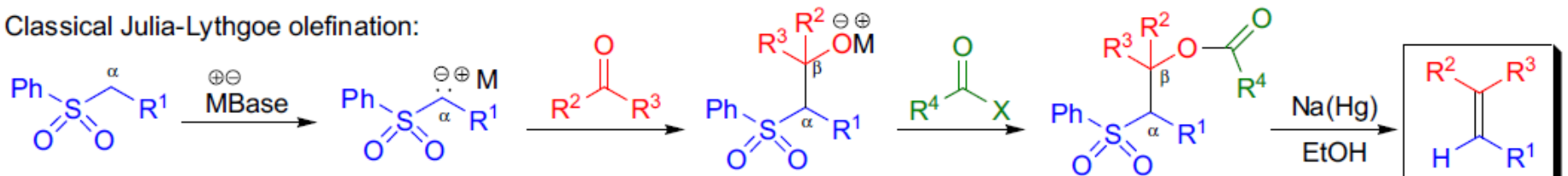
JULIA-LYTHGOE OLEFINATION

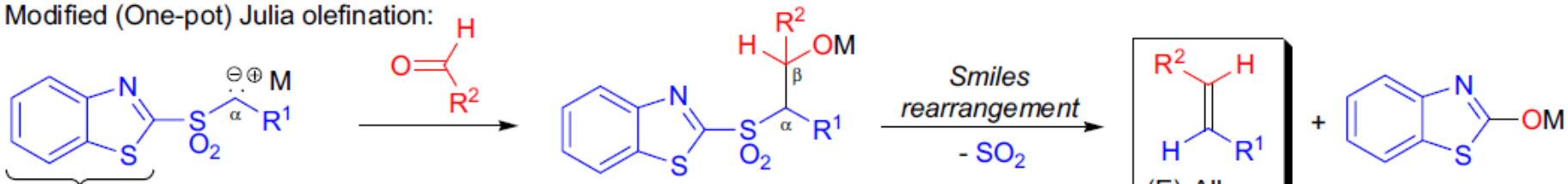
Classical Julia-Lythgoe olefination:



alkylphenyl sulfone | α-metalated alkylphenylsulfone | β-alkoxy sulfone | β-acyloxy sulfone

R^1 = H, alkyl, aryl; R^2, R^3 = H, alkyl, aryl, alkenyl; R^4 = alkyl, aryl; X = Cl, Br, OCOR

Modified (One-pot) Julia olefination:



Het = benzothiazol-2-yl (BT) | β-alkoxysulfone | metal salt of benzothiazol-2-ol

R^1 = H, alkyl, aryl; R^2 = alkyl, aryl,alkenyl; Het = benzothiazol-2-yl (BT), pyridin-2-yl (PYR), 1-phenyl-1*H*-tetrazol-5-yl (PT)

This olefin synthesis requires the following steps

- 1) addition of an α-metalated phenylsulfone to an aldehyde or ketone;
- 2) acylation of the resulting β-alkoxysulfone
- 3) reductive elimination of the β-acyloxysulfone with a single-electron donor to yield the desired alkene.

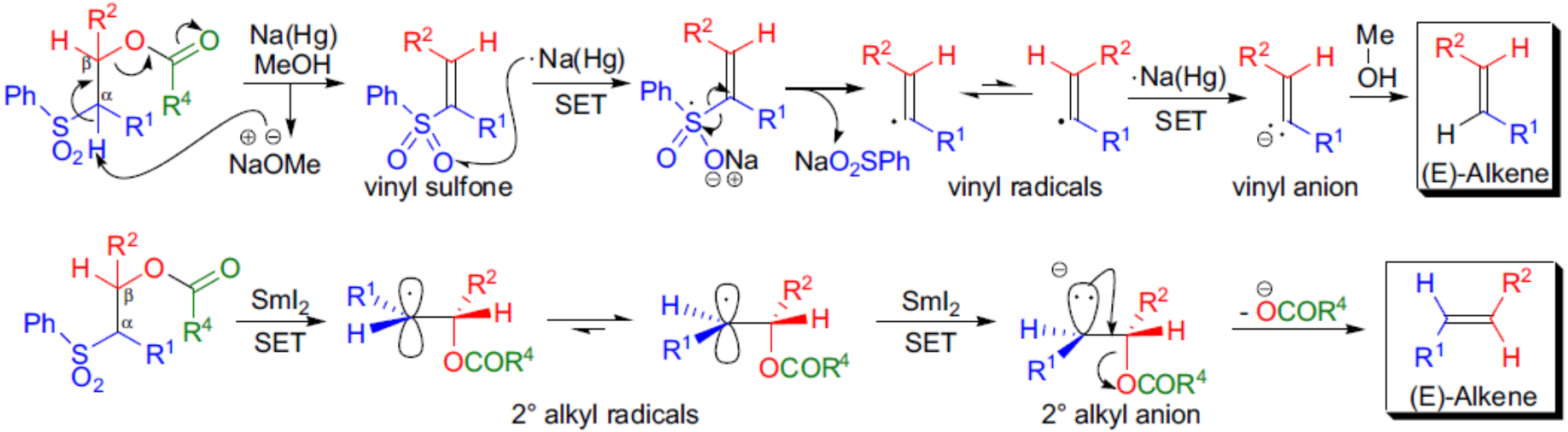
general features

- 1) high (*E*)-stereoselectivity;
- 2) the (*E*)-selectivity is increased with increasing chain branching around the newly formed double bond;
- 3) the relative stereochemistry in the intermediate β-acyloxysulfones does not influence the geometry of the alkene product

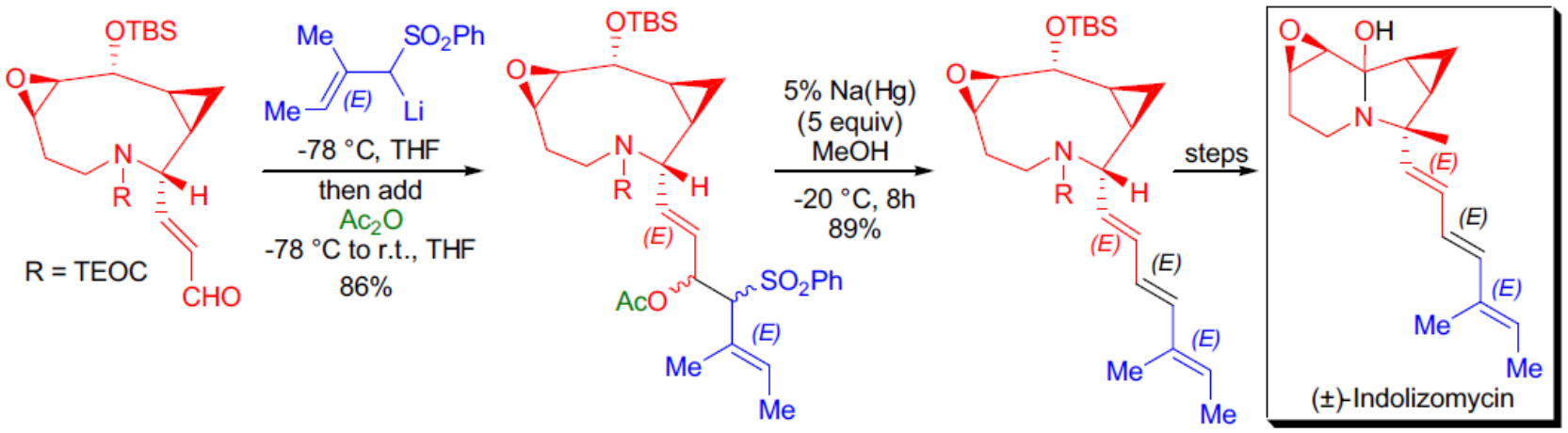
One-pot

- Since the classical procedure was quite tedious (3 steps) to carry out in the laboratory, a more convenient *one-pot modification* was developed by S.A. Julia and co-workers who added α-metalated heteroarylsulfones to carbonyl compounds instead of the traditional phenylsulfones. The initial intermediate β-alkoxy heteroarylsulfone is very labile, and it quickly undergoes the *Smiles rearrangement* in which the heterocycle is transferred from the sulfur to the oxygen atom to afford yet another unstable intermediate, a sulfinate salt. This sulfinate salt readily decomposes to the desired (*E*)-alkene, sulfur dioxide and the metal salt of benzothiazol-2-ol. Several heteroaromatic activators were examined, and it was revealed that not all heteroarylsulfones worked equally well in terms of product yield and stereoselectivity. The BT-sulfones react with α,β-unsaturated or aromatic aldehydes to give conjugated 1,2-disubstituted (*E*)-alkenes. Kocienski found that the PT-sulfone (1-phenyl-1*H*-tetrazol-5-yl sulfone) provides nonconjugated 1,2-disubstituted alkenes with high (*E*)-selectivity if no significant electronic or steric bias is present (*Kocienski-modified Julia olefination*). For the preparation of conjugated 1,2-disubstituted (*Z*)-alkenes, the use of allylic or benzylic TBT-sulfones (1-*t*-butyl-1*H*tetrazol-5-yl sulfones) is recommended

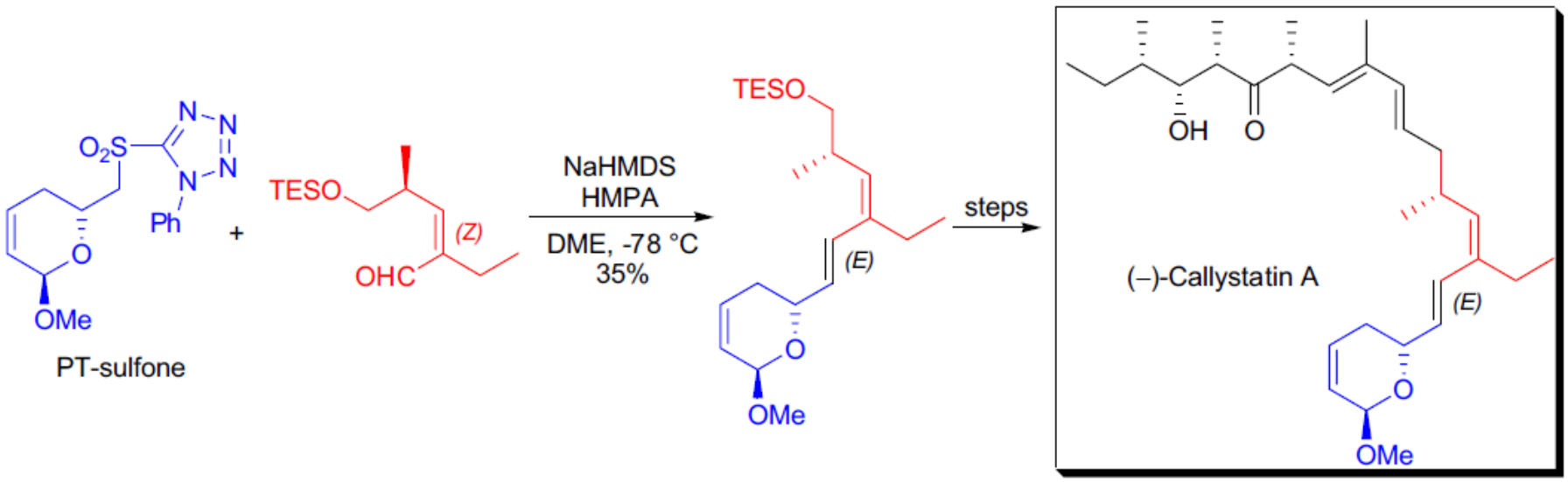
Mechanism


Na(Hg)
MeOH
NaOMe
vinyl sulfone
·Na(Hg)
SET
NaO2SPh
vinyl radicals
·Na(Hg)
SET
vinyl anion
Me
OH
(E)-Alkene
SmI2
SET
2° alkyl radicals
SmI2
SET
2° alkyl anion
- OCOR4
(E)-Alkene

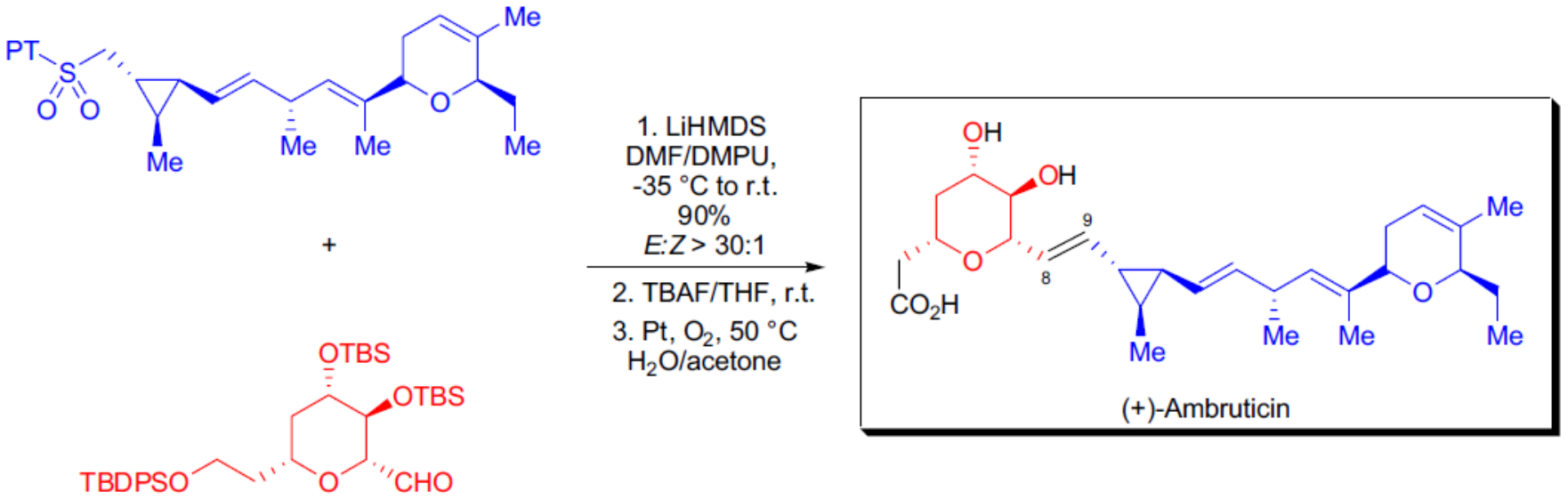
Synthetic Applications



Synthetic Applications



Synthetic Applications



Thanks