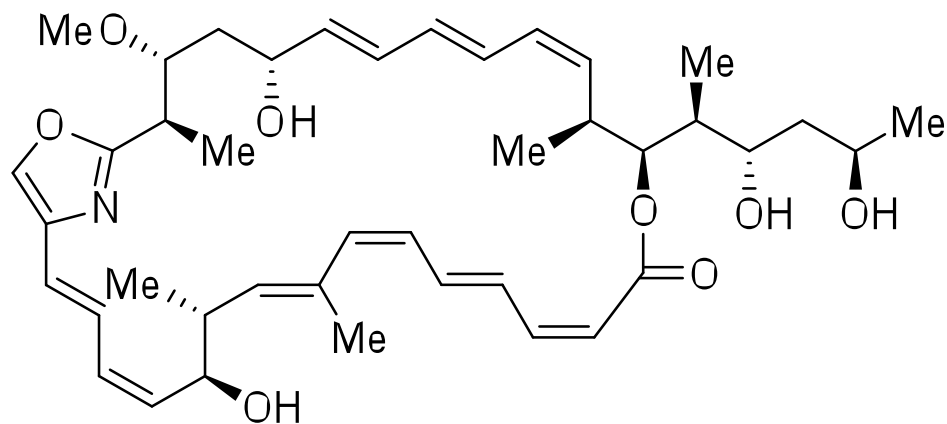


Total Synthesis of Chivosazole F

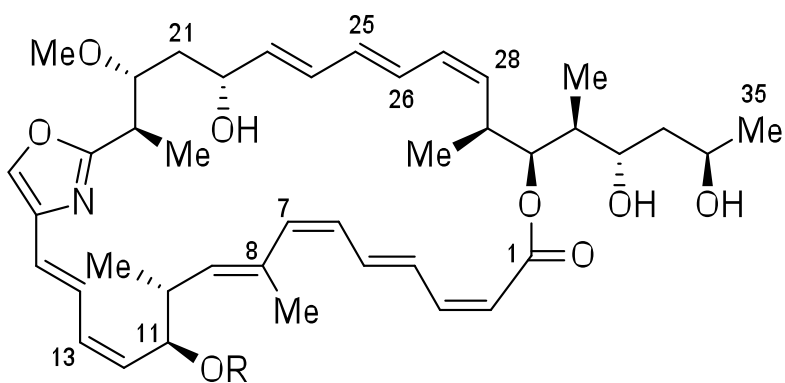
Brodmann, T.; Janssen, D.; Kalesse, M.* *J. Am. Chem. Soc.* **2010**, *132*, 13610.



Dimas Paz
Wipf group - Current Literature
October 4, 2010

Chivosazoles – Isolation and Biological Activity

- Chivosazoles are polyene macrolides isolated by Höfle and Reichenbach from the myxobacterium *Sorangium cellulosum*.



Chivosazoles (A-E) R = 6-desoxyglucopyranose
Chivosazole (F) R = H

- 31-membered macrolactone ring
- 1 oxazole,
- 10 stereocenters
- 3 polyene moities

Absolute and relative configuration

- NMR
- Chemical degradation
- Partial synthesis
- Genetic analysis

- Active against yeasts and filamentous fungi
- They are highly cytotoxic against mammalian cell cultures (IC₅₀ 9ng/mL (L929) and HeLa cells).

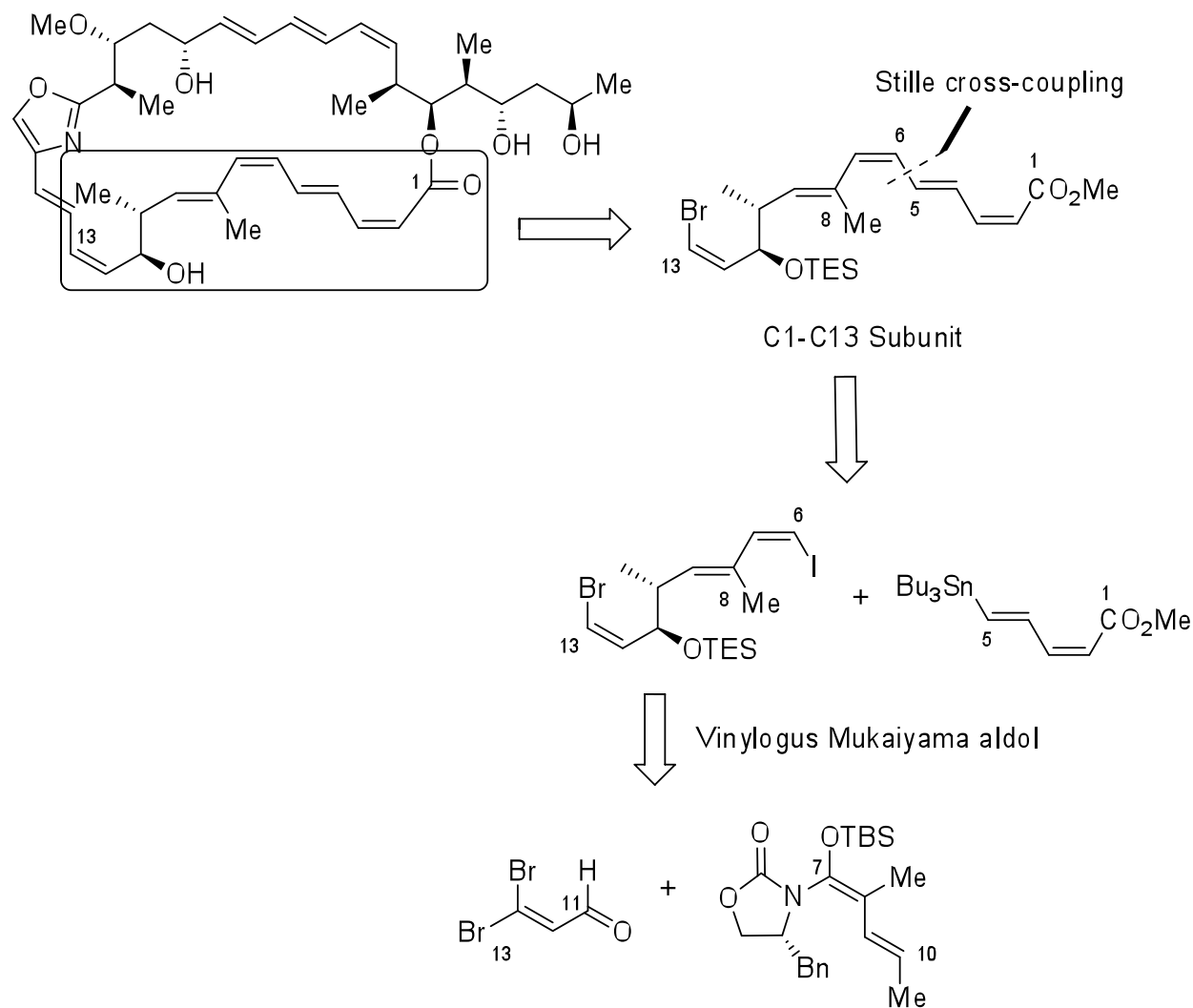
Irschik, H.; Jansen, R.; Gerth, K.; Höfle, G.; Reichenbach, H. *J. Antibiot.* **1995**, *48*, 962

Jansen, R.; Irschik, H.; Reichenbach, H.; Höfle, G. *Liebigs Ann. Chem.* **1997**, 1725

Diestel, R.; Irschik, H.; Jansen, R.; Mohammed, W. K.; Reichenbach, H.; Sasse, R. *ChemBioChem* **2009**, *10*, 2900

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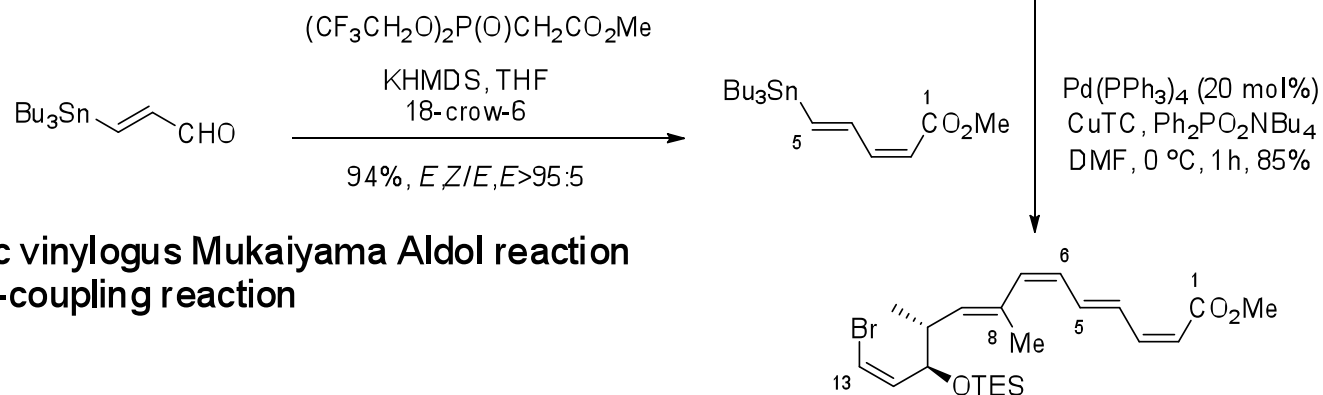
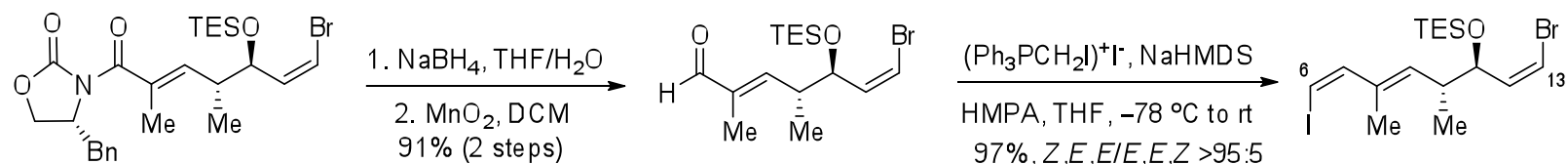
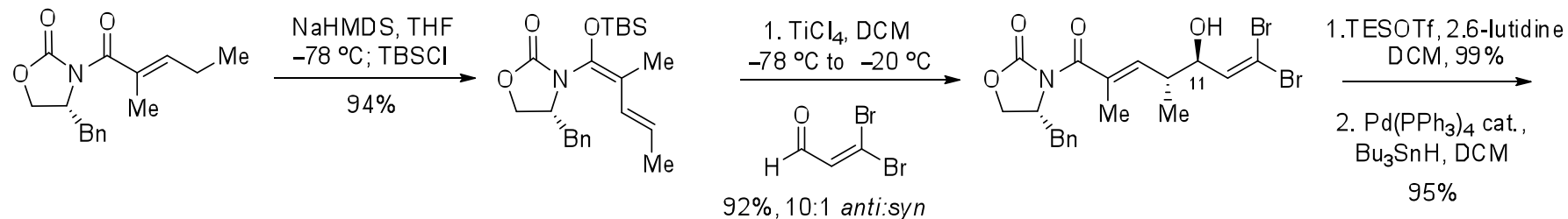
Paterson's group Synthesis of the C1-C13 Subunit of the Chivosazoles



Paterson, I.; Kan, S. B. J.; Gibson, L. J. *Org. Lett.* **2010**, *12*, 3724

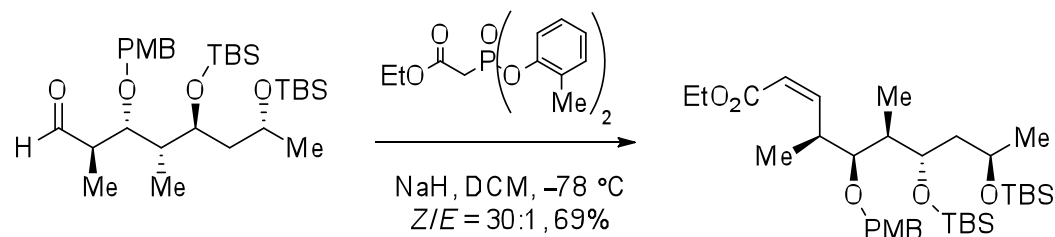
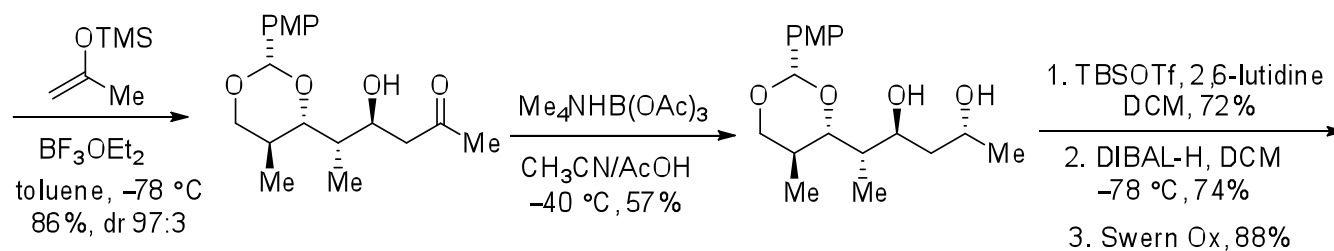
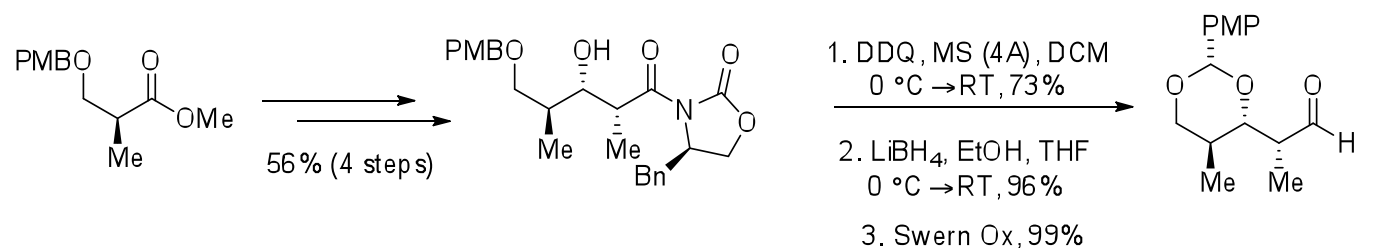
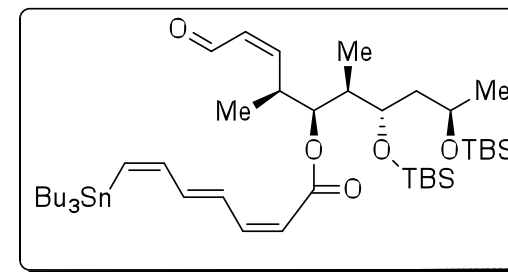
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Paterson's group Synthesis of the C1-C13 Subunit of the Chivosazoles



- * Asymmetric vinylogous Mukaiyama Aldol reaction
- * Stille cross-coupling reaction

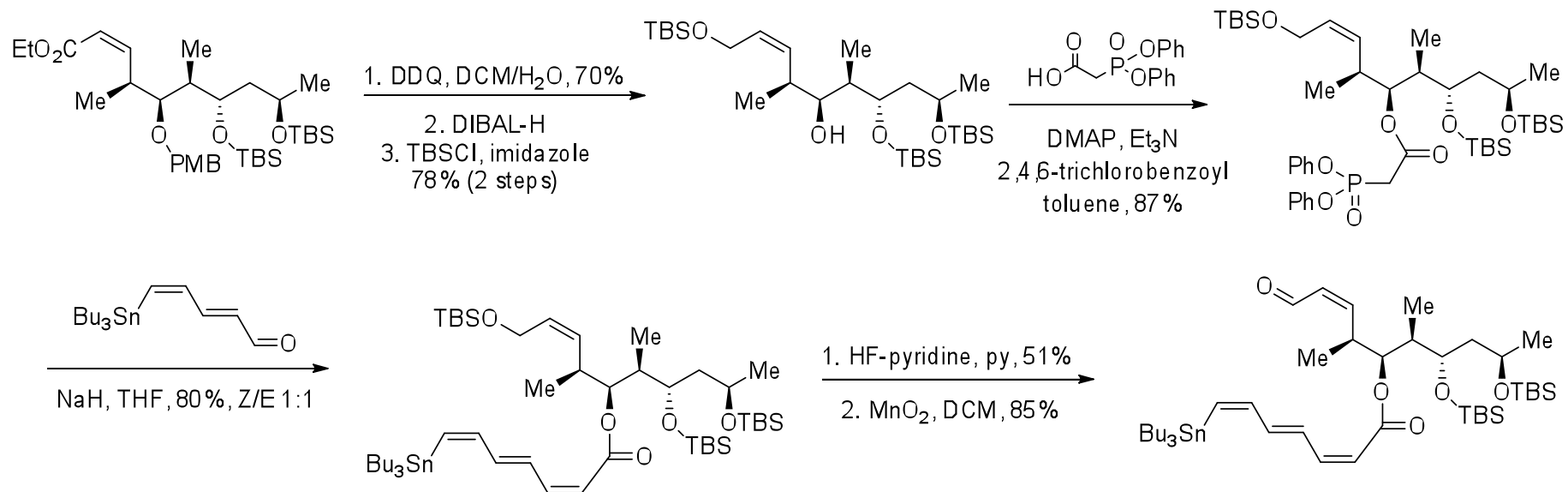
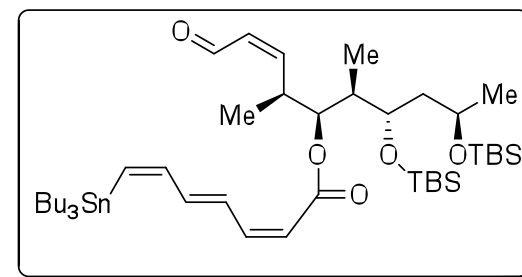
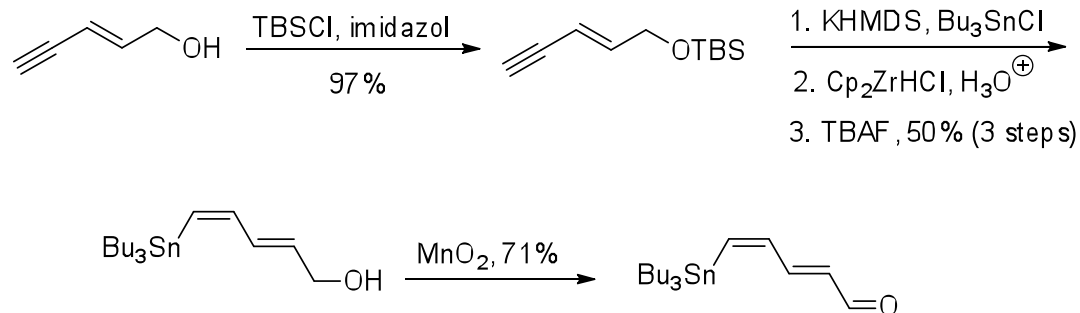
Total Synthesis of Chivosazole F



Janssen, D.; Albert, D.; Jansen, R.; Müller, R.; Kalesse, M. *Angew. Chem. Inter. Ed.* **2007**, *46*, 4898

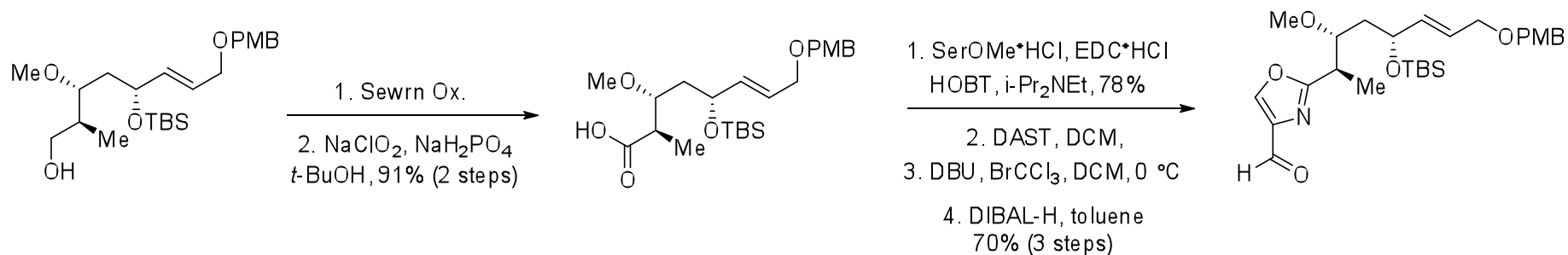
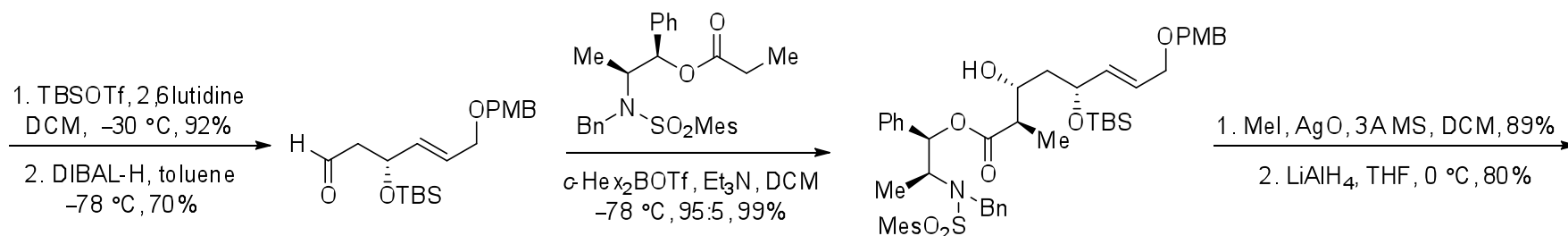
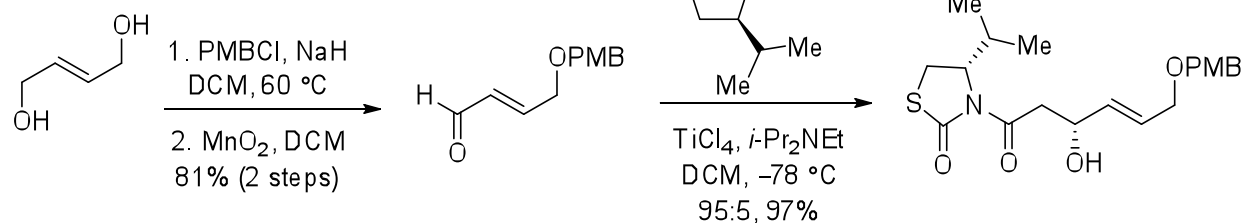
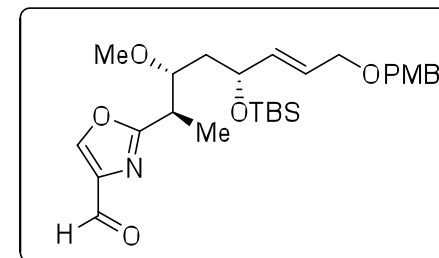
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Total Synthesis of Chivosazole F



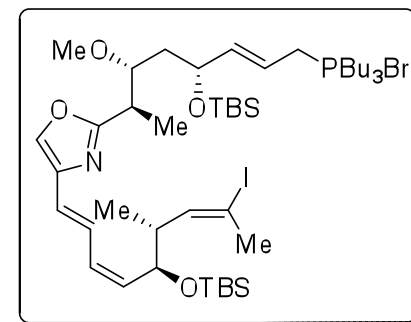
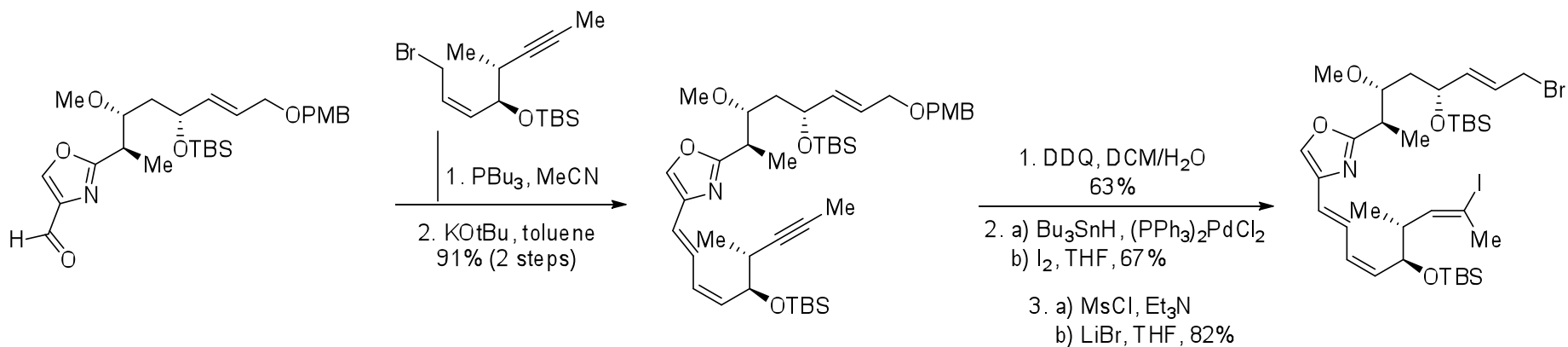
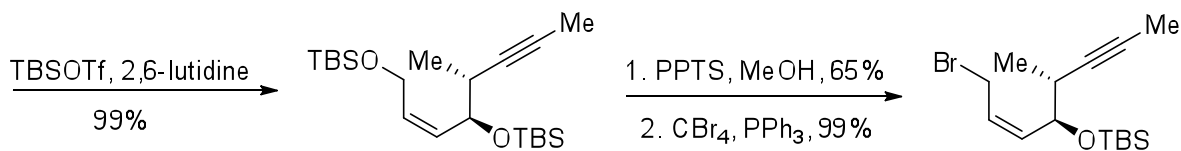
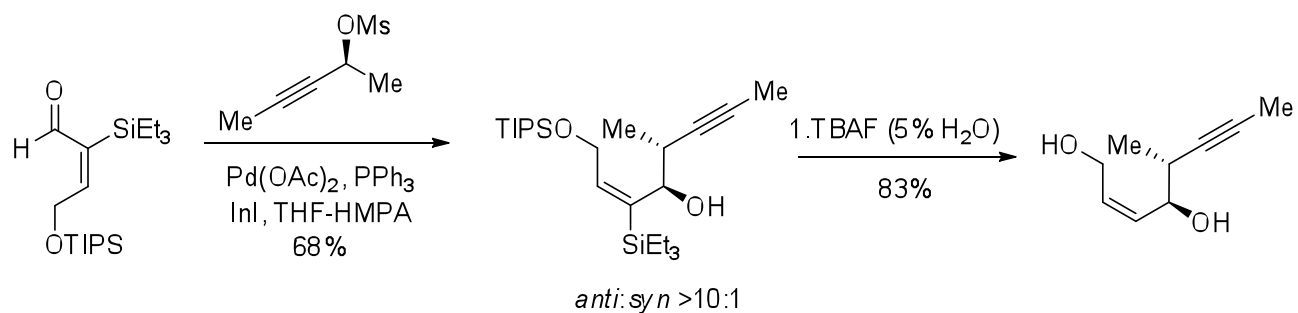
Mapp, A. K.; Heathcock, C. H. *J. Org. Chem.* **1999**, *64*, 23
 Janssen, D.; Kalesse, M. *Synlett* **2007**. 2667

Total Synthesis of Chivosazole F

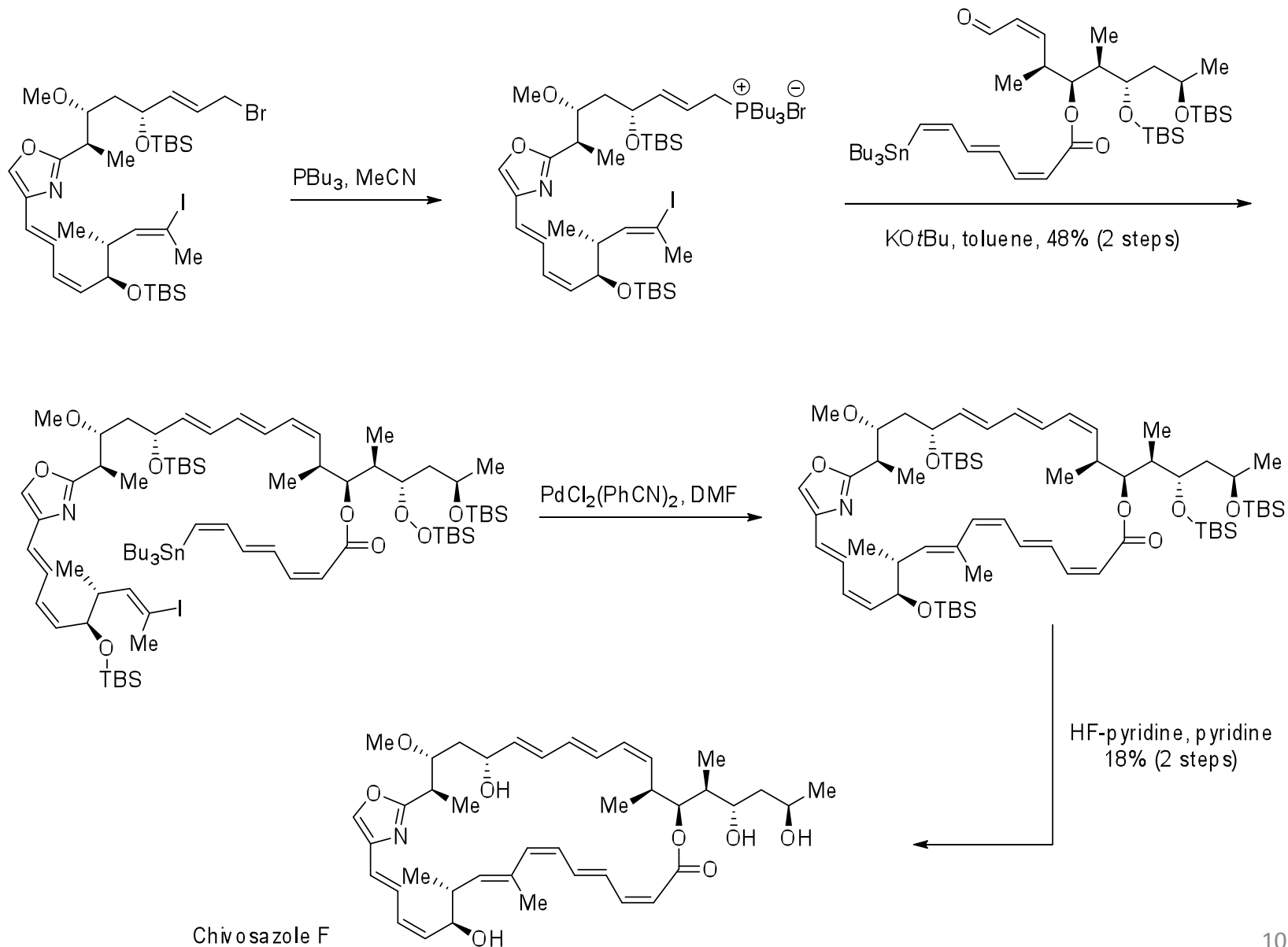


Janssen, D.; Kalesse, M. *Synlett* **2007**, 2667.

Total Synthesis of Chivosazole F



Total Synthesis of Chivosazole F



10

Summary and Outlook

- Chivosazole F was synthesized in 24 steps in 0.087% overall yield from Roche ester.
- Key transformations include selective Evans aldol reaction, Mukayama aldol reaction, Wittig reaction and intramolecular Stille coupling for the macrolactone formation.