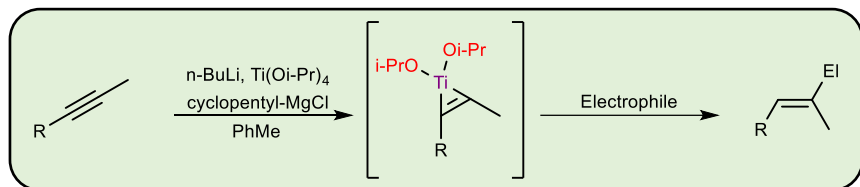


A General Scheme



Micalizio, G. *J. Org. Chem.* **2009**, Vol. 74, No. 19 <https://doi.org/10.1021/jo901451c>

Glenn Micalizio

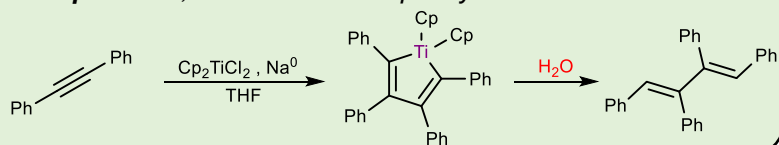
* Works on the development of novel C-C bond connections, the synthesis of rare and complex natural products, and optimizing strategies for achieving various complex scaffolds.

***Professor at Dartmouth: 2013-present**

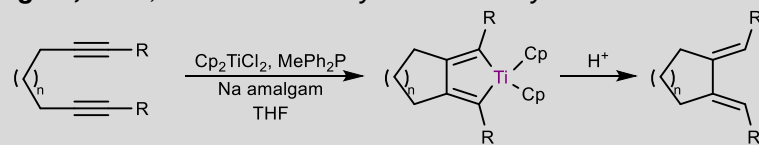


Previous Work

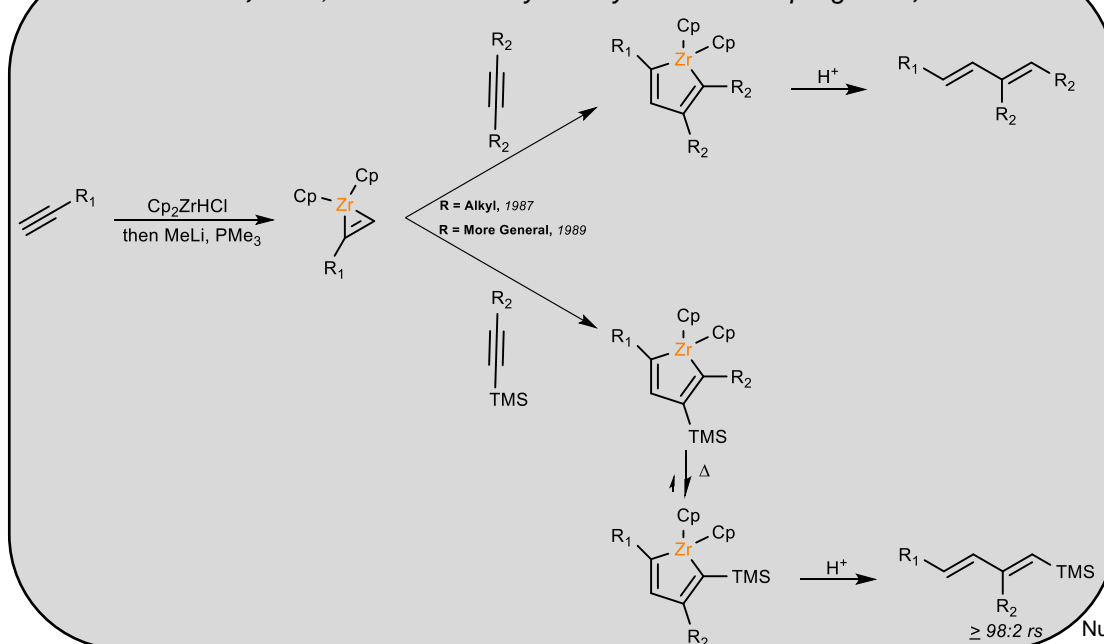
Vol'pin et. al, Dimerization of diphenylacetonide 1963



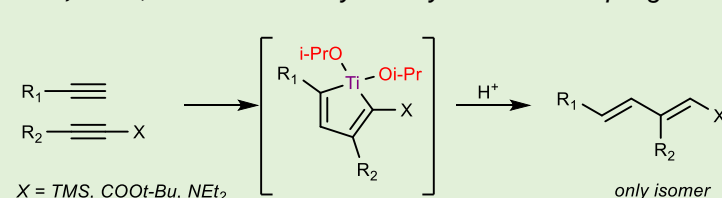
Nugent, et. al, Intramolecular Cyclization of Diynes 1984



Buchwald, et. al, Zr-Mediated Alkyne-Alkyne Cross-Coupling 1987, 1989



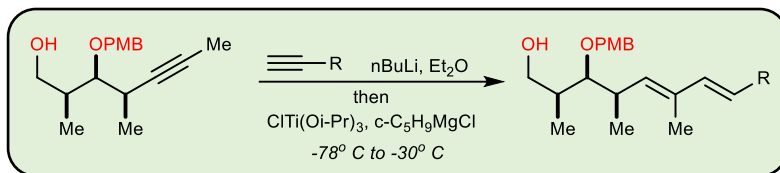
Sato, et. al, Ti-Mediated Alkyne-Alkyne Cross-Coupling 1999



Methods up to this point were well established to couple alkynes, however, the methods lacked generality and functional group compatibility. The transformation, however, was well established and demonstrated promise for further development.

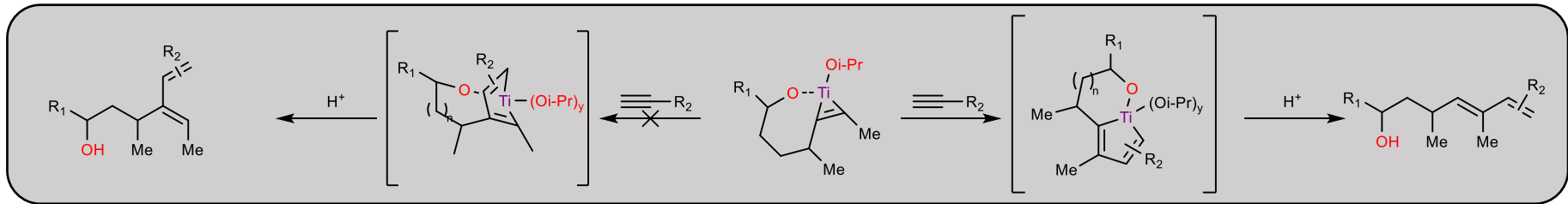
Micalizio, G. *J. Org. Chem.* **2009**, 74. <https://doi.org/10.1021/jo901451c>
Nugent, W.A. *J. Am. Chem. Soc.* **1984**, 106, 6422. <https://doi.org/10.1021/ja00333a055>
Buchwald, S. J. *Am. Chem. Soc.* **1987**, 109, 2544. <https://doi.org/10.1021/ja00242a066>
Vol'pin, M. *Dokl. Akad. Nauk SSSR.* **1963**, 151, 1100. <http://mi.mathnet.ru/eng/dan28435>

Substrate Scope – A Focus on Developing a Broad Alkyne-Alkyne Coupling with Good Regioselectivity



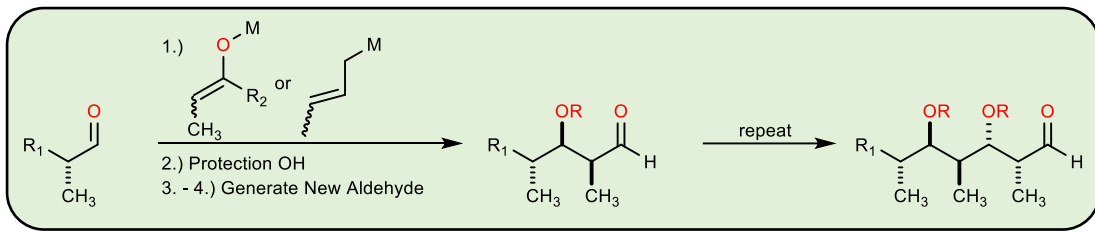
The selectivity is generated by the directing capacity of the metal alkoxy residue generated during the reaction.

Mechanism and Selectivity Rationale



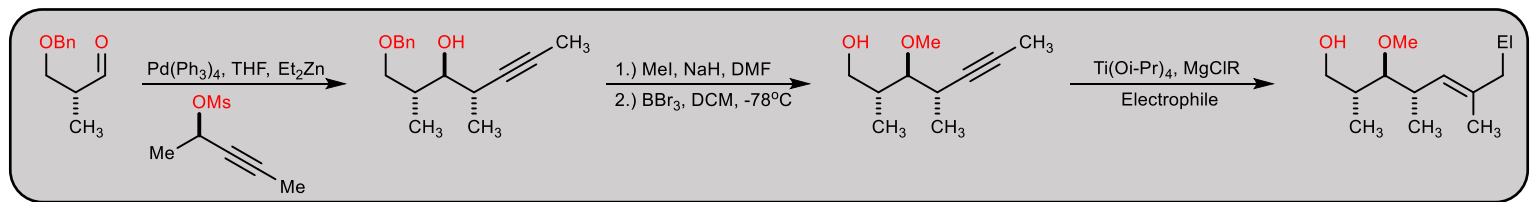
Utility in Polyketide Synthesis

The Conventional Approach to Polyketide Synthesis



6-8 Steps

This Approach

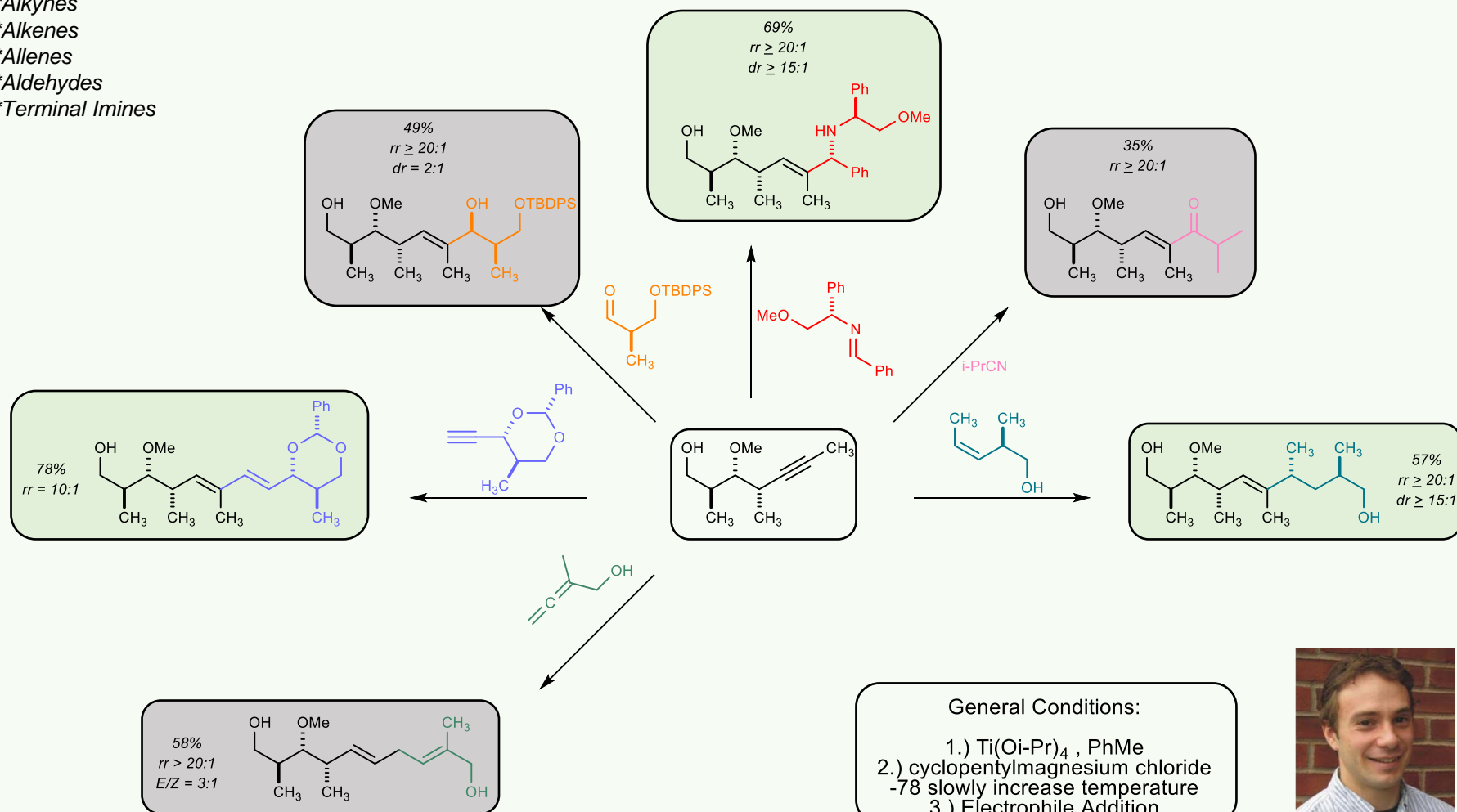


4 Steps

Substrate Scope – A Wide Range of Electrophiles

Compatible Electrophiles include:

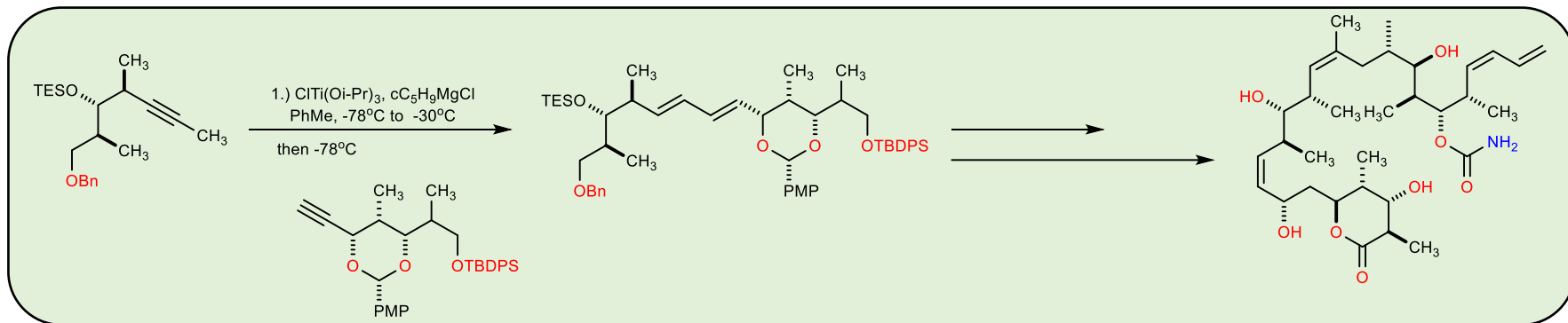
- *Alkynes
- *Alkenes
- *Allenenes
- *Aldehydes
- *Terminal Imines



Lark Perez

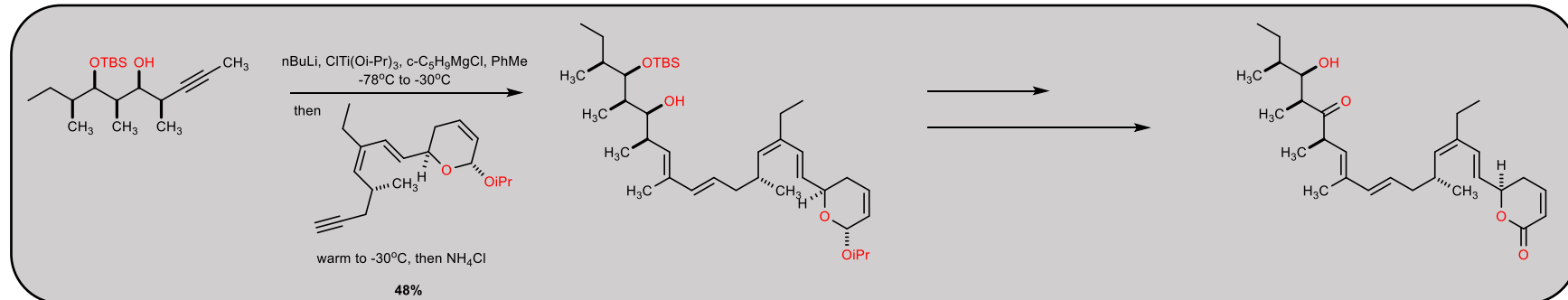
Examples in Total Synthesis

A Formal Total Synthesis of dictyostatin



Micalizio, G. *Tetrahedron*, **2009**, 69, 5908 <https://doi.org/10.1016/j.tet.2009.04.073>

Total Synthesis of callystatin A by Titanium-Mediated Reductive Alkyne-Alkyne Cross-Coupling



Micalizio, G. *Angew.* **2008**, 47, 7837. <https://doi.org/10.1002/anie.200803031>