

Enantioselective Synthesis of Oasomycin A, Part II: Synthesis of the C29-C46 Subunit

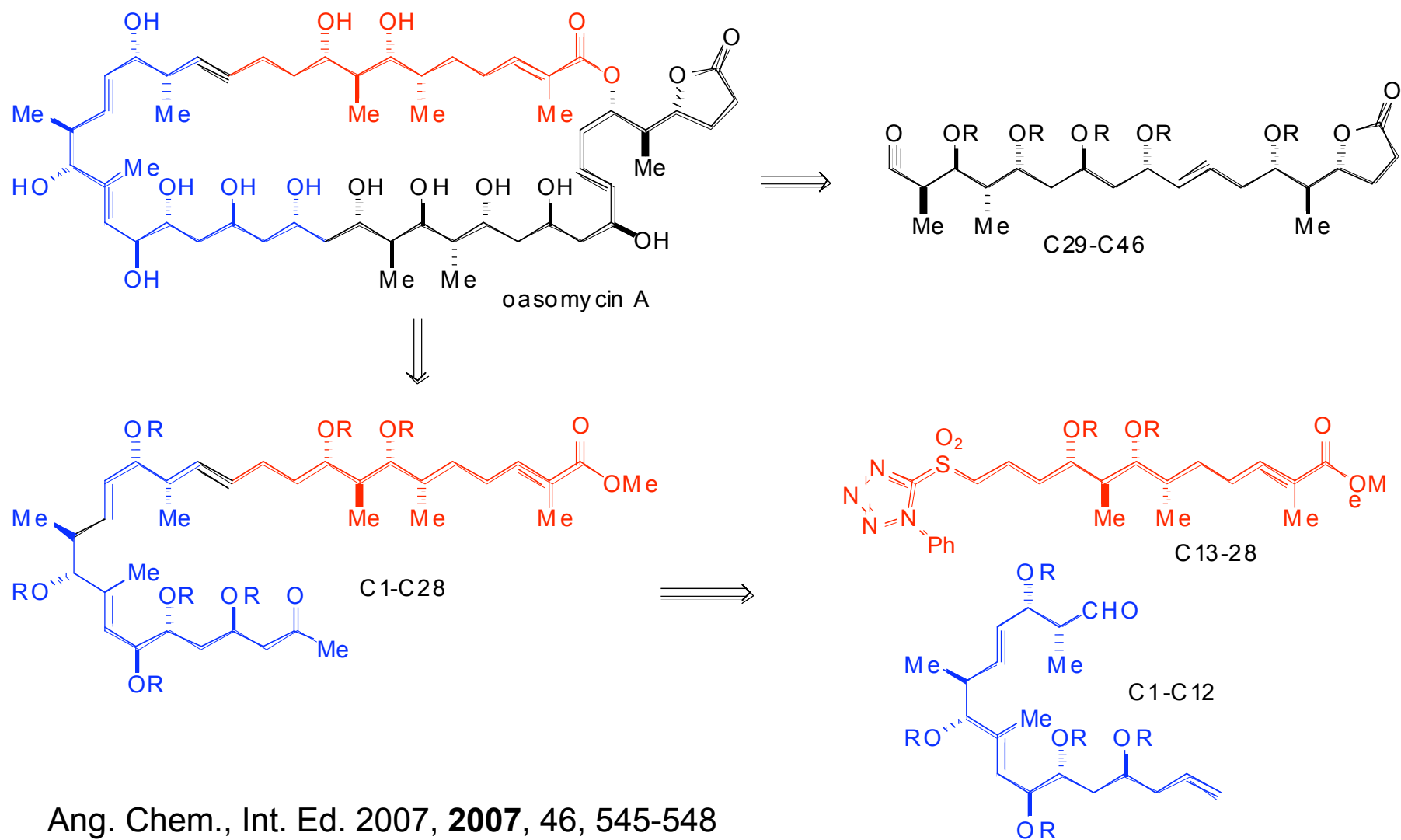
Angew. Chem., Int. Ed. 2007, 46, 541-544

Evans, D.A.; Nagorny, P.; Reynolds, D.J.; McRae K.J.

Discovery and Biological Implications

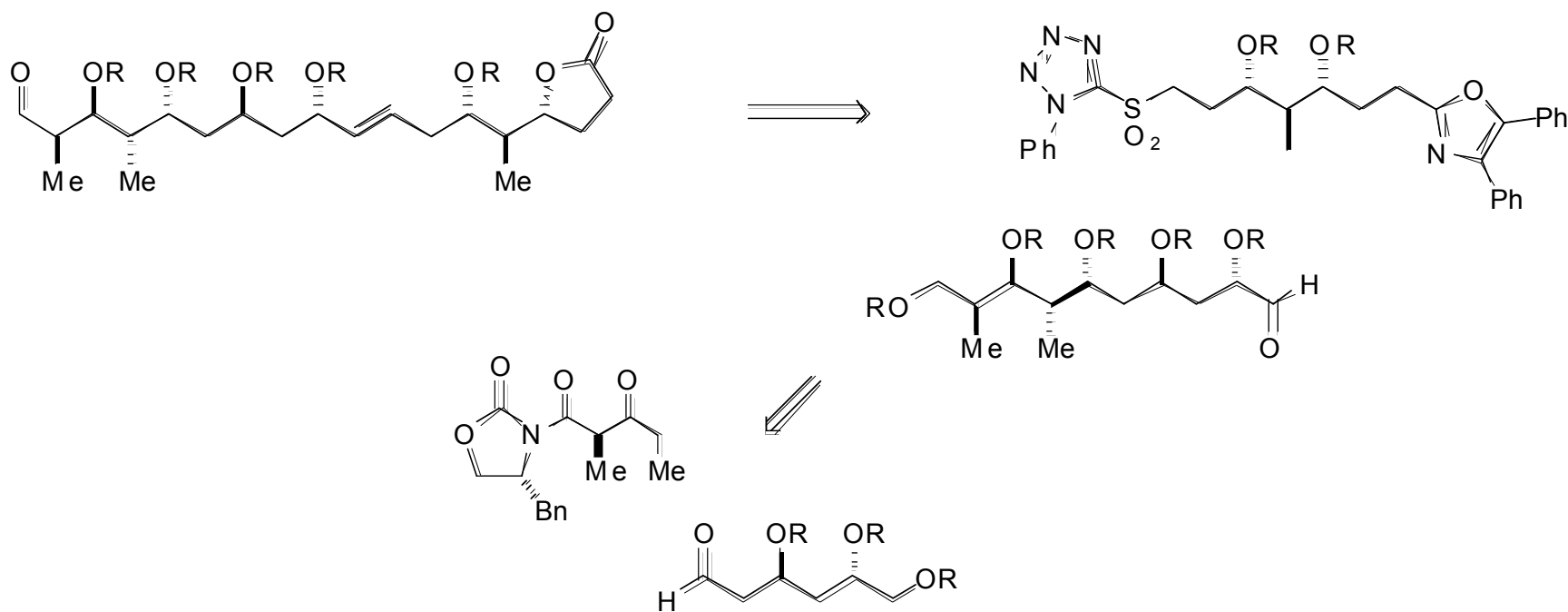
- Produced by Streptoverticillium and Streptomyces strains (Streptomyces olivaceus Tu 4081).
- Potential antibiotic and inhibitor of cholesterol biosynthesis.

Retrosynthesis: Oasomycin A

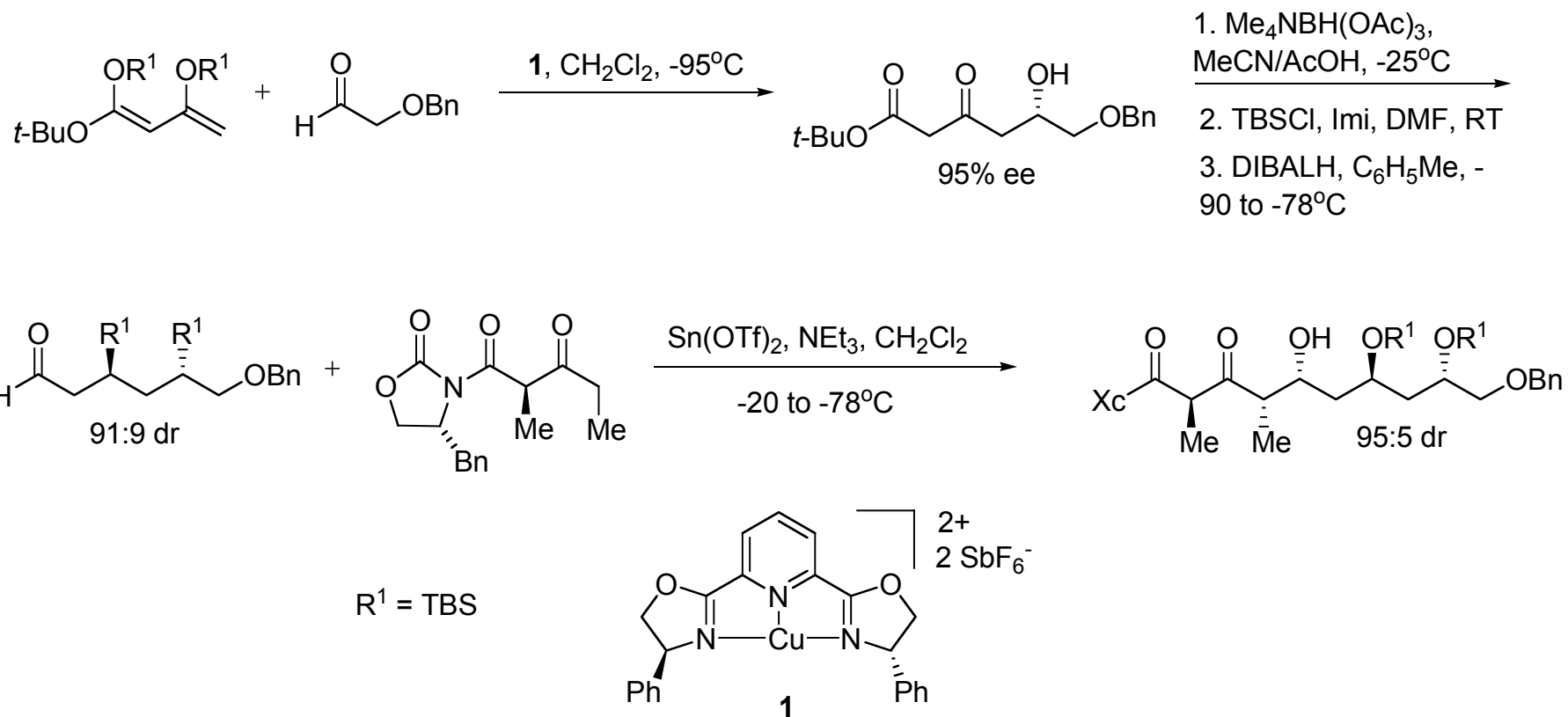


Ang. Chem., Int. Ed. 2007, **2007**, 46, 545-548

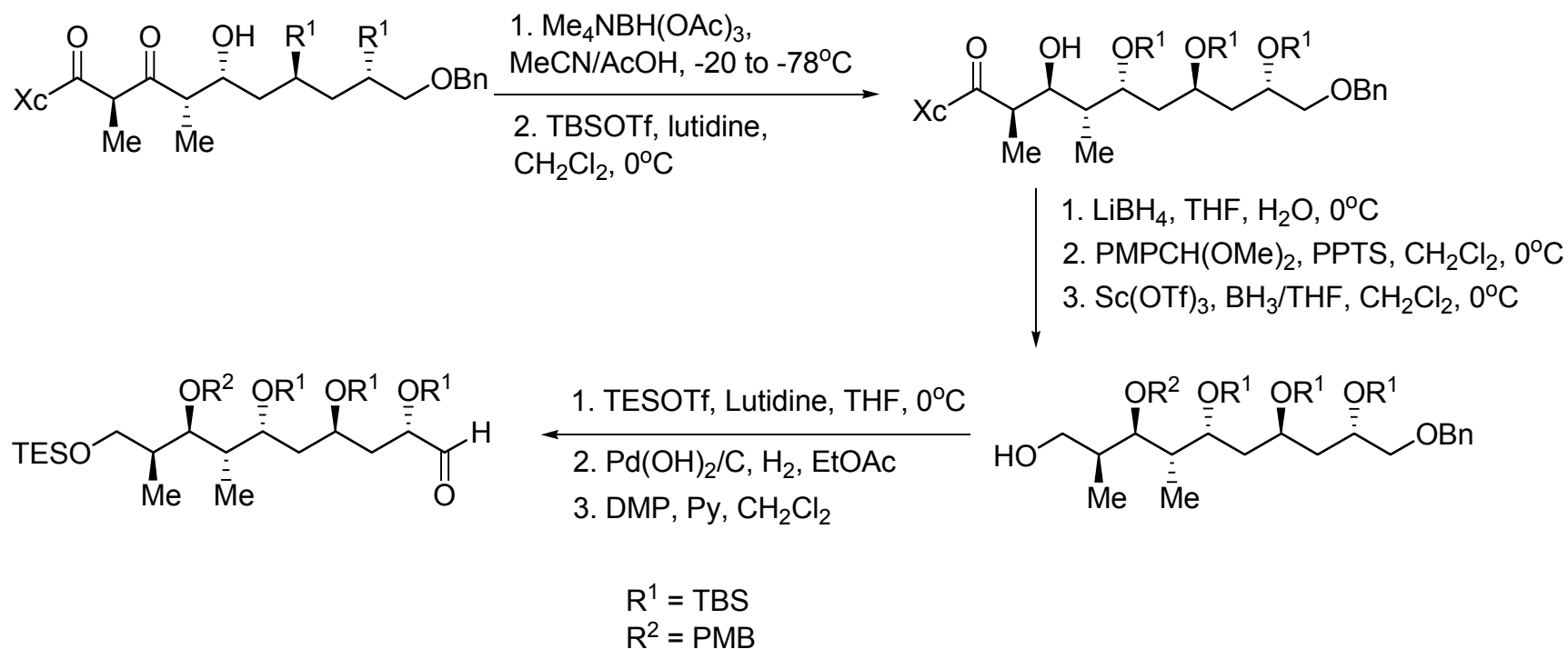
Retrosynthesis: C29-C46 Fragment



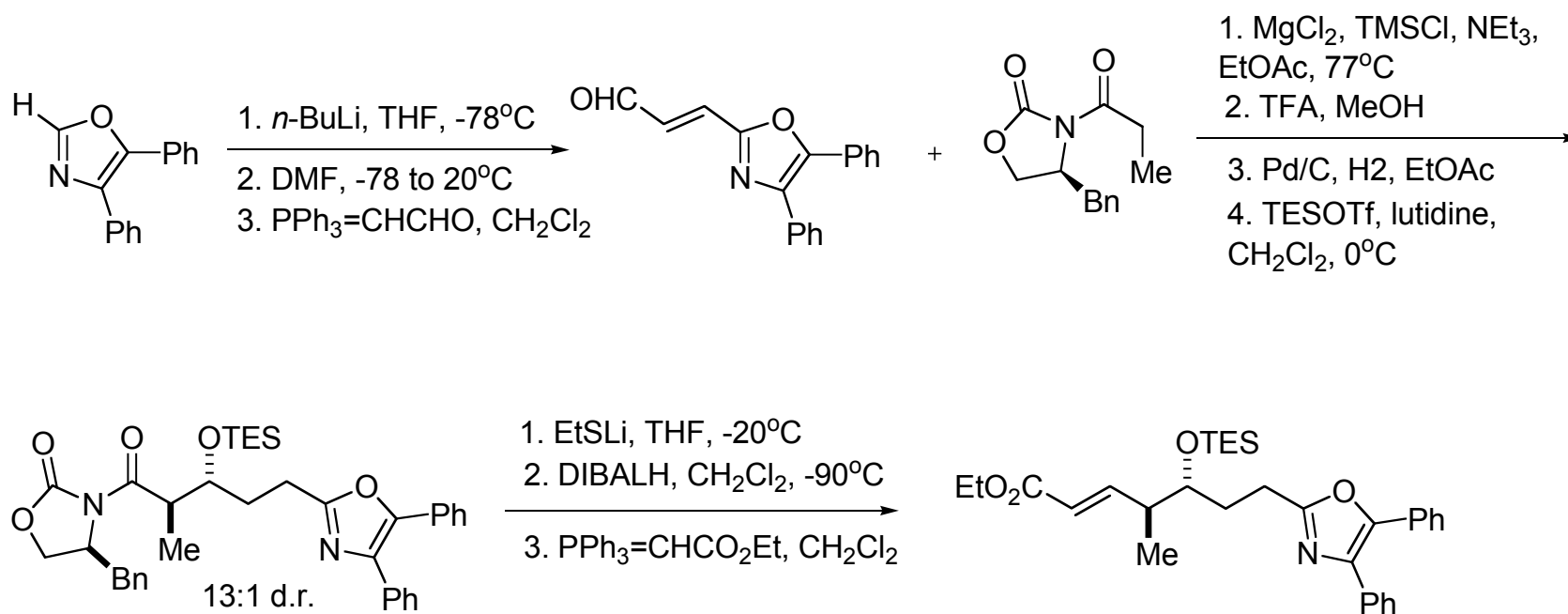
Synthesis: C29-C38 Fragment



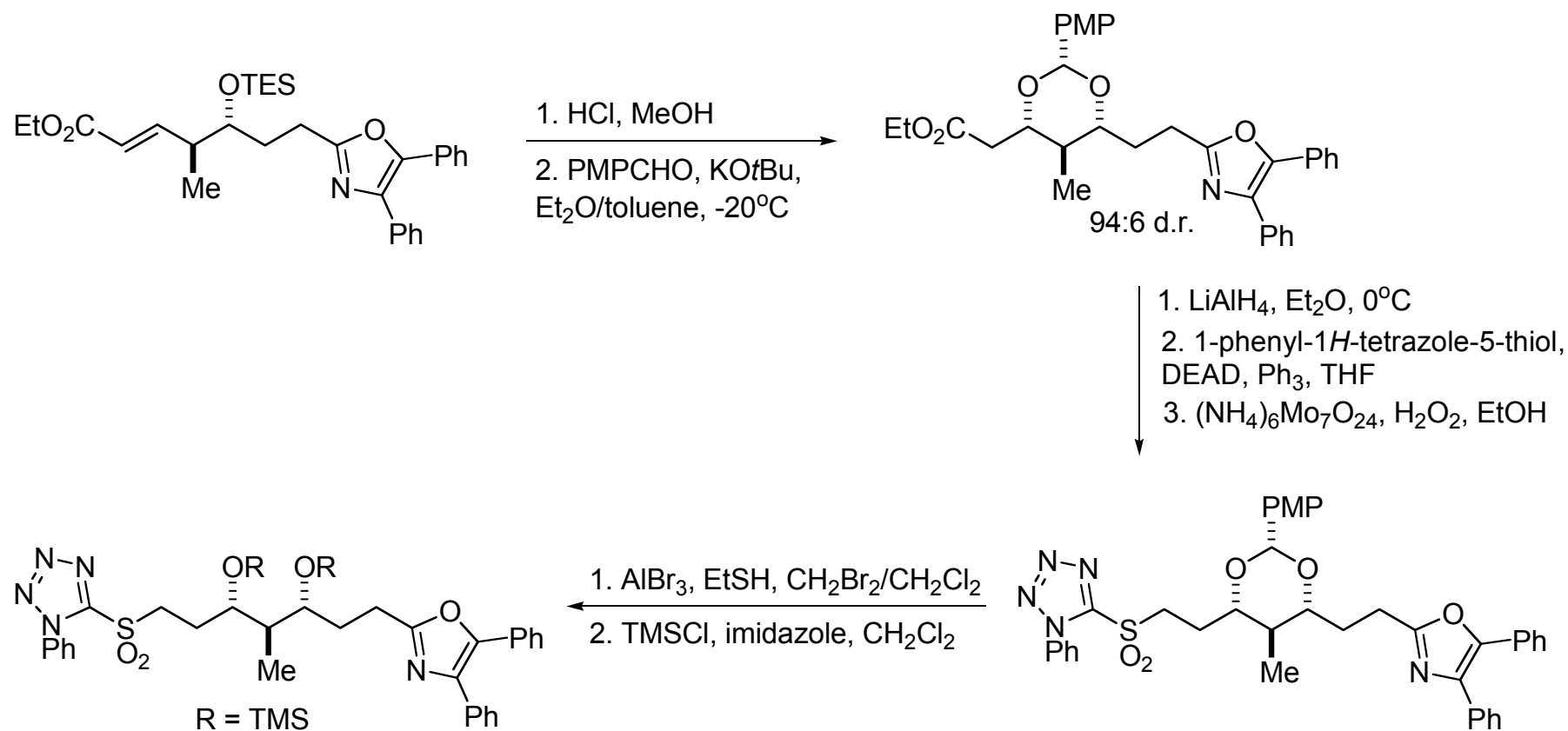
Synthesis: C29-C38 Fragment



Synthesis: C39-C46 Fragment



Synthesis: C39-C46 Fragment



Reaction scheme showing the synthesis of a complex molecule:

Starting materials:

- Aldehyde: $\text{TESO}-\text{CH}_2-\text{CH}(\text{Me})-\text{CH}(\text{OR}^2)-\text{CH}(\text{Me})-\text{CH}(\text{OR}^3)-\text{CH}_2-\text{CH}(\text{OR}^3)-\text{CH}_2-\text{CHO}$
 $\text{R}^2 = \text{PMB}$
 $\text{R}^3 = \text{TBS}$
- Intermediate: $\text{Ph}-\text{N}=\text{N}-\text{C}(\text{Ph})=\text{S}(\text{O})_2-\text{CH}_2-\text{CH}(\text{OR}^1)-\text{CH}(\text{Me})-\text{CH}(\text{OR}^1)-\text{CH}_2-\text{CH}_2-\text{C}_2\text{H}_4-\text{O}-\text{C}_2\text{H}_3-\text{N}=\text{C}(\text{Ph})-\text{C}(\text{Ph})=\text{O}$
 $\text{R}^1 = \text{TMS}$

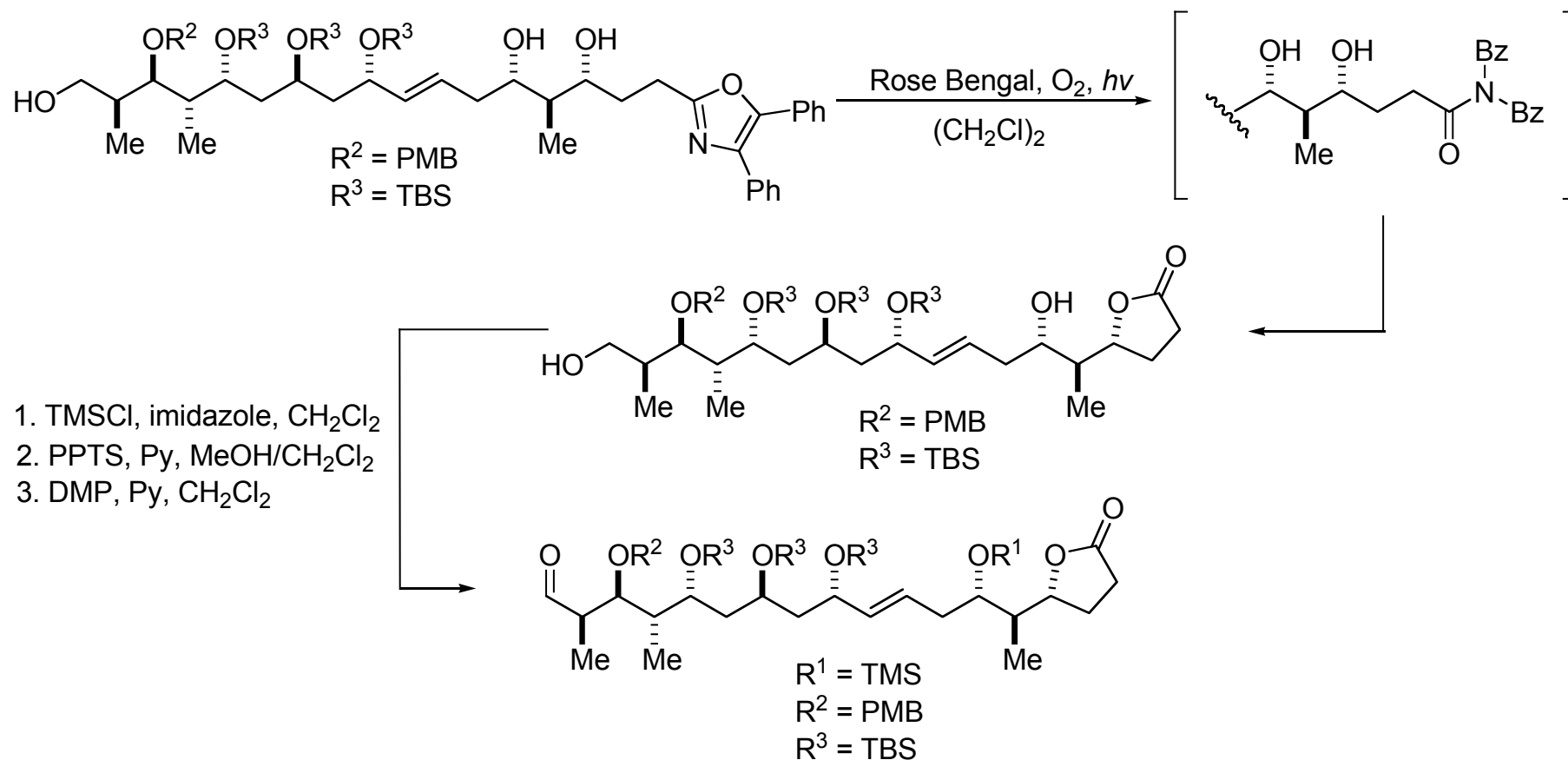
Reaction conditions:

1. KHMDS, DME, -48 to -20°C
2. PPTS, $\text{MeOH}/\text{CH}_2\text{Cl}_2$

Product:

$\text{HO}-\text{CH}_2-\text{CH}(\text{Me})-\text{CH}(\text{OR}^2)-\text{CH}(\text{Me})-\text{CH}(\text{OR}^3)-\text{CH}_2-\text{CH}(\text{OR}^3)-\text{CH}_2-\text{CH}=\text{CH}-\text{CH}_2-\text{CH}(\text{OH})-\text{CH}(\text{Me})-\text{CH}_2-\text{CH}_2-\text{O}-\text{C}_2\text{H}_3-\text{N}=\text{C}(\text{Ph})-\text{C}(\text{Ph})=\text{O}$
 $\text{R}^2 = \text{PMB}$
 $\text{R}^3 = \text{TBS}$

Synthesis: C29-C46 Fragment



Conclusion

- Subunit C29-C46 of oasomycin A was synthesized with high enantioselectivity.
- Enantioselective aldol reactions were highly utilized for the formation of C29-C38 and C39-C46 subunits.
- Julia-Kocienski olefination used as a key step in the formation of the C29-C46 fragment.