

Total Synthesis of (-)-Kendomycin

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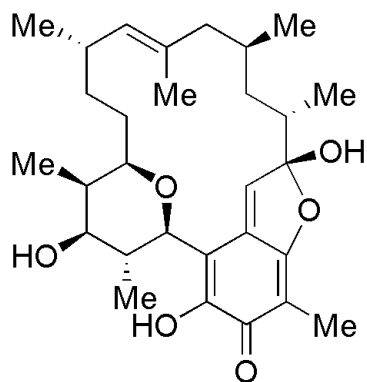
GMSchaaf

Crimmins Group Meeting

Monday, April 03, 2006

(-)-Kendomycin

- Isolated in 1996 by Funahashi and co-workers from *Streptomyces violaceoruber*
- Absolute stereochemistry determined by Zeeck in 2000
- Architecturally novel polyketide macrocycle
- Biological data:



*Proposed
Biosynthesis*

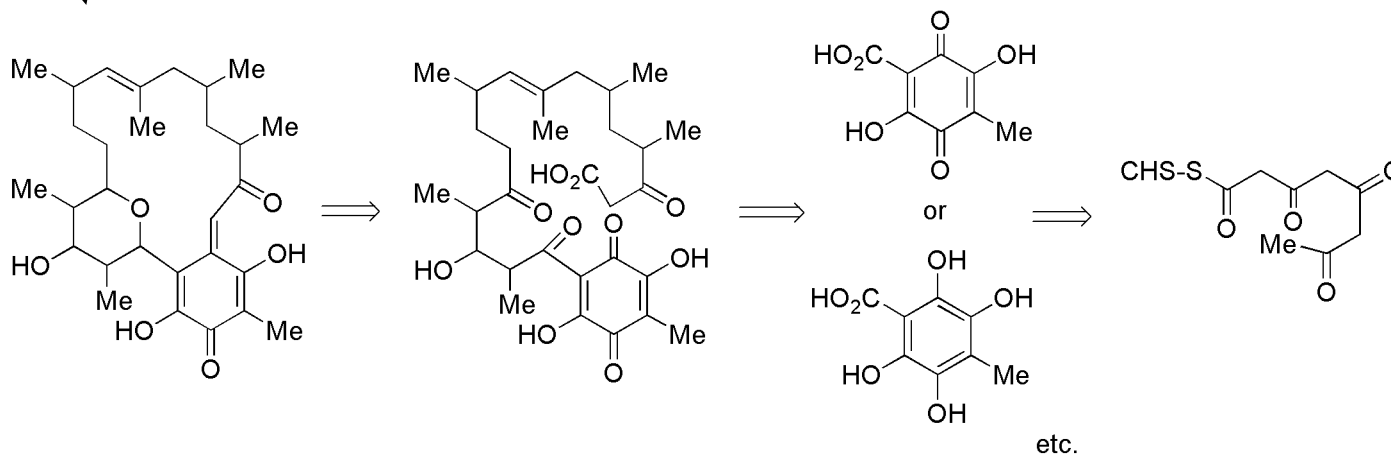
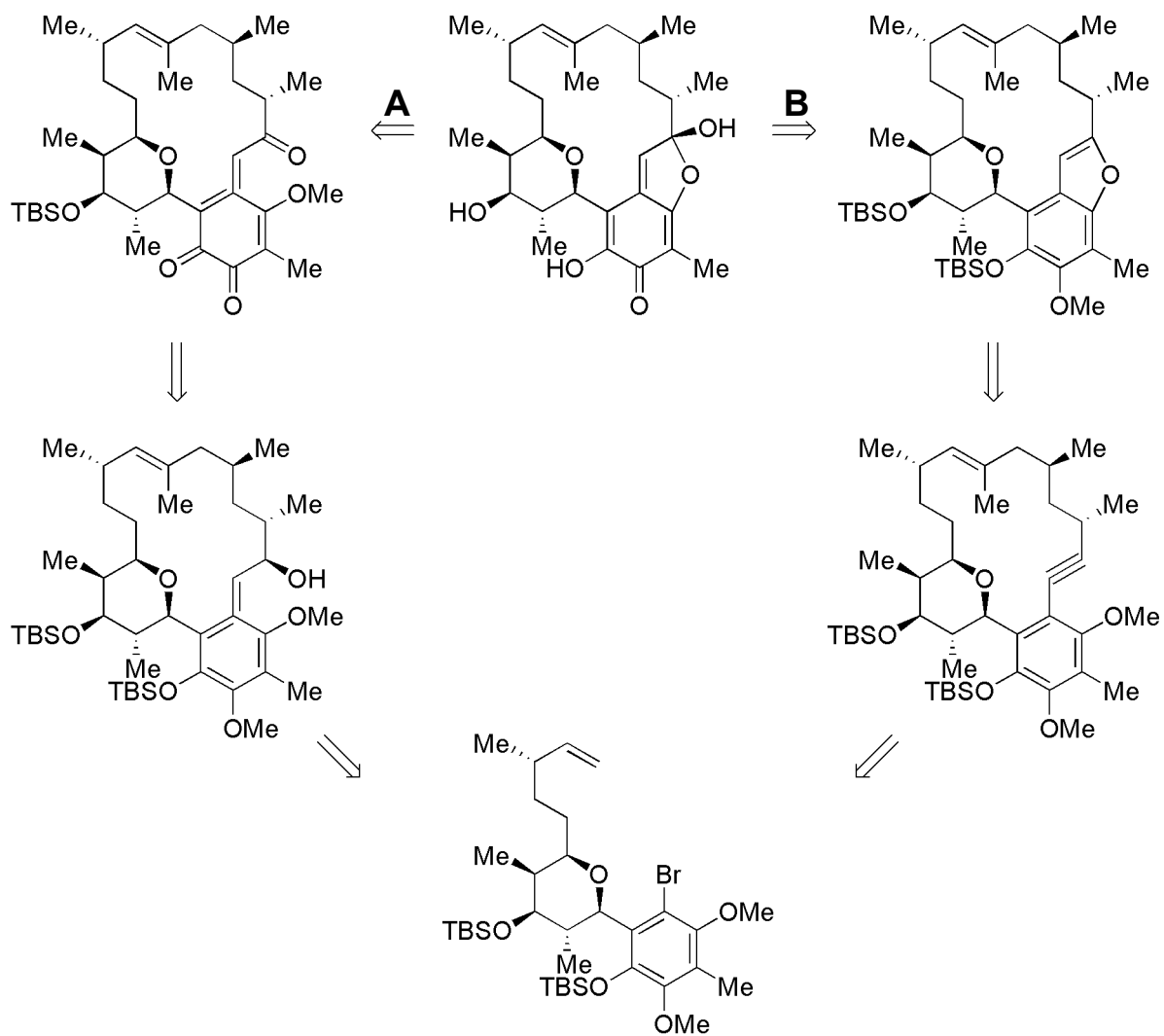


Table 3 Cytotoxic activity of 1 and 2 (in $\mu\text{mol l}^{-1}$)

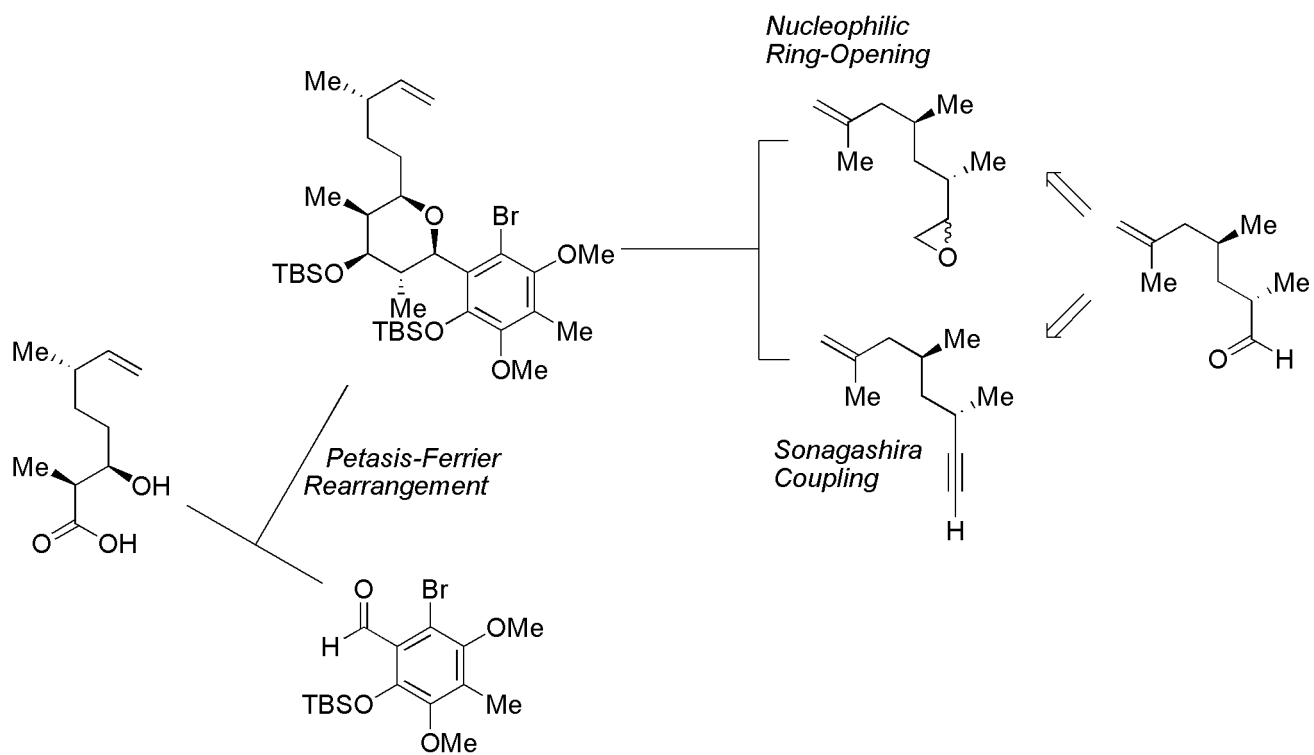
Compound	HMO2 ^a		HEP G2 ^b		MCF7 ^c	
	GI ₅₀ ^d	TGI ^e	GI ₅₀	TGI	GI ₅₀	TGI
1	<0.1	0.2	<0.1	0.2	<0.1	0.5
2	0.1	0.4	0.8	48	0.2	0.6
Doxorubicin	<0.1	0.1	0.3	1.0	<0.1	0.2
Cisplatin	0.2	1.5	0.5	5.0	0.1	10

^a Stomach adenocarcinoma. ^b Hepatocellular carcinoma. ^c Breast adenocarcinoma. ^d 50% growth inhibition. ^e Total growth inhibition.

Retrosynthesis

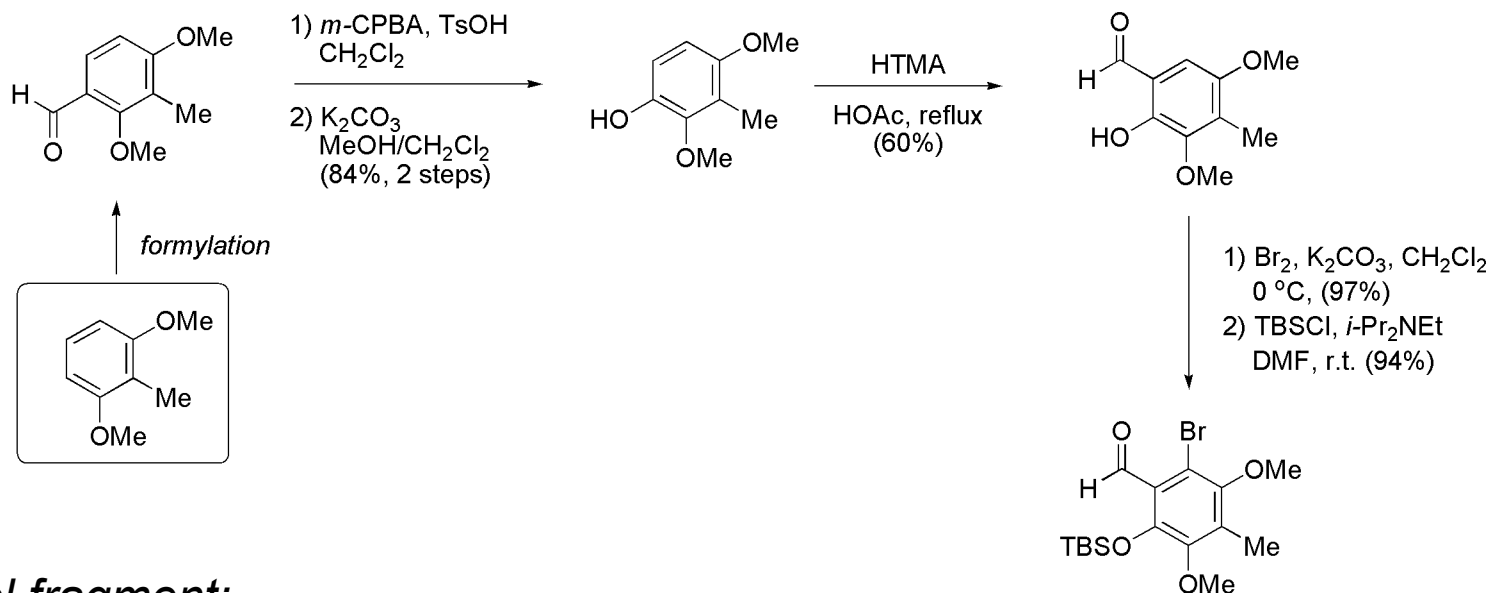


Retrosynthesis

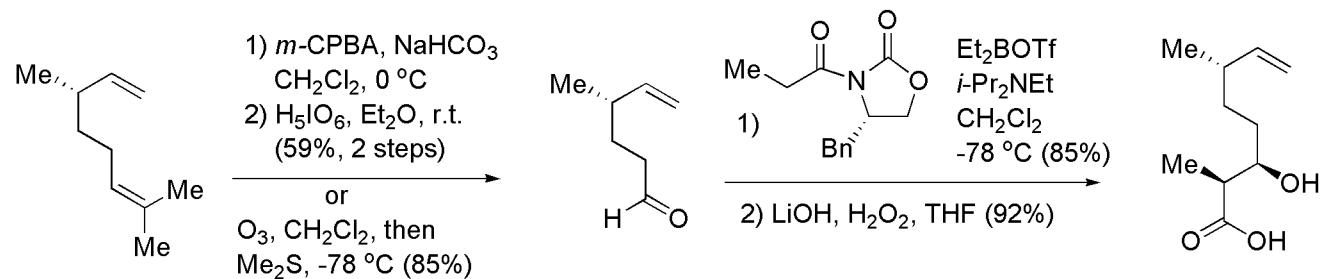


Fragment Synthesis

Aromatic fragment:

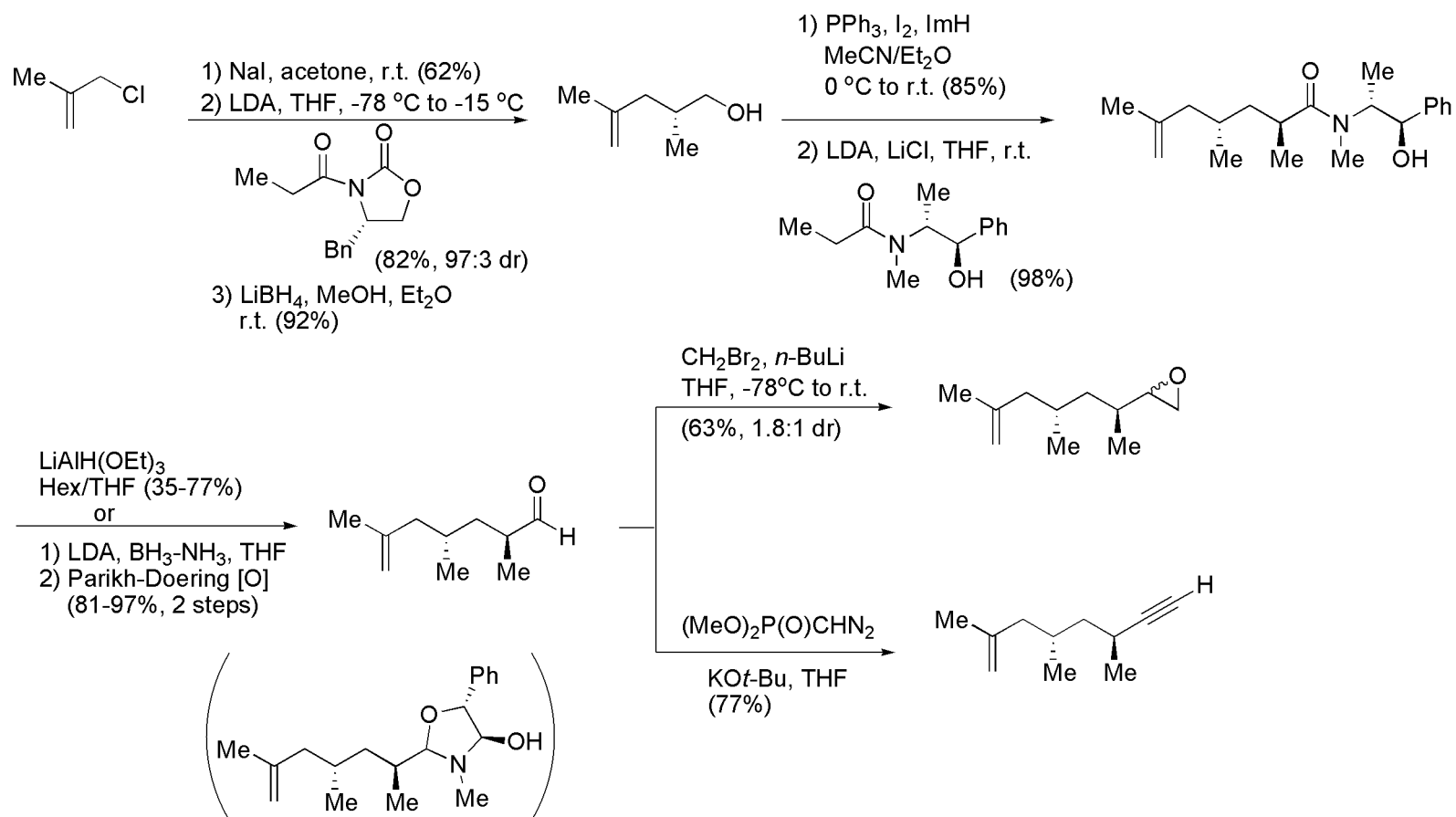


Aldol fragment:

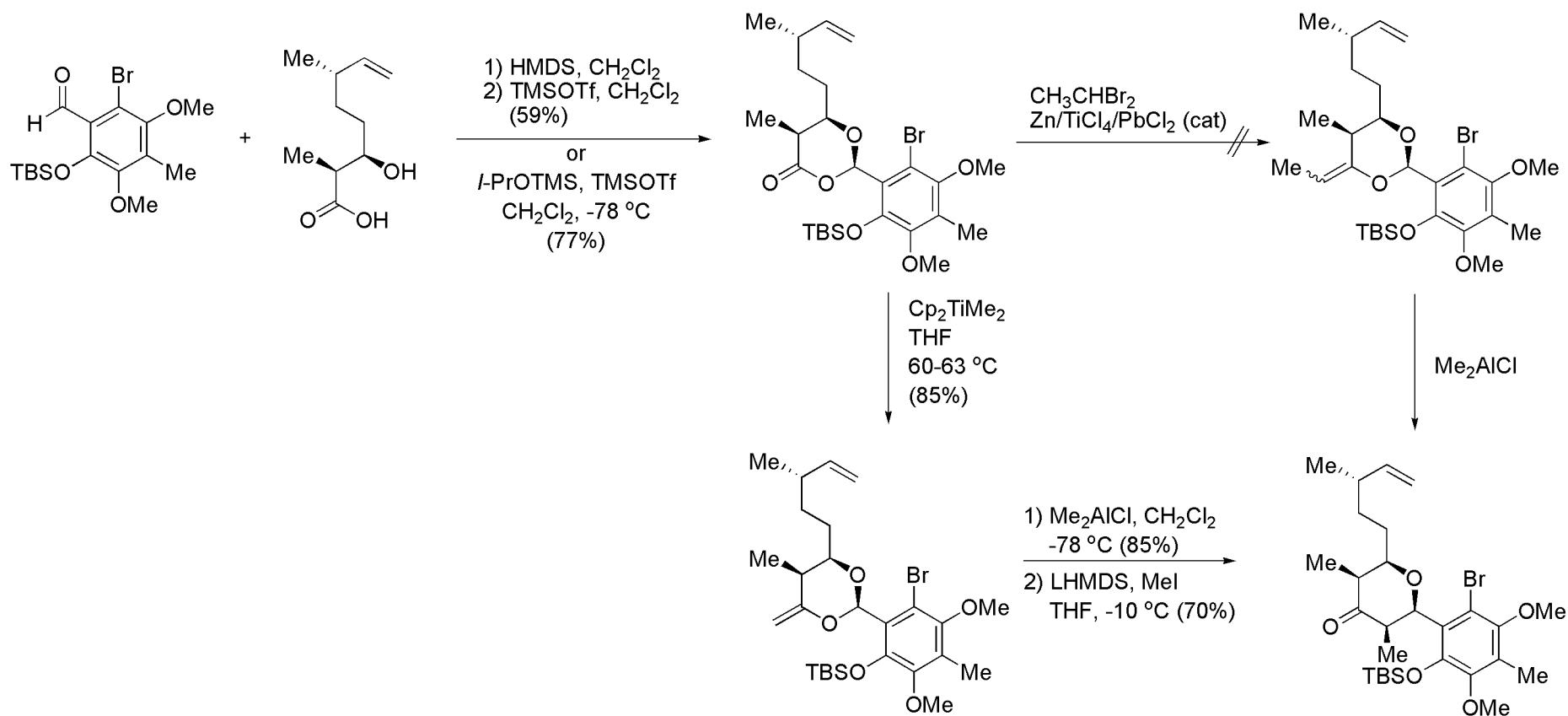


Fragment Synthesis

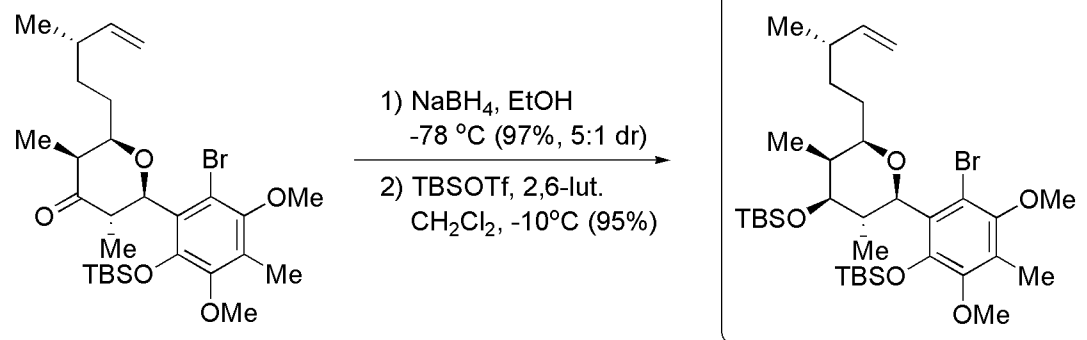
Alkyne/Epoxide Fragment:



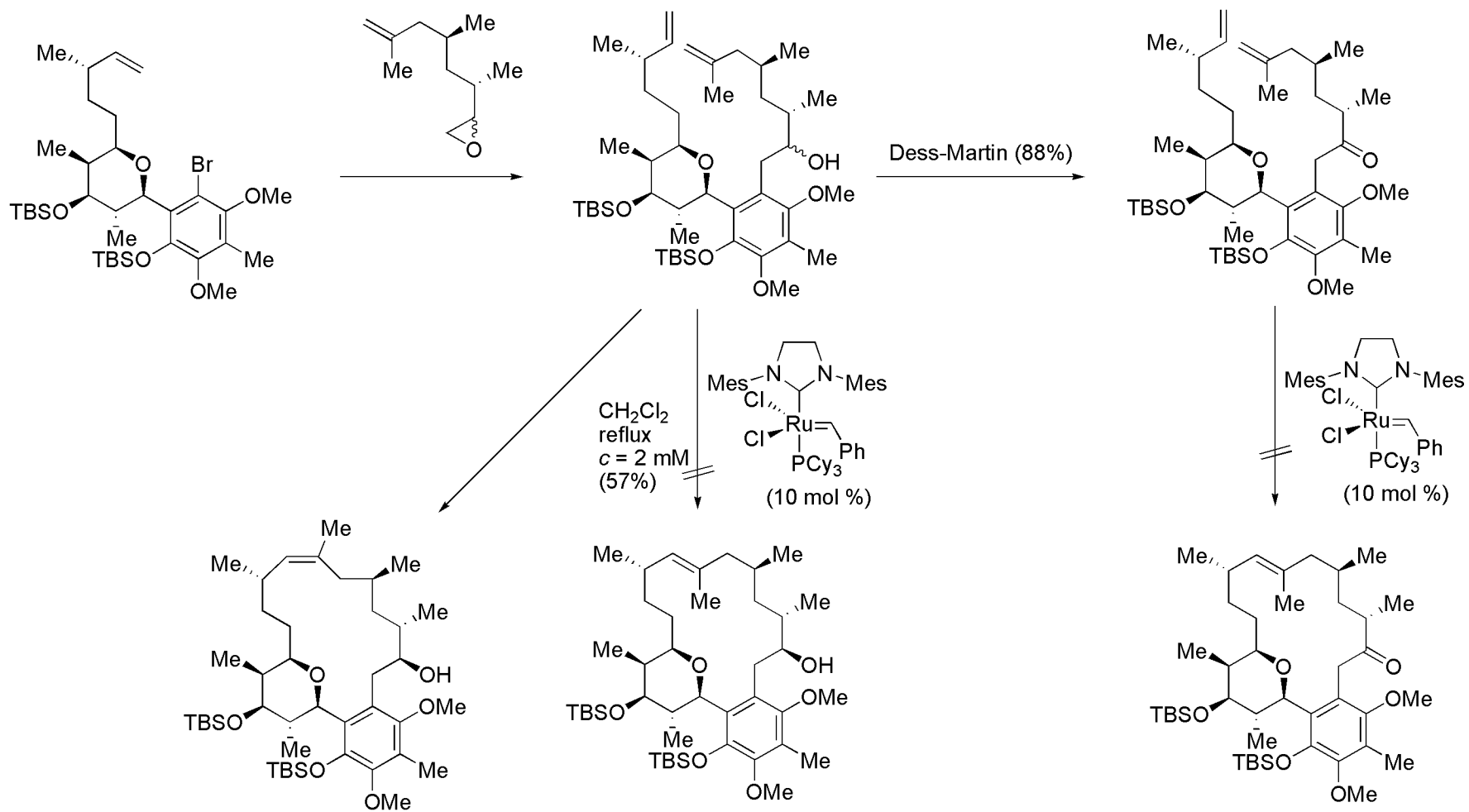
Common Intermediate



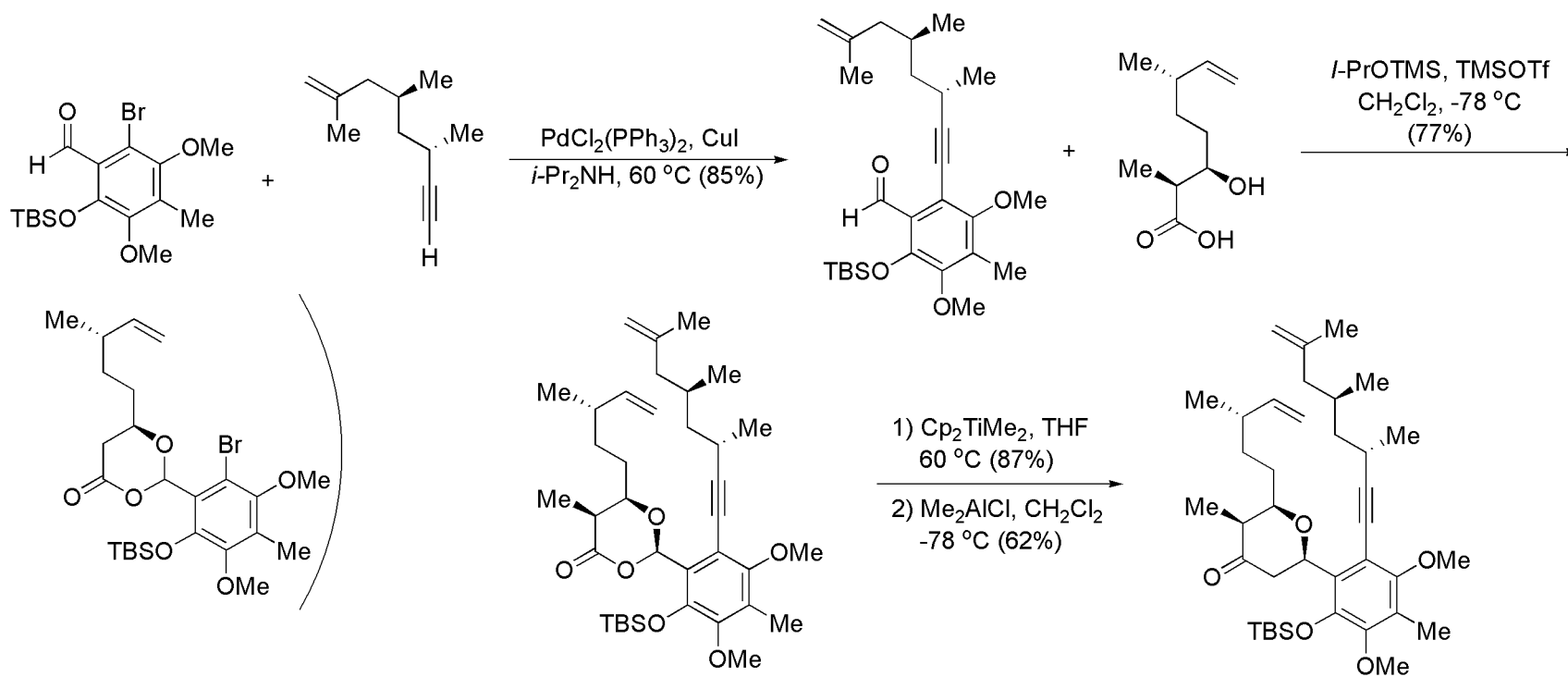
Common Intermediate



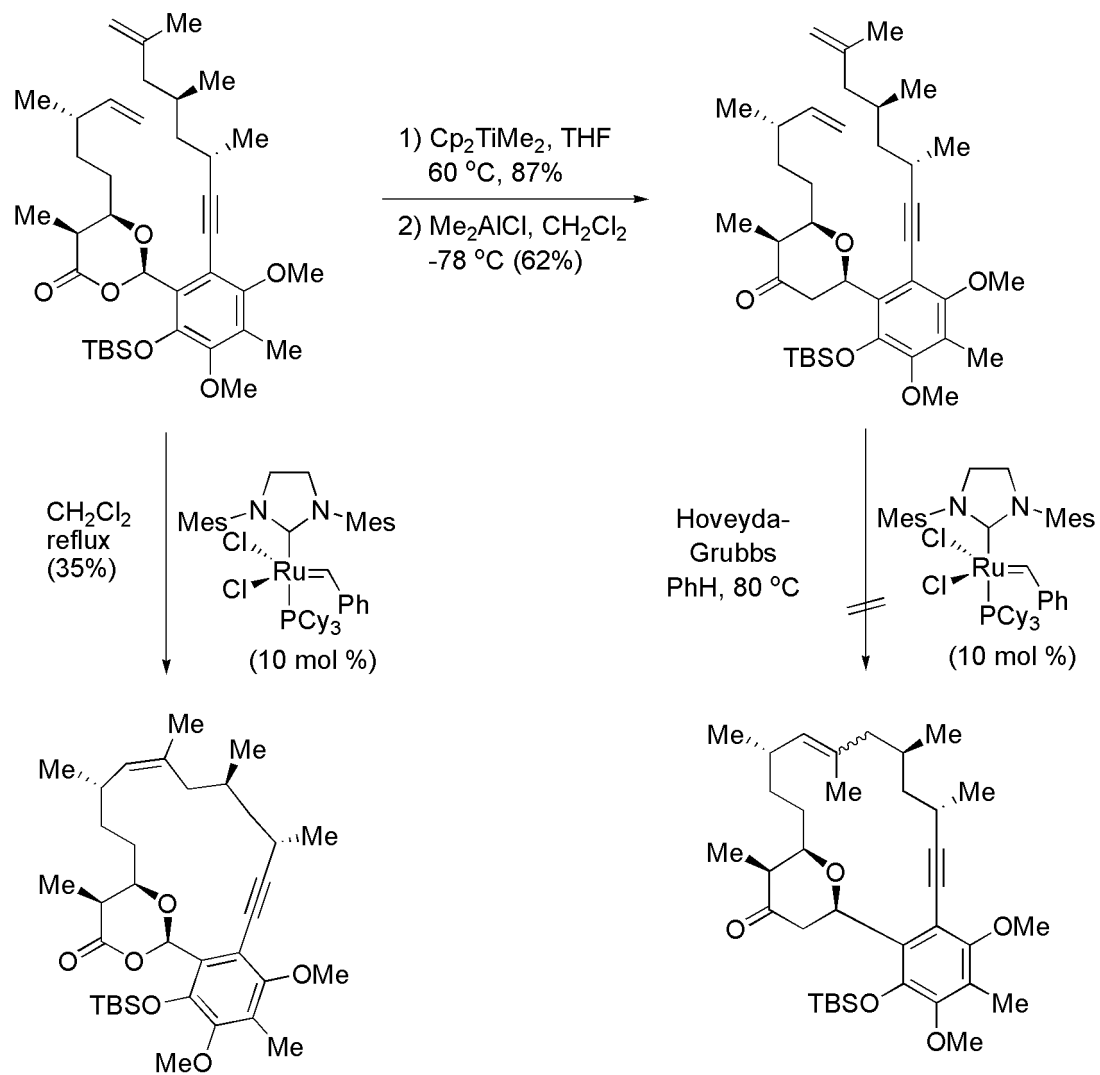
Pathway A



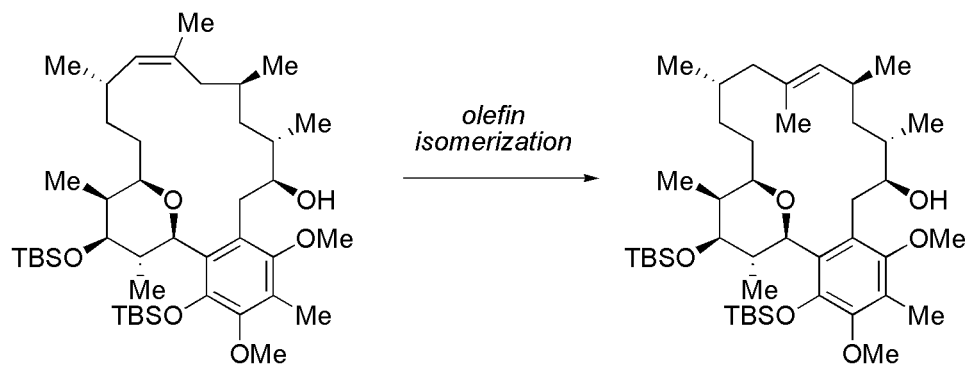
Pathway B



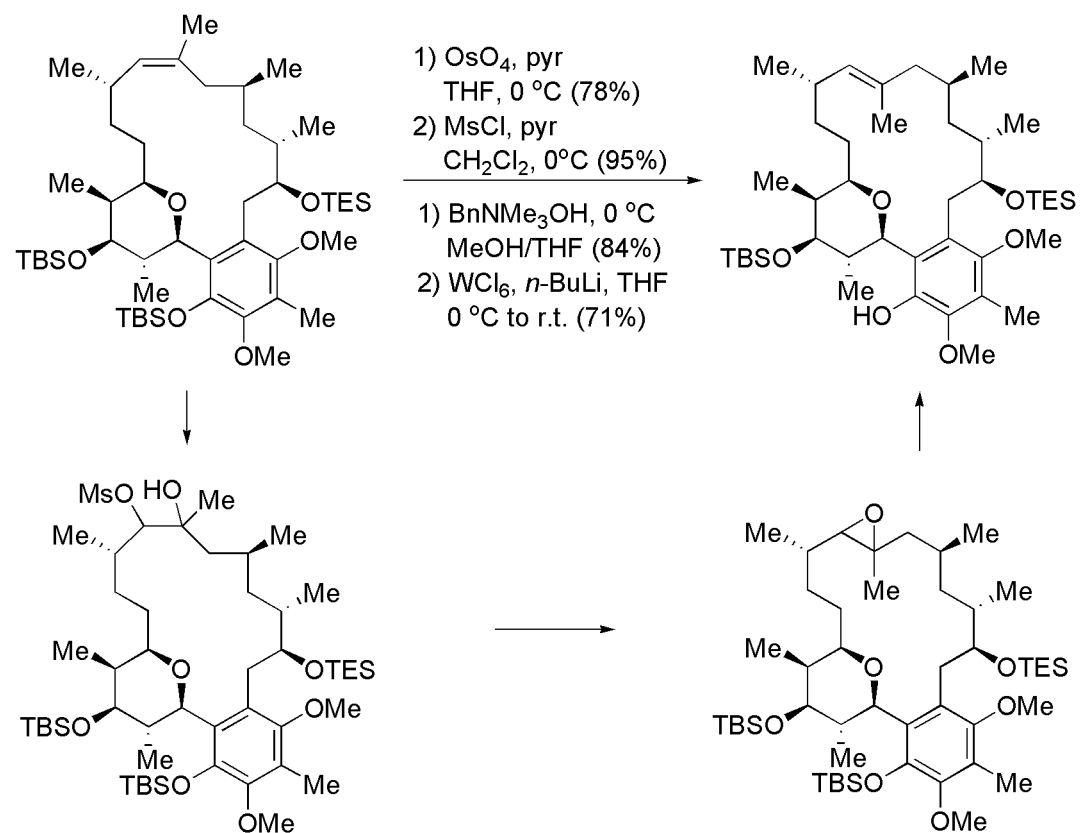
Pathway B



So...what DOES work??



Pathway A - Redux



Finishing Touches

