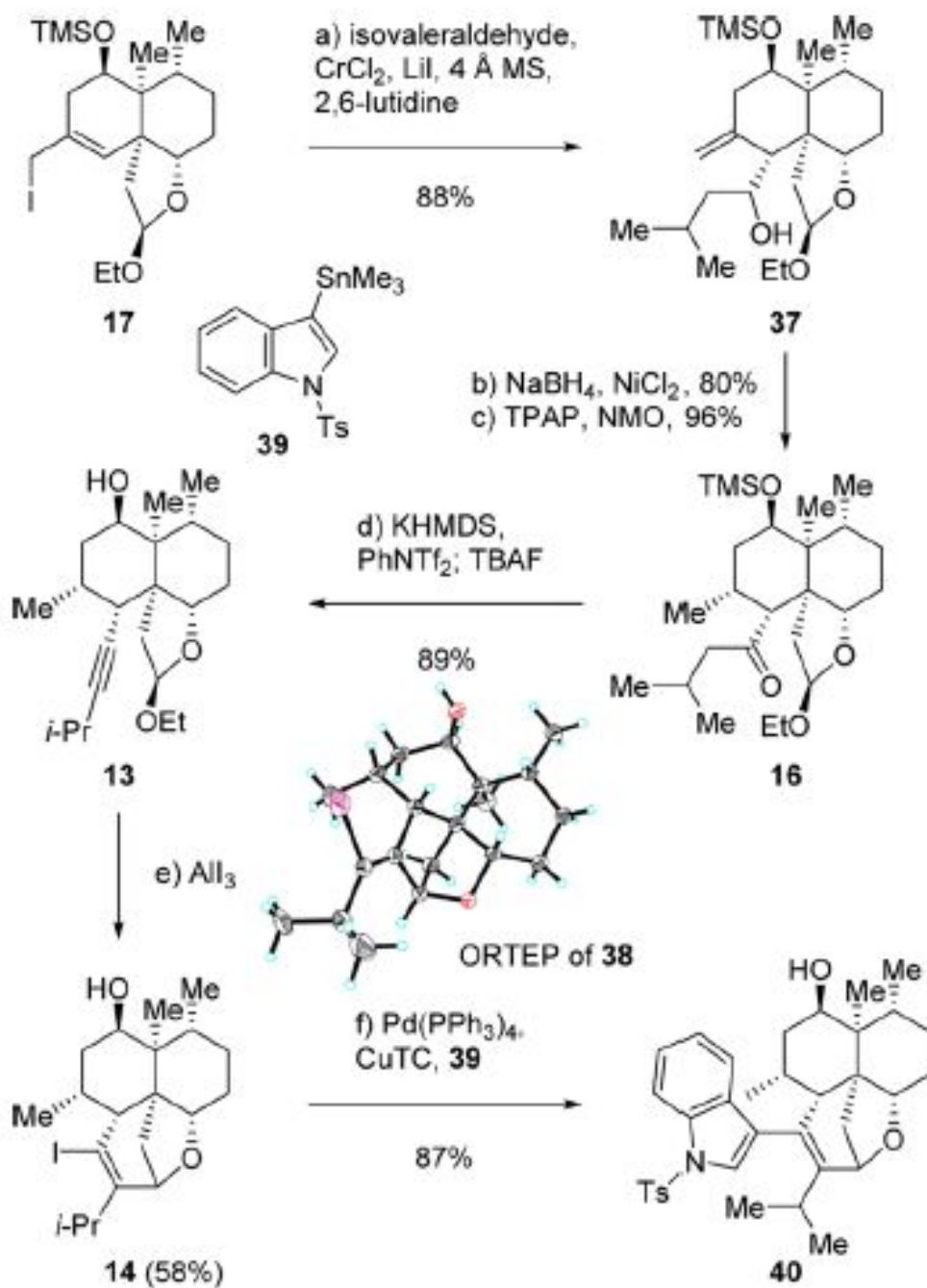
89%

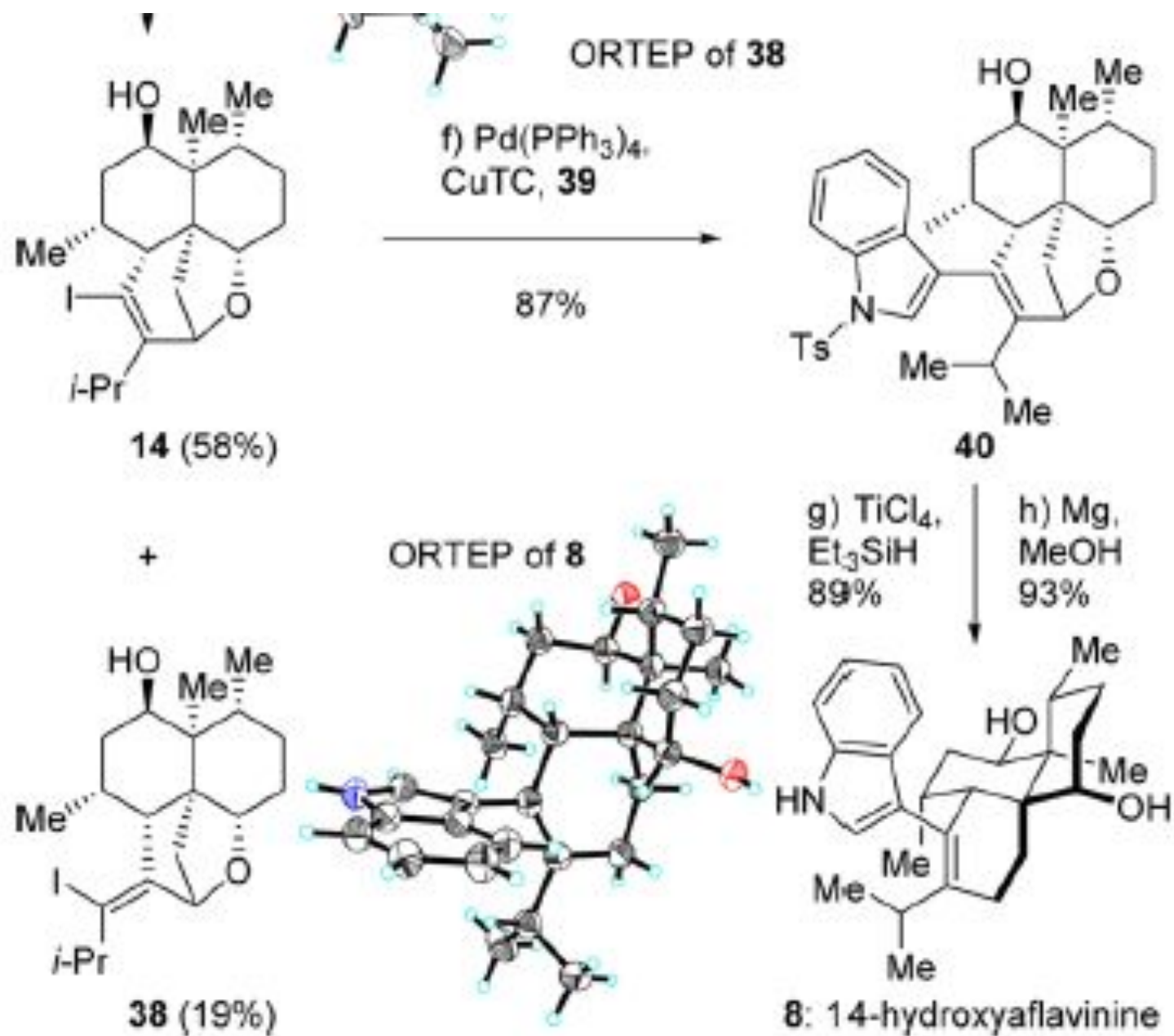








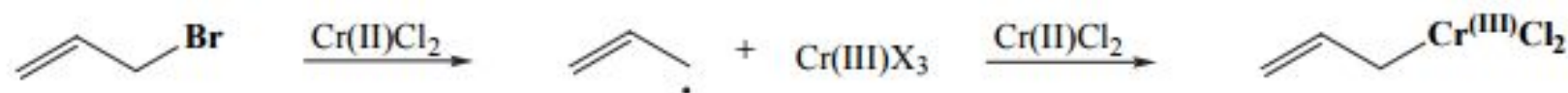
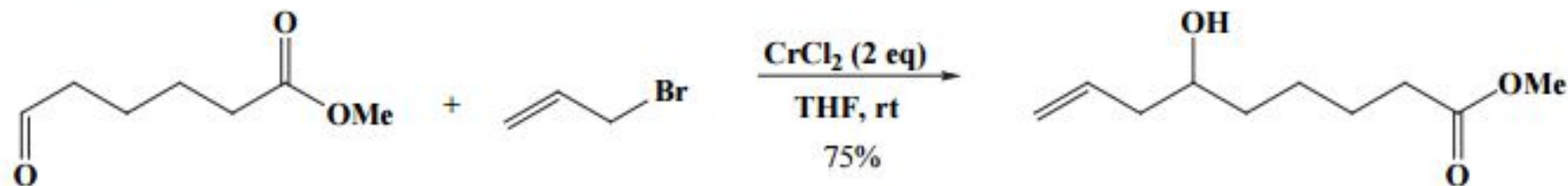




Nozaki-Hiyama Reaction

In 1977, Nozaki and Hiyama reported a remarkably chemoselective Cr(II)-mediated "Barbier-type" coupling of allyl halides with aldehydes. Unlike a Mg(0)-mediated Barbier coupling, aldehydes may be coupled in the presence of ketones and esters.

Nozaki, Hiyama. *JACS* 1977 (99) 3179.



Insertion of Cr occurs *via* 2 single electron transfer events (hence the requirement for 2 eq. of Cr(II) salt). This avoids oxidative addition which would result in a high energy Cr(IV) species. Kochi *JACS* 1964 (86) 5264; *JACS* 1968 (90) 1582.

