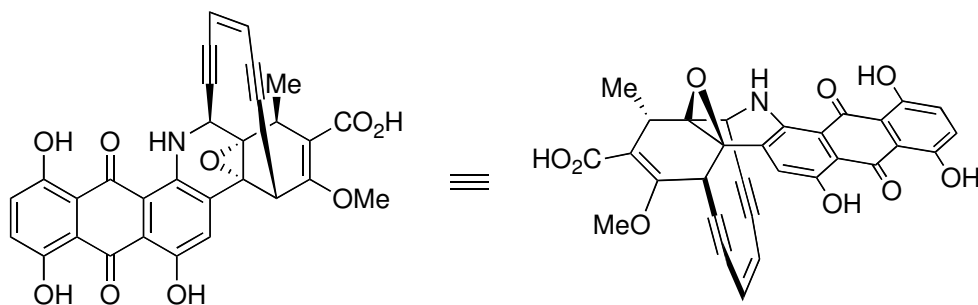


# Dynemicin A



## Molecule in Review

Adel ElSohly  
Snyder Group  
June 12, 2009

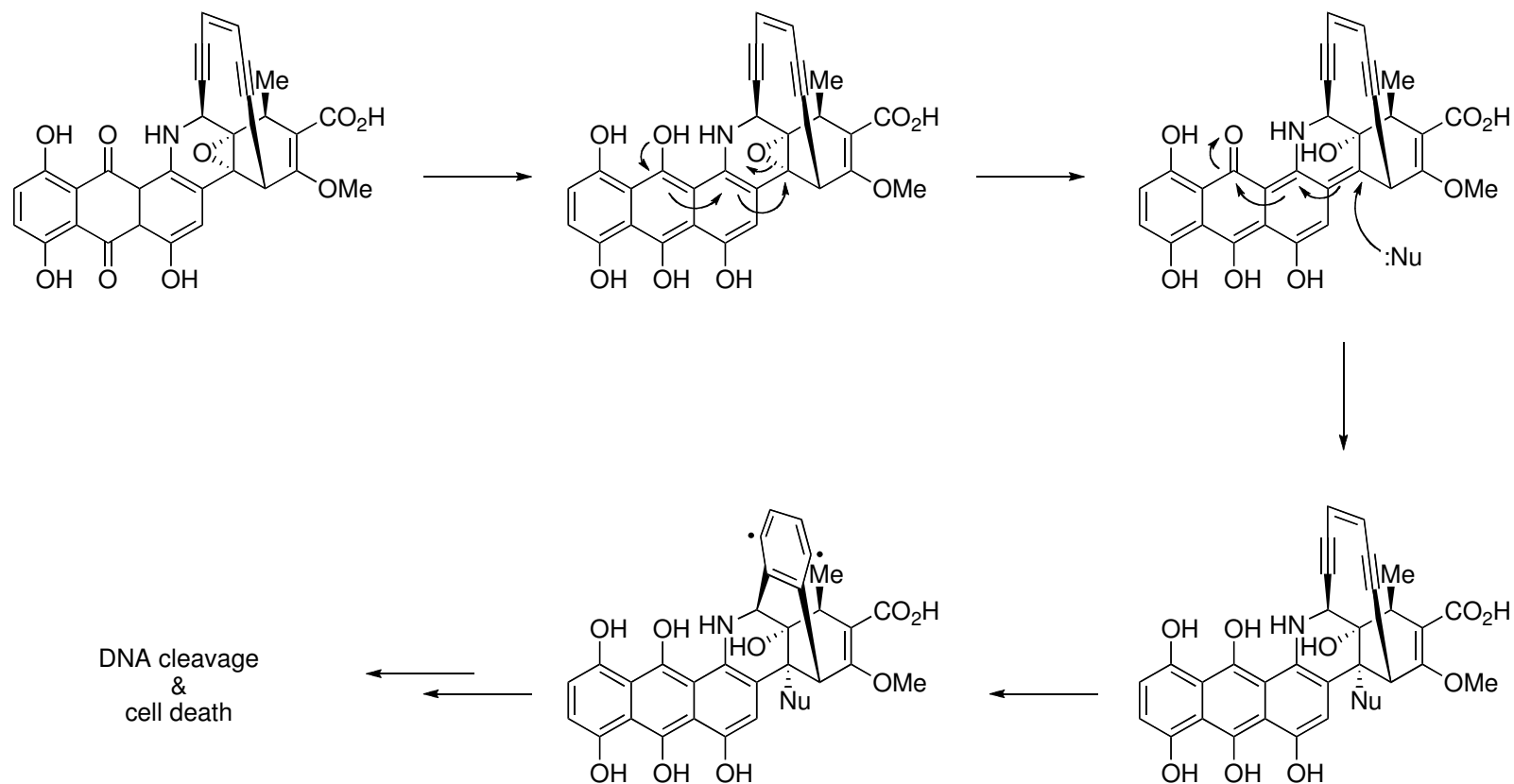
Synthesis Literacy Group  
Columbia University  
Chemistry

# *Isolation & Characterization*

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- First isolated in mid 80s from Indian soil bacteria *Micromonospora chernisa*
- Structure elucidated by Bristol-Myers in Japan
- Anthraquinone chromophore makes NP bright violet
- Potent Antitumor agent
  - Unlike other ene-diyne NPs, doesn't possess any carbohydrate subunits
  - Makes this NP relatively unselective in its cleavage of single and double-stranded DNA
- Isolation is difficult since NP is not very stable above r.t.

# Proposed Mechanism of Action



DNA cleavage  
&  
cell death

EISohly 3 - CU Synthesis Lit Group - Dynemicin A

# *Synthetic Approaches Toward Dynemicin A*

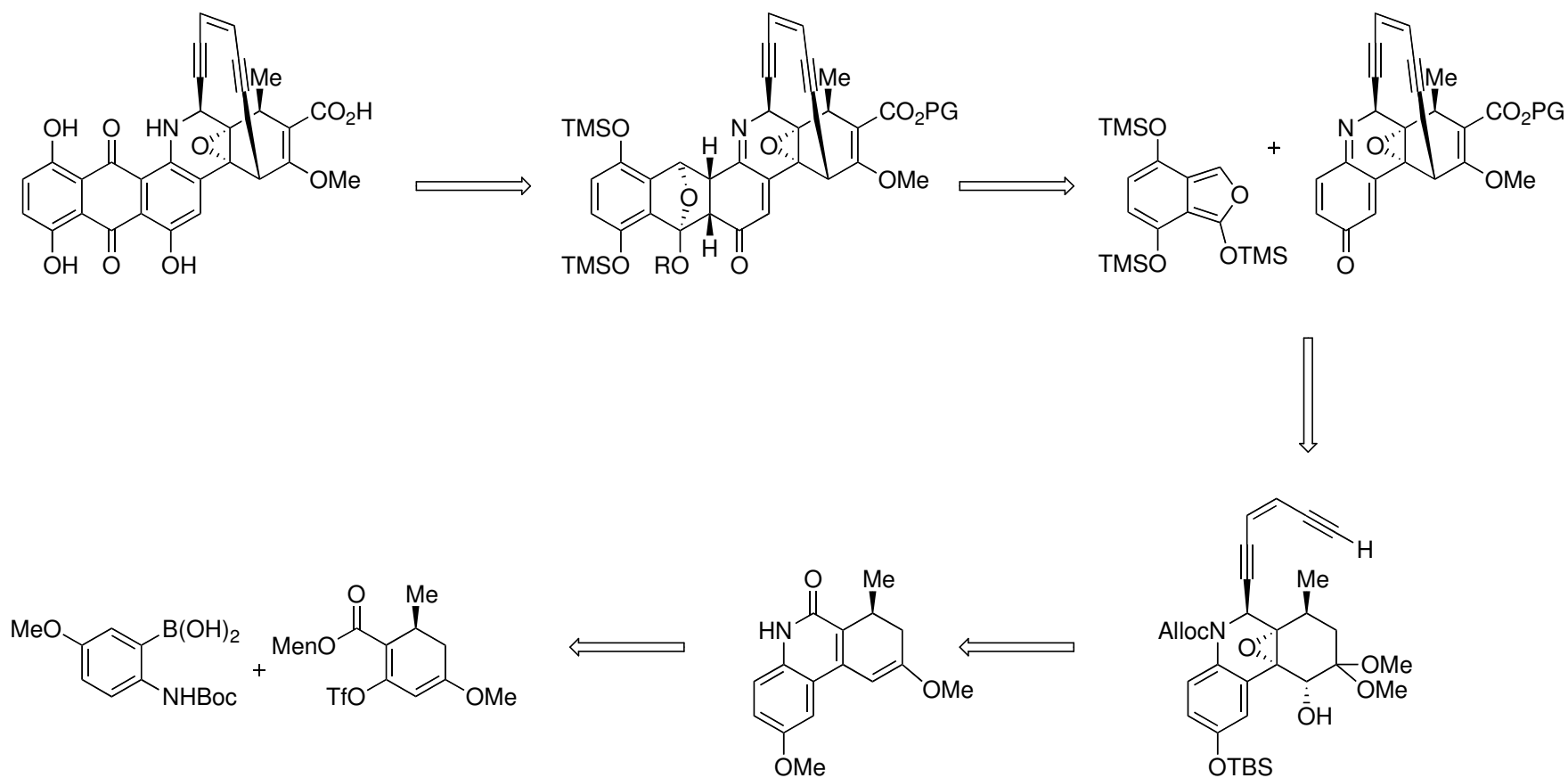
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- Andy Myers
  - JACS. **1997**, *119*, 6072. -- full account
  - Chem. & Biol. **1995**, *2*, 33 -- initial disclosure
- Sam Danishefsky
  - JACS. **1996**, *118*, 9509. -- full account
  - ACIE. **1995**, *34*, 1721. -- initial disclosure
- Stuart Schreiber
  - JACS. **1993**, *115*, 10378. -- final account\*

\*Synthesis of Tri-O-Methyl derivative

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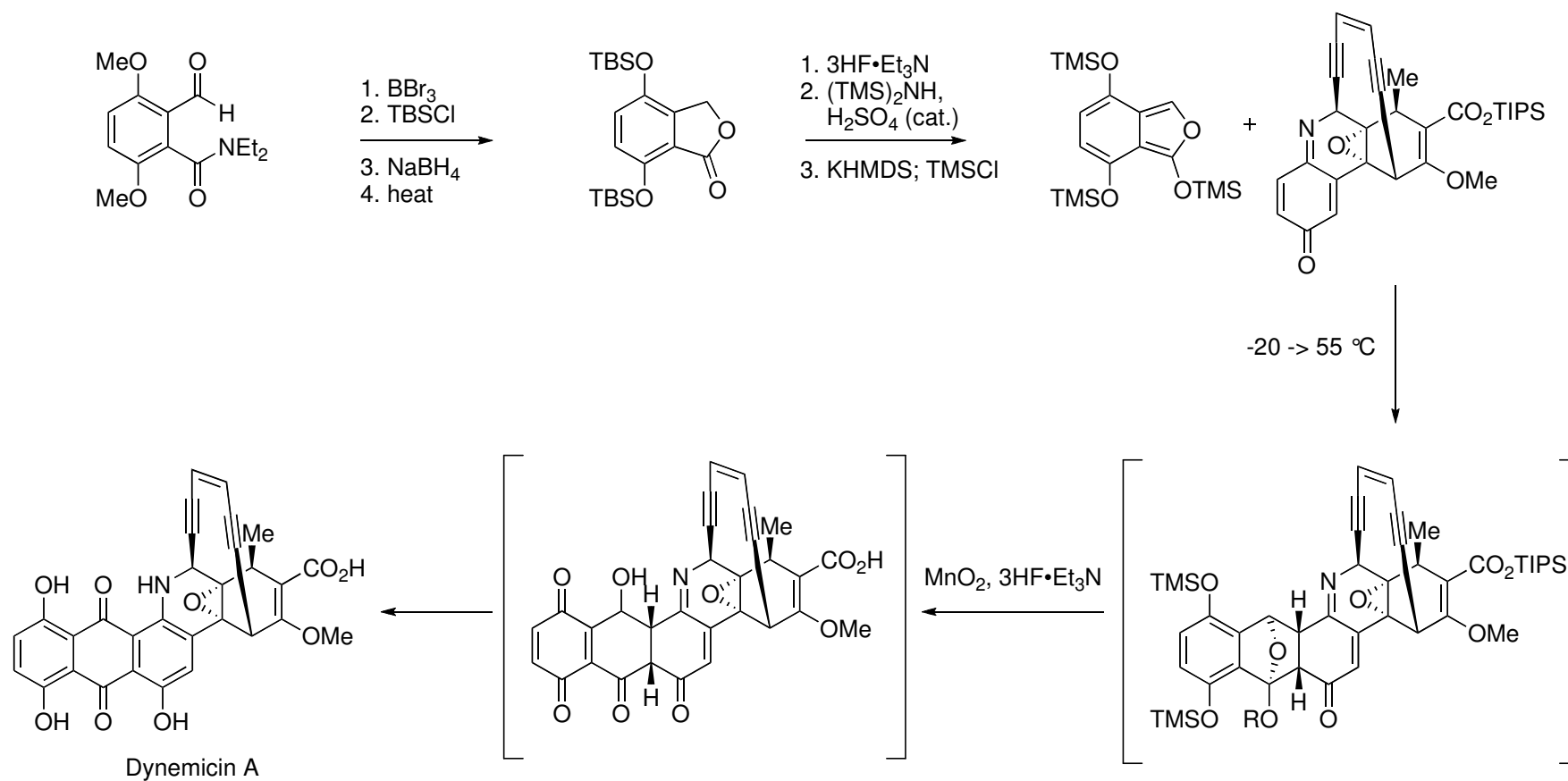
# Myers' Approach: Retrosynthesis



EISohly 5 - CU Synthesis Lit Group - Dynemicin A

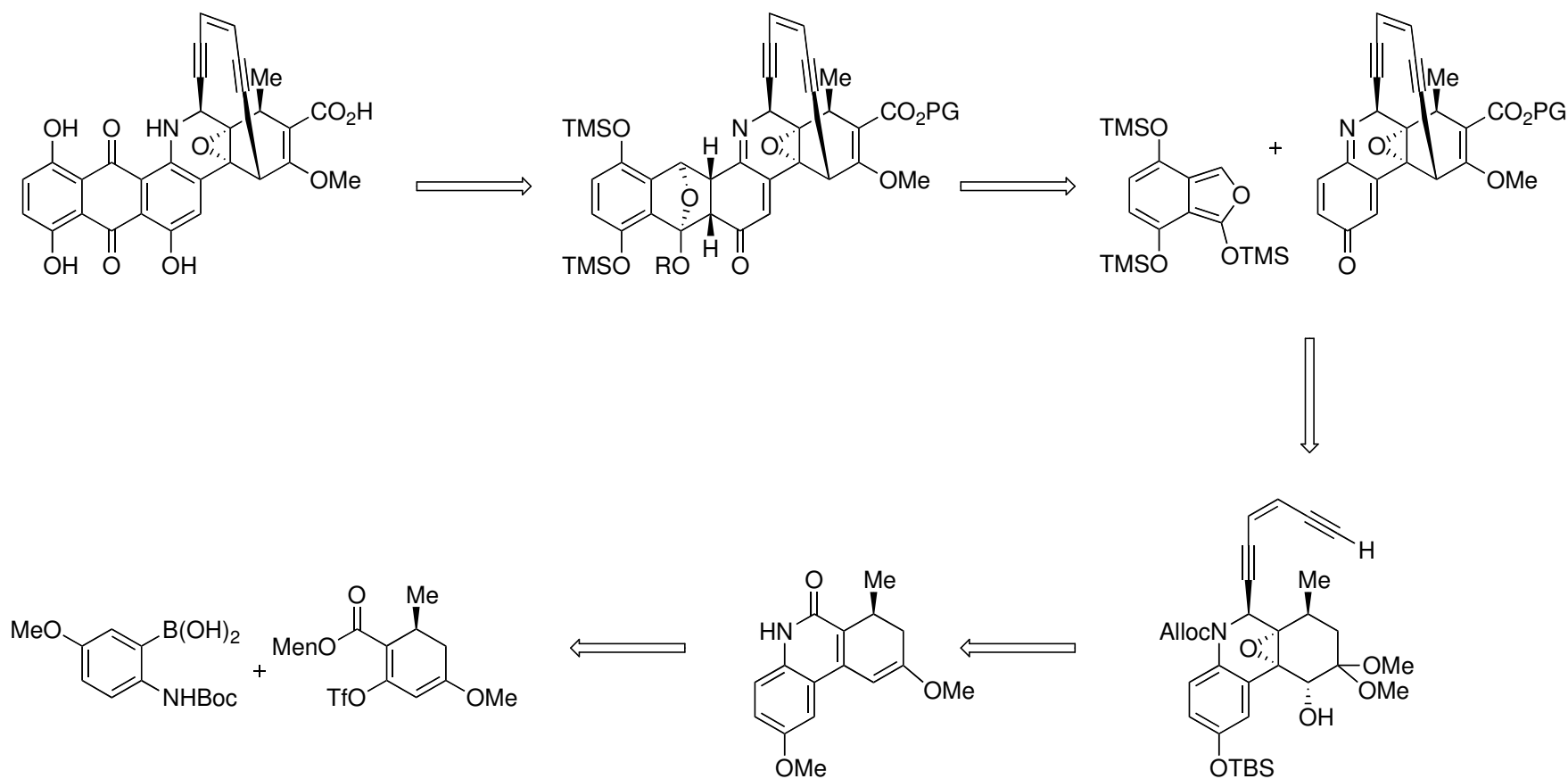


# Myers' Approach: Total Synthesis



EISohly 7 - CU Synthesis Lit Group - Dynemicin A

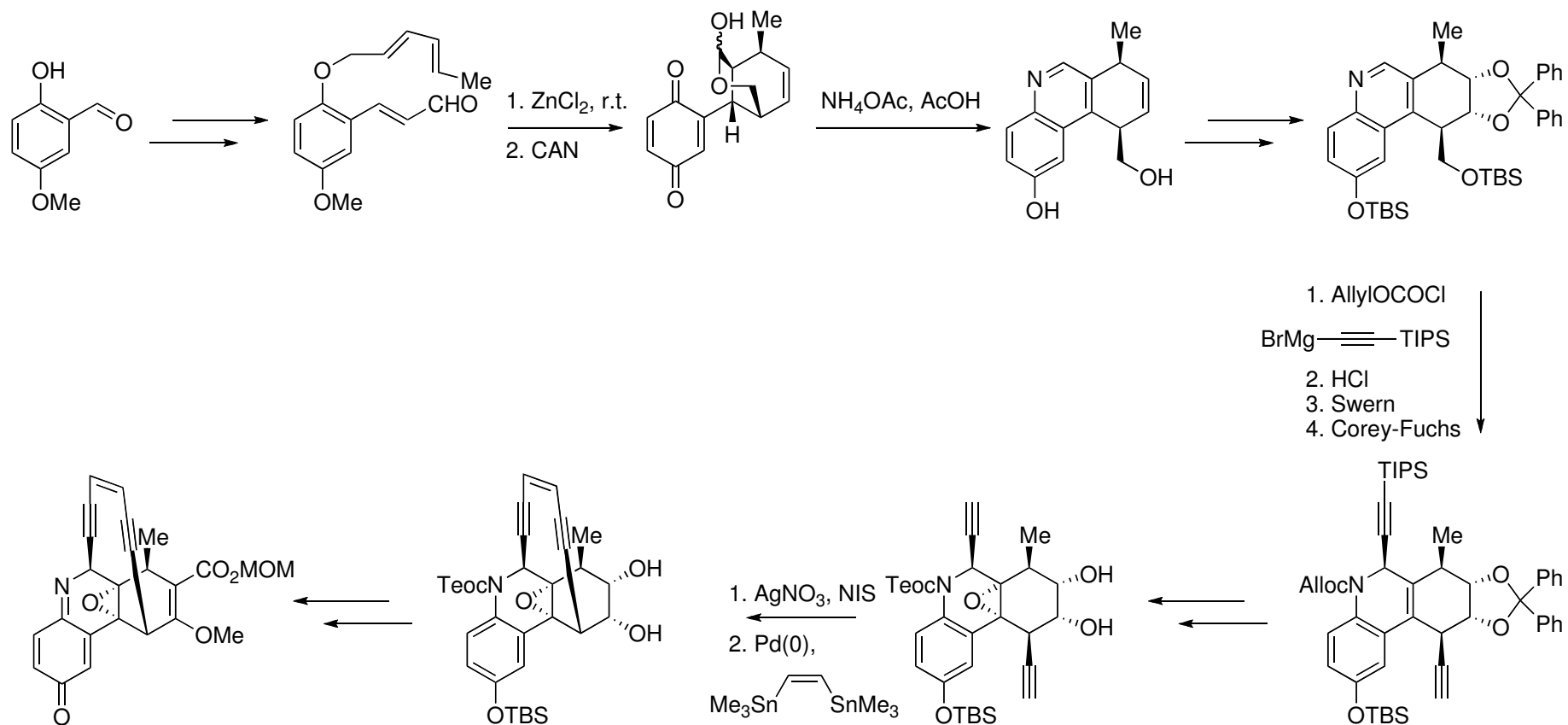
# Myers' Approach: Retrosynthesis



EISohly 8 - CU Synthesis Lit Group - Dynemicin A



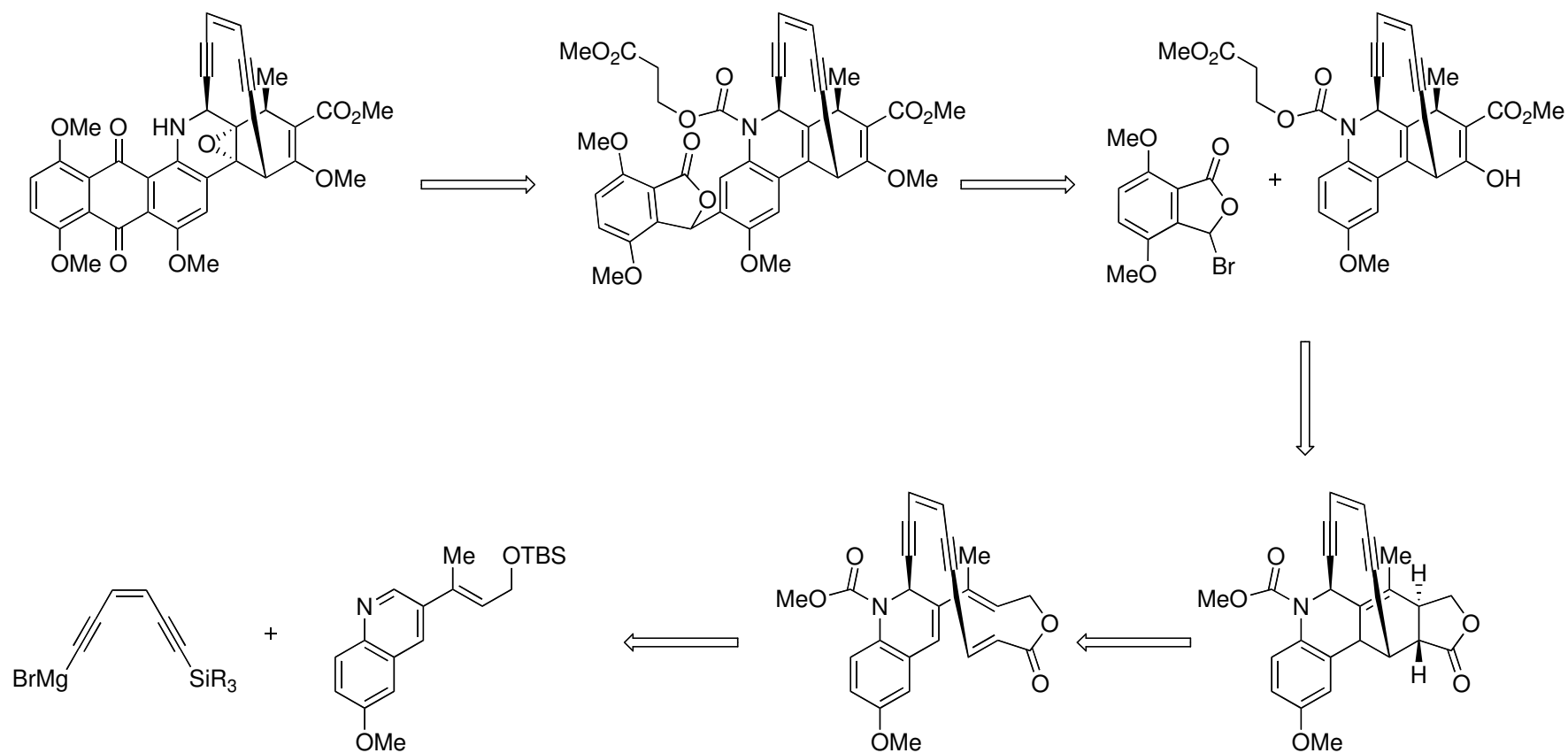
# Danishefsky's Approach: Total Synthesis



EISohly 10 - CU Synthesis Lit Group - Dynemicin A

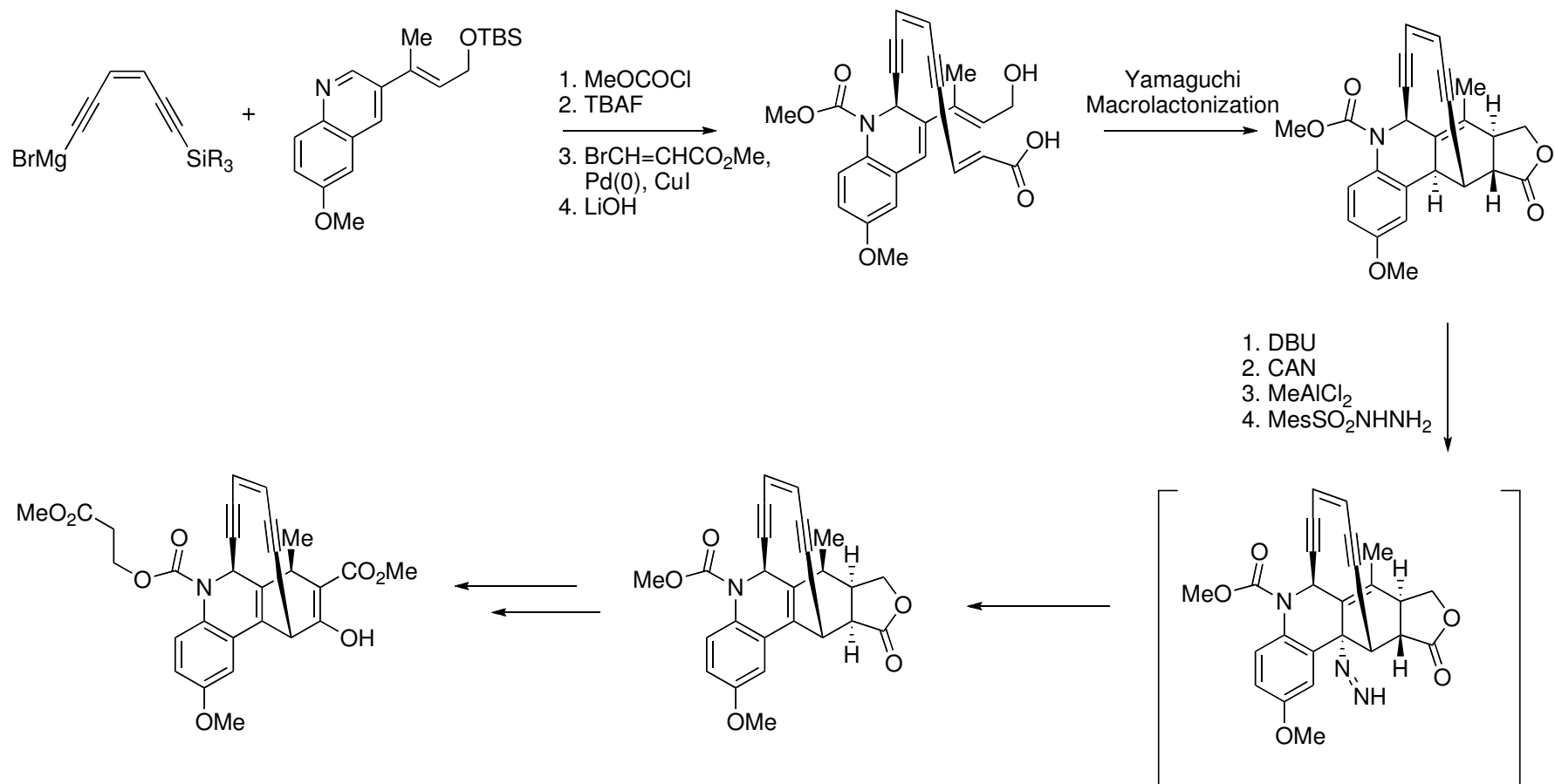


# Schreiber's Approach: Retrosynthesis



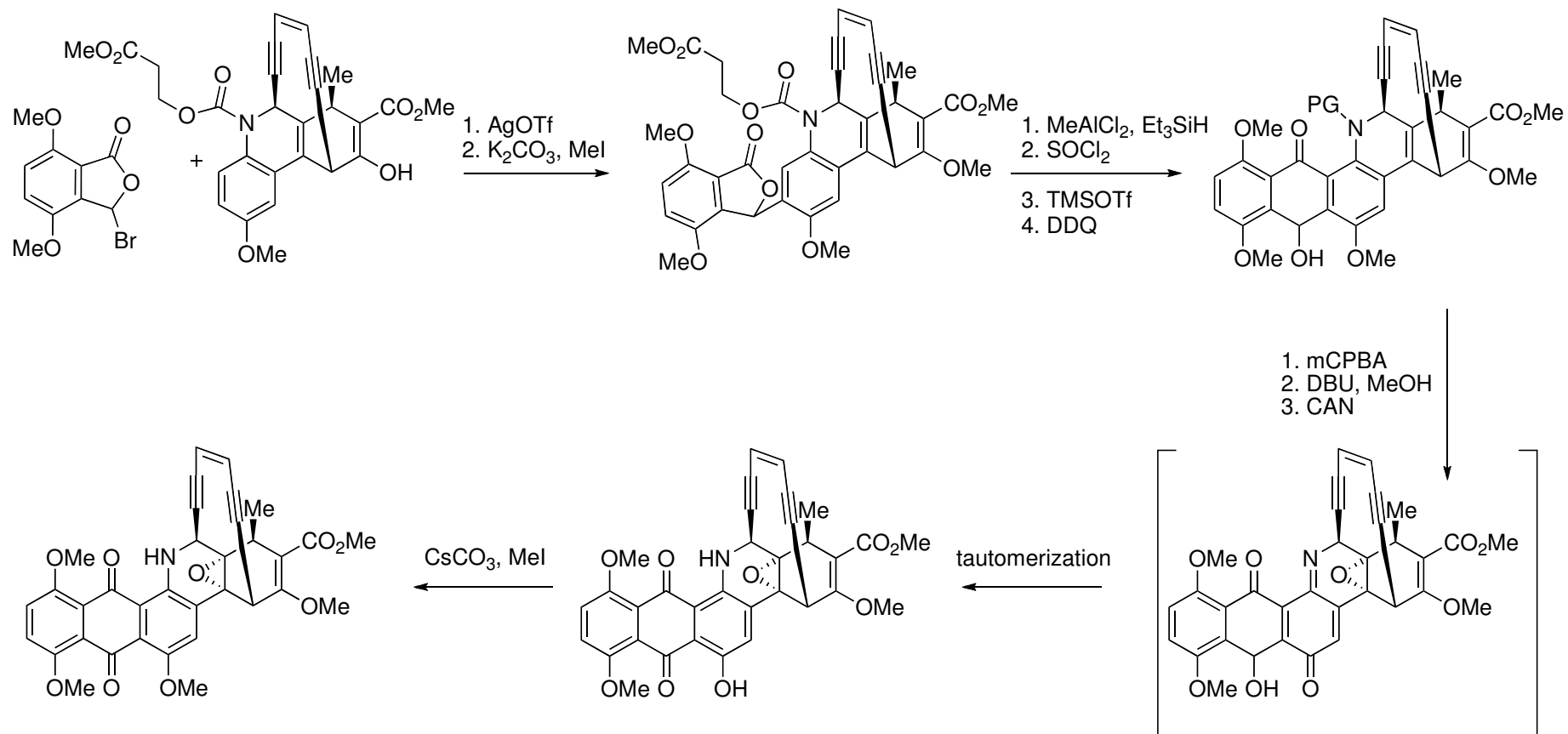
EISohly 12 - CU Synthesis Lit Group - Dynemicin A

# Schreiber's Approach: Synthesis



EISohly 13 - CU Synthesis Lit Group - Dynemicin A

# Schreiber's Approach: Synthesis



EISohly 14 - CU Synthesis Lit Group - Dynemicin A

# Summary of Syntheses

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- Andy Myers
  - Diels-Alder reaction of isobenzofuran assembles anthraquinone ring system
  - Yamaguchi alkynylation & nucleophilic addition fashions ene-diyne
- Sam Danishefsky
  - Diels-Alder reaction of homophthalic anhydride enolate to forge anthraquinone ring system
  - Yamaguchi alkynylation, Corey-Fuchs homologation, and double Stille reactions complete ene-diyne system
- Stuart Schreiber\*
  - Iterative Friedel-Crafts alkylations complete anthraquinone moiety
  - Yamaguchi alkynylation/macrolactonization and intramolecular Diels-Alder completes ene-diyne structure

\*Synthesis of Tri-O-Methyl derivative