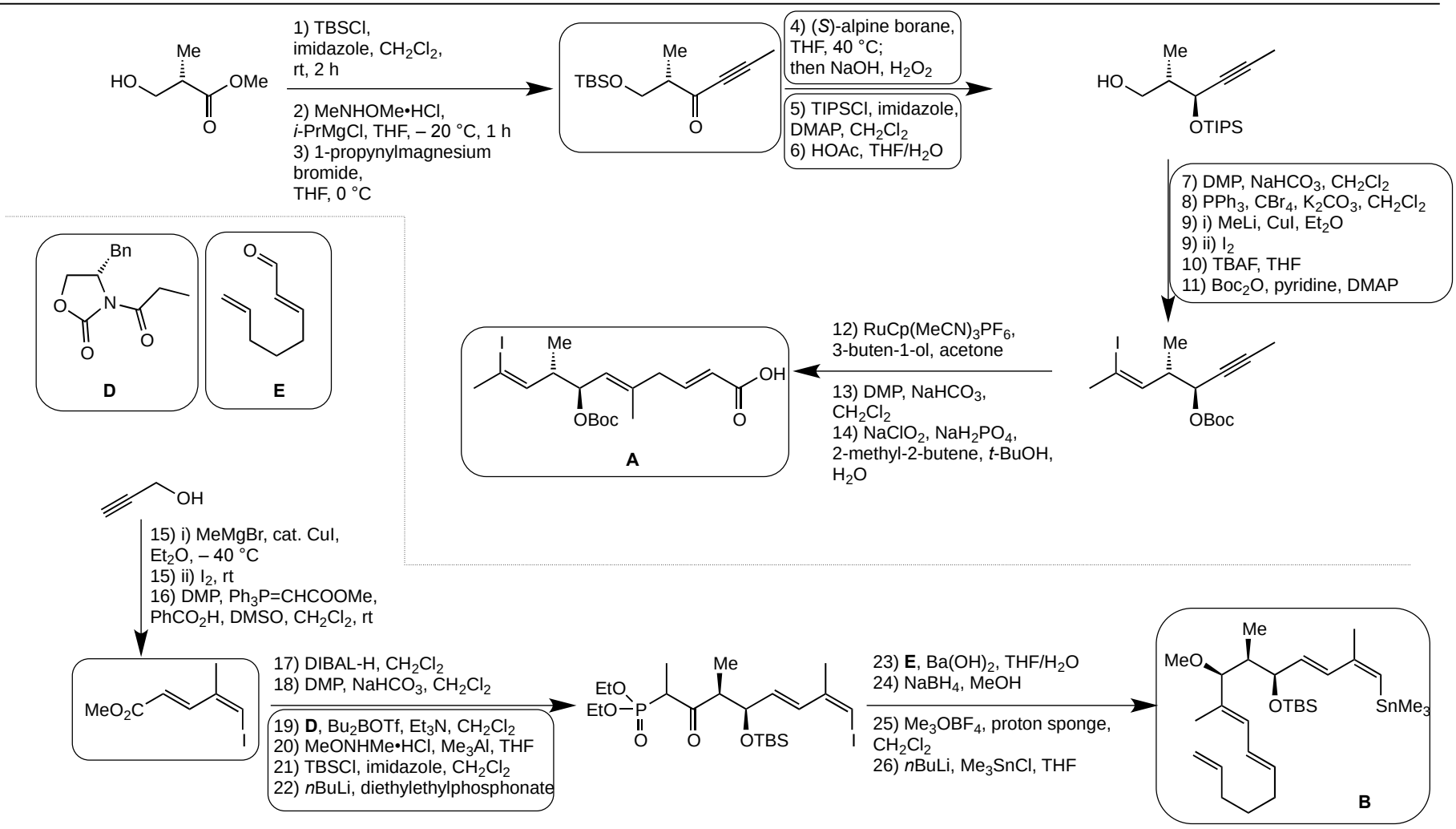
E56: Total Synthesis of (–)-Archazolid B



P. A. Roethle, I. T. Chen, D. Trauner, *J. Am. Chem. Soc.* **2007**, *129*, 8960; U. Schmidt, P. Gleich, H. Griesser, R. Utz, *Synthesis* **1986**, *12*, 992; C. M. Beaudry, D. Trauner, *Org. Lett.* **2002**, *4*, 2221; B. M. Trost, J. L. Gunzner, *J. Am. Chem. Soc.* **2001**, *123*, 9449.

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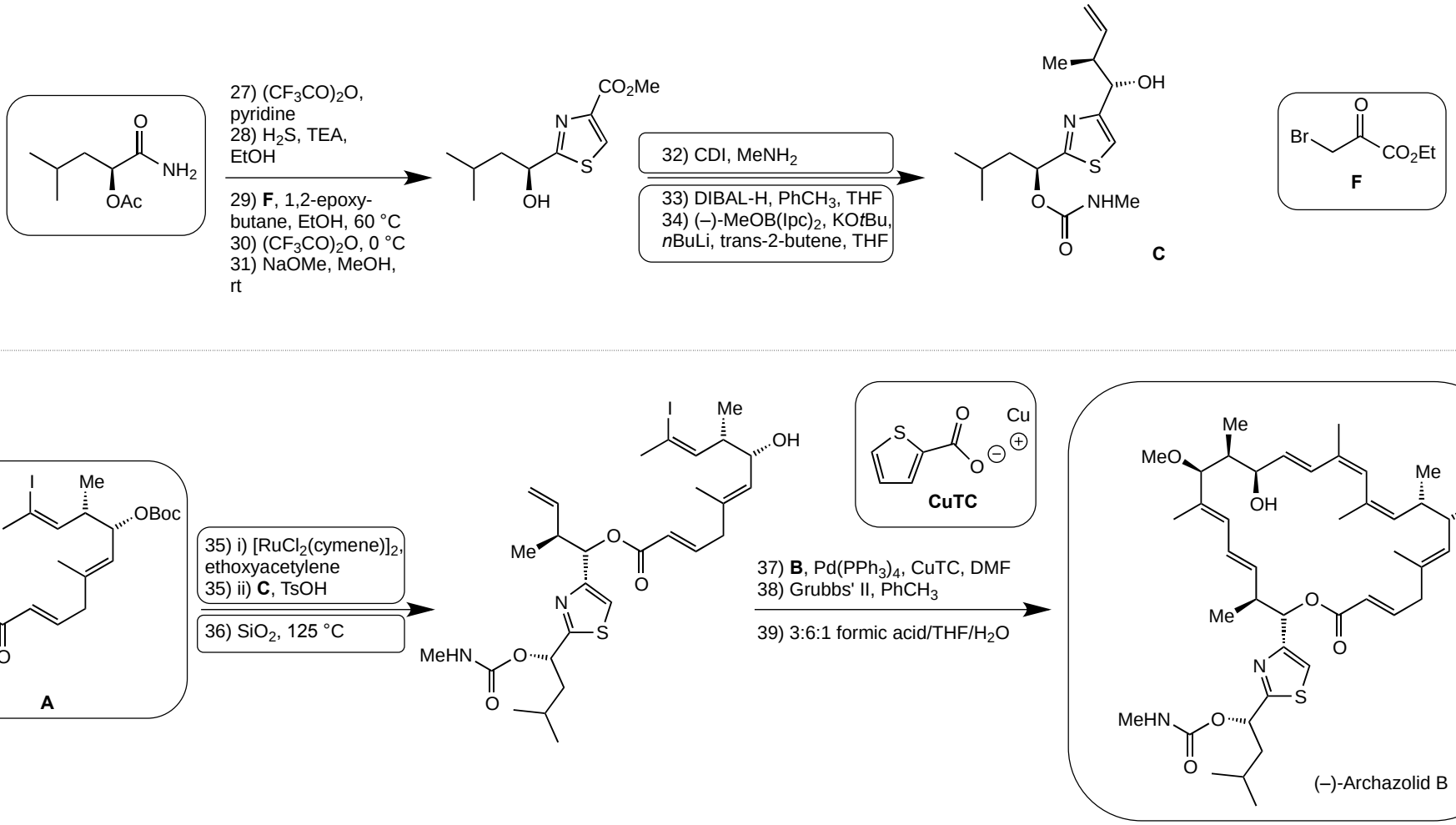

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E56: Total Synthesis of (–)-Archazolid B

Reaction Key:

1) TBS Protection
2) Weinreb Amide Formation
3) 1-propynil Addition
4) Midland Alpine Borane Reduction
5) TIPS Protection
6) TBS Deprotection
7) Alcohol to Aldehyde Oxidation
8) Corey-Fuchs Reaction
9) Installation of (Z)-vinyl iodide, „Tanino and Miyashita Method“
10) TIPS Deprotection
11) Boc Protection
12) Trost Alder-ene Reaction
13) Alcohol to Aldehyde Oxidation
14) Pinnick Oxidation
15) Carbocupration / Iodination Sequence
16) Allylic Oxidation and Concominant Olefination
17) Ester to Alcohol Reduction
18) Alcohol to Aldehyde Oxidation
19) Evans syn-Aldol Addition
20) Transamination
21) TBS Protection
22) Phosphonate Claisen Reaction
23) Horner-Wasdworth-Emmons Reaction
24) Diastereoselective Reduction (Ketone to Alcohol)
25) Etherification
26) Iodine-Tin Exchange
27) Amide to Nitrile Conversion
28) Thioamide Formation
29) Hantzsch Thiazole Synthesis (1,2-Epoxybutane stops reaction before dehydration)
30) Cautious Dehydration
31) Transesterification
32) Carbamoylation
33) Ester to Aldehyde Reduction
34) Brown Crotylation
35) Esterification
36) Thermal Boc Deprotection
37) Stille Coupling (Both Cu and Pd necessary according to authors)
38) Hoye Relay Ring-Closing Metathesis
39) Careful Deprotection of the Base-Sensitive Macrolactone

Steps 27 and 28 can also be done in one step with the Lawesson Reagent

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