

Synthesis of a Ring-Expanded Bryostatin Analogue

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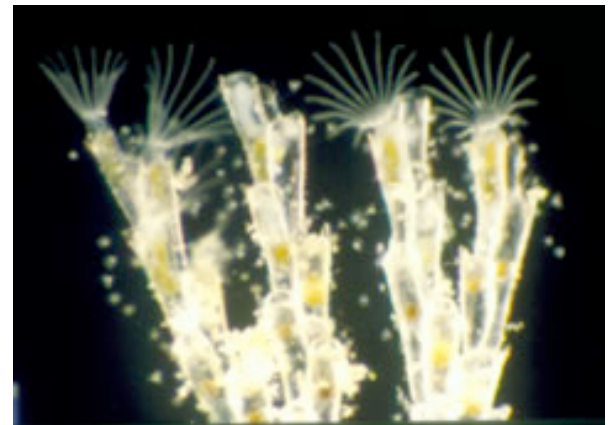
Outline

- Background
- Previous total synthesis of bryostatin
- Retrosynthetic analysis
- Ring-expanded bryostatin synthesis

Bryostatins

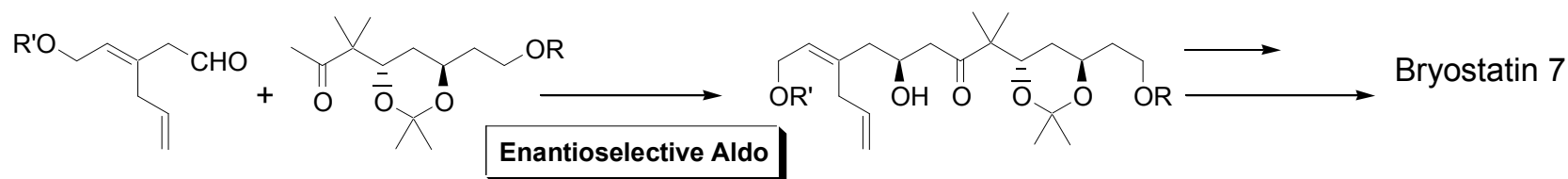
- Marine macrolides isolated from bryozoan invertebrates
- First discovered by G. Petit *et al.*
- To date, 18 bryostatin has been isolated
- Bryostatin 1 has shown to modulate protein kinase C (PKC) isozymes in cell-signal transduction

Hale, K. J.; Hummersone, M. G.; Manaviazar, S.; Frigerio, M. *Nat. Prod. Rep.* **2002**, 19, 413



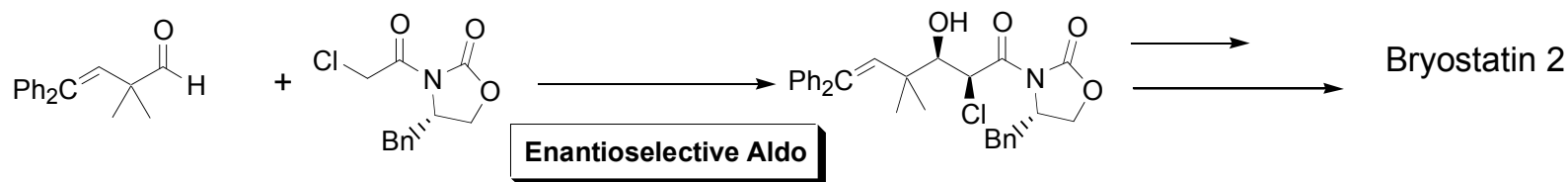
Previous Total Synthesis of Bryostatin

Masamune synthesis (1990):



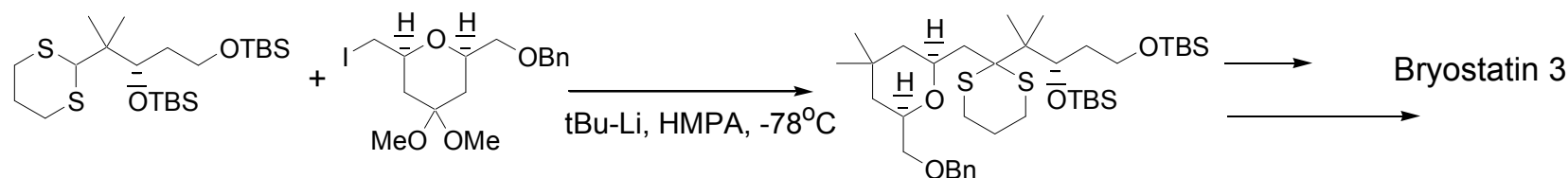
Masamune *et al.* JACS **1990**, 112, 7407

Evans synthesis (1999):



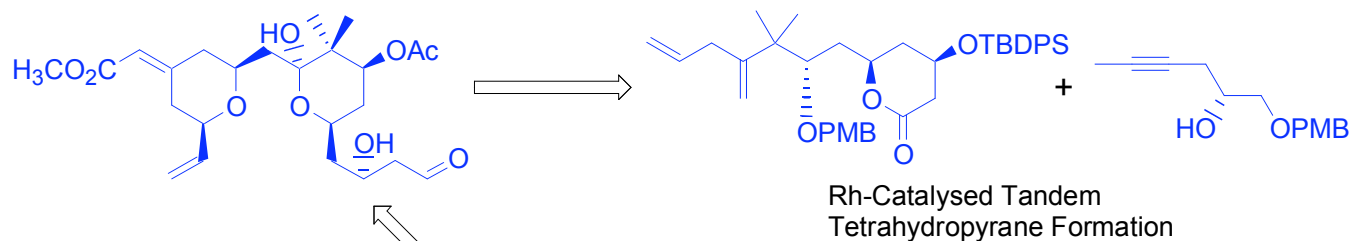
Evans *et al.* JACS **1999**, 121, 7540

Yamamura synthesis (2000):

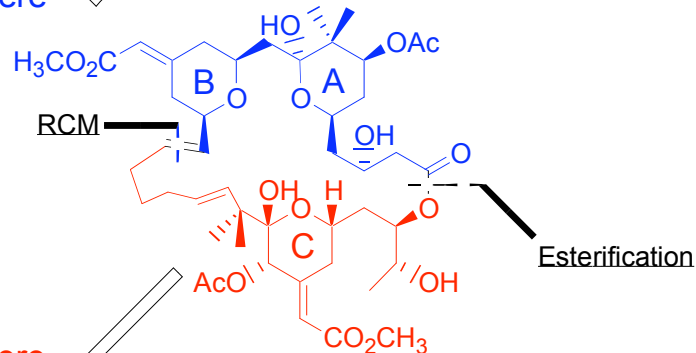


Yamamura *et al.* Angew., Int. Ed. **2000**, 39, 2290

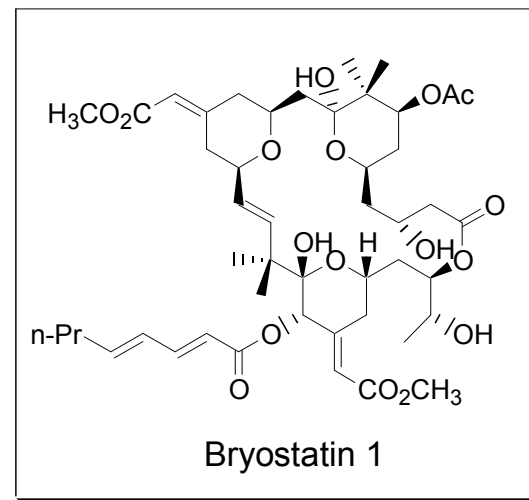
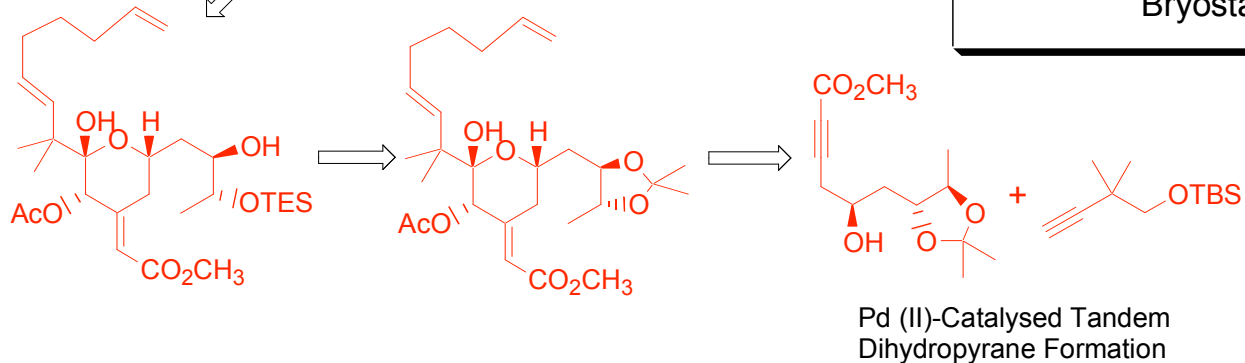
Retrosynthetic analysis



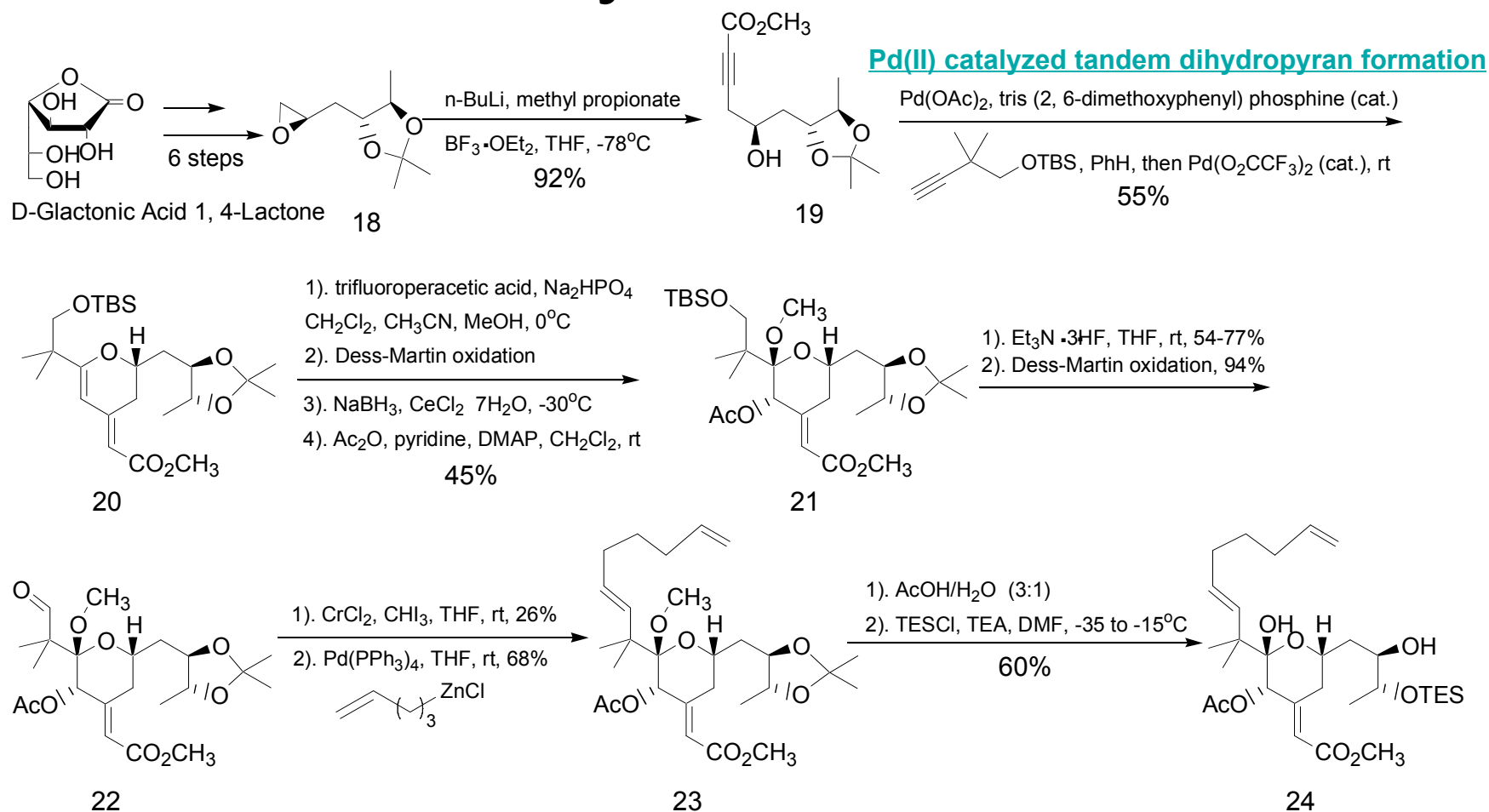
Northern Hemisphere



Southern Hemisphere

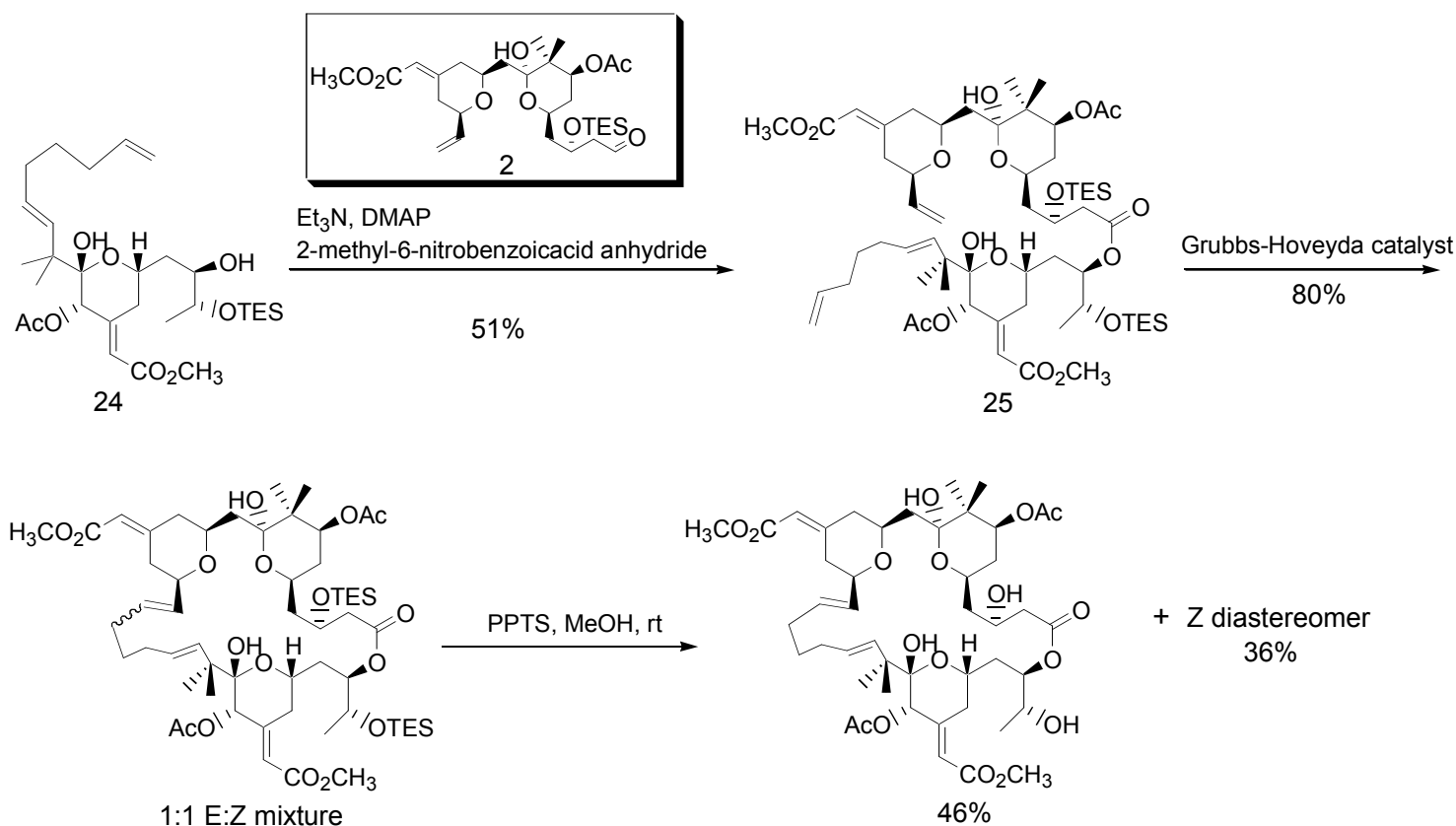


Synthesis of Ring-Expanded Bryostatin 1



Trost, B. M.; Yang, H.; Thiel, O. R.; Frontier, A. J.; Brindle, C. S. *J. Am. Chem. Soc.* **2007**, ASAP

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