Some Approaches to Synthesis of Marine Natural Products Containing Medium-Sized Rings

Literature Presentation
Alexander V. Predeus, MSU

Representative C15 Medium-Sized Ring Ether Marine Metabolites

(+)-laurencin
(+)-prelaureatin
(+)-laurallene
(-)-isolaurallene
(+)-obtusenyne
(+)-brasilenyne (1)
1. Total Synthesis of (+)-Laurencin: The Key Reaction

31%, X = Me₃Si (SnCl₄, CH₂Cl₂, -60 to -20°C)
78%, X = PhS (BF₃*Et₂O, t-BuOMe, -78 to -30°C)

1. Total Synthesis of (+)-Laurencin: Cyclization
1. Total Synthesis of (+)-Laurencin: Final Steps

(+)-laurencin: 24 steps, ~2% overall yield
2. Total Synthesis of (+)-Prelaureatin and (+)-Laurallene: The Key Step and The Ring Closure

2. Total Synthesis of (+)-Prelaureatin and (+)-Laurallene: Finishing Steps

(+)-Prelaureatin

1. CBr₄, Oct₃P, C₆H₆, 70°C
2. HF-pyr, pyridine
3. Swern
4. Ph₃P=CHOME

(+)-Laurallene

1. Hg(OAc)₂, THF-H₂O
2. ICH=PPh₃
THF, HMPA

Me₃Si≡
Pd(PPh₃)₄
Cul, Et₂NH

(+)-prelaureatin
20 steps, 5.2% overall yield

(+)-laurallene
19 steps, 3.6% overall yield
3. Total Synthesis of (+)-Brasilenyne: Beginning

![Chemical diagram](image)

3. Total Synthesis of (+)-Brasilenyne: The End

(+)-brasilenyne: 19 steps, 5.1% overall yield
Conclusions:

• Medium-sized rings are very common to many classes of natural products, especially marine metabolites

• Even relatively simple natural products, containing medium-sized rings, are challenging synthetic targets, requiring individual approach

• Among others, metathesis and coupling reactions are most popular means of medium size ring construction