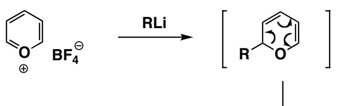
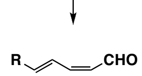
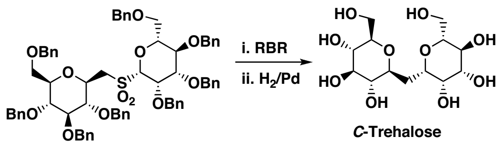
New Methodology



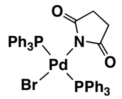


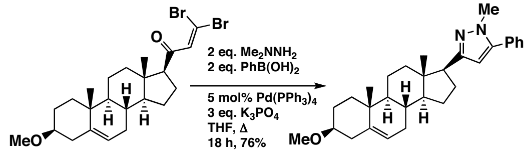
Stereoselective dienal synthesis:
J. Chem. Soc., Perkin Trans. I, 1995, 2385



C-Glycoside and *C*-oligosaccharide synthesis:
Carbohyd. Res., 2006, *341*, 1298

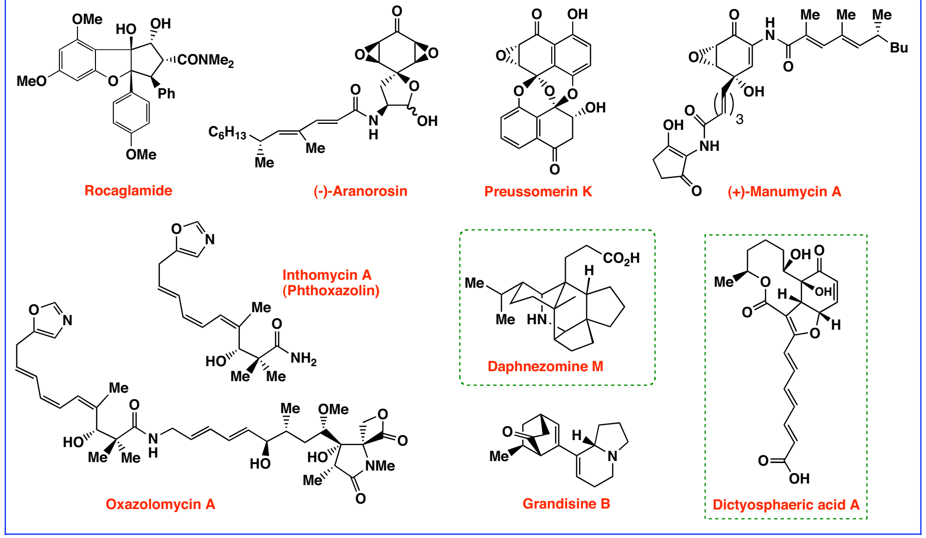
Novel Pd(0) catalysts:
Org. Lett., 2007, *9*, 5397



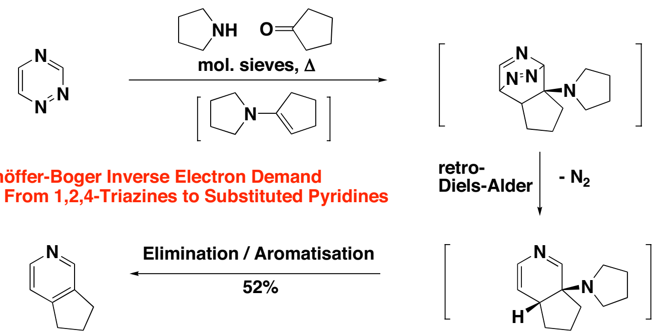


One-pot tandem processes: *Synlett*, 2010, 602
(including TOP: *Acct. Chem. Res.*, 2005, *38*, 851)

Natural Product Targets



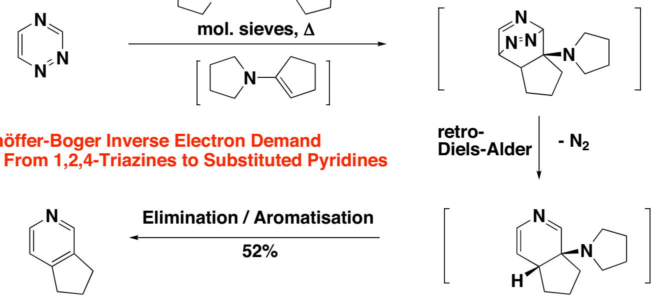
How Can We Efficiently Prepare Polysubstituted Pyridines?



Neunhöffer-Boger Inverse Electron Demand
Route From 1,2,4-Triazines to Substituted Pyridines

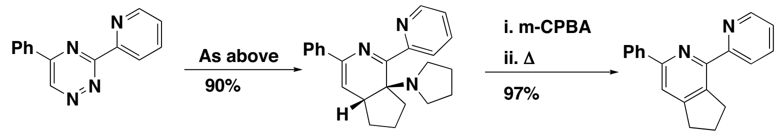
Dale Boger *et al.*, *J. Am. Chem. Soc*, 1985, *107*, 5745 and references therein

How Can We Efficiently Prepare Polysubstituted Pyridines?



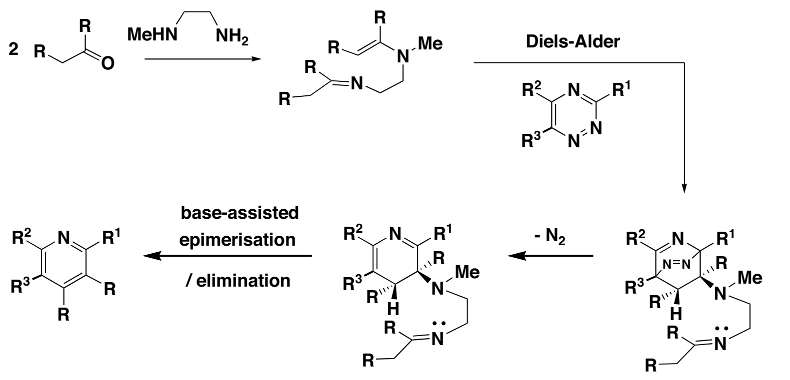
Neunhöffer-Boger Inverse Electron Demand
Route From 1,2,4-Triazines to Substituted Pyridines

Dale Boger *et al.*, *J. Am. Chem. Soc*, 1985, *107*, 5745 and references therein



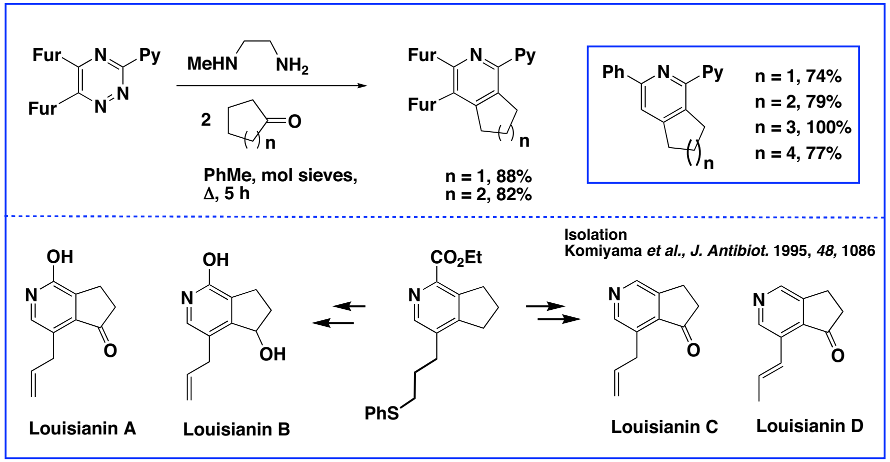
Steve Raw

Tethered Imine-Enamine (TIE) Methodology for Polysubstituted Pyridine Synthesis



Steve Raw

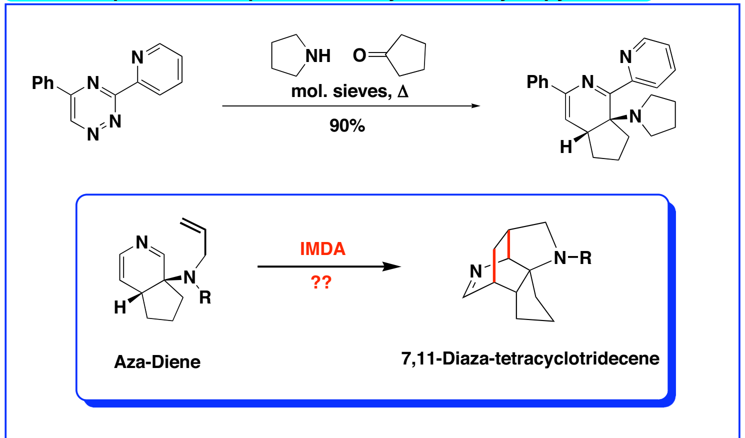
TIE Methodology for Polysubstituted Pyridine Synthesis



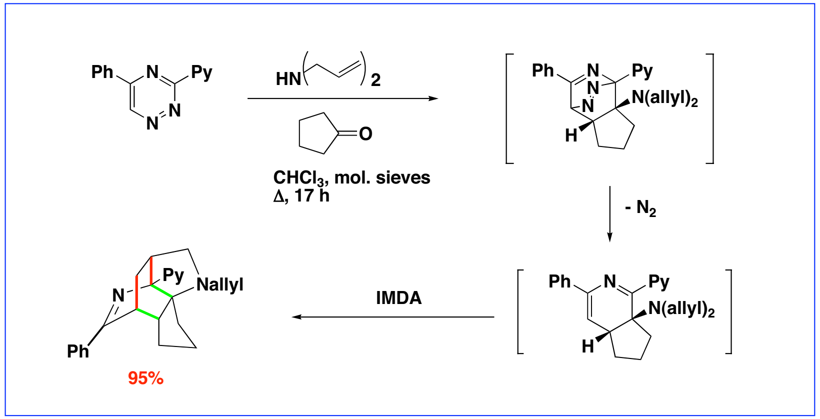
Steve Raw, Peter Geyelin
Nicola Catozzi, Pierre Wasnaire
Mike Edwards

J. Org. Chem. 2005, *70,* 10086
Synlett 2007, 2217
J. Org. Chem. 2009, *74,* 8343

Can We Exploit the Unexpected Stability of the Dihydropyridines?



Triple Diels-Alder Cascades for Polycycle Synthesis

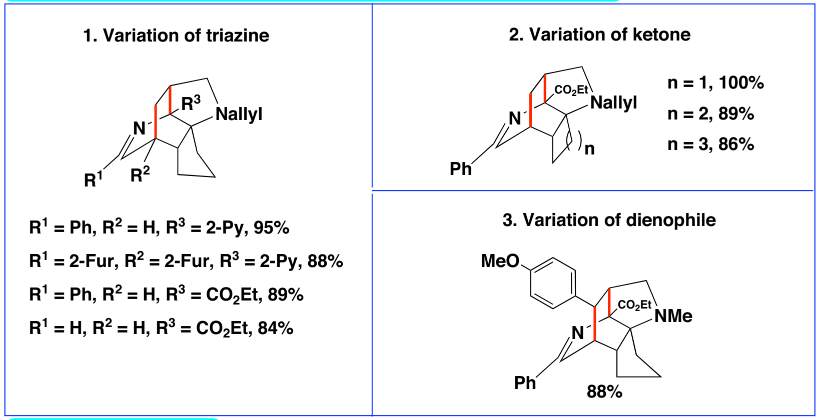


Steve Raw

Inverse electron-demand D-A
Retro-D-A
IMDA

Four new carbon-carbon bonds
Five new stereogenic centres
Two new rings
ONE-POT

Triple Diels-Alder Cascades for Polycycle Synthesis: Scope

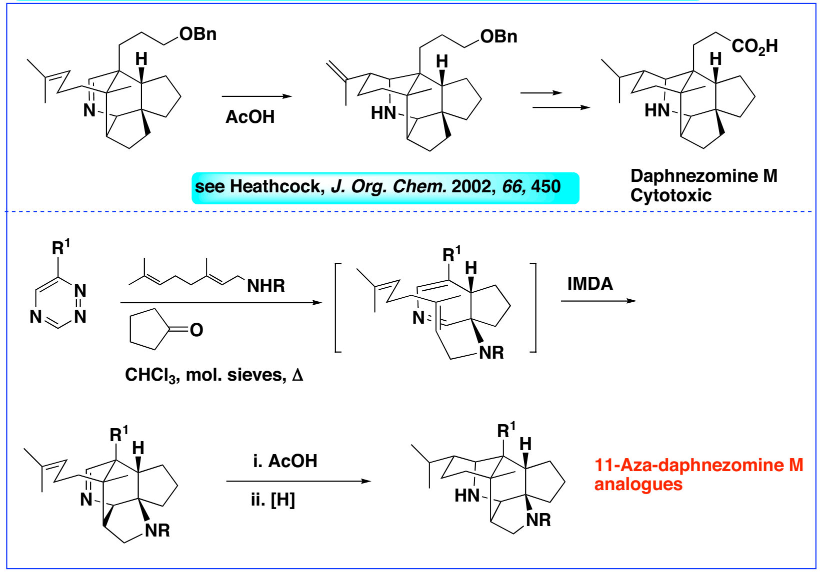


Steve Raw, Will Bromley

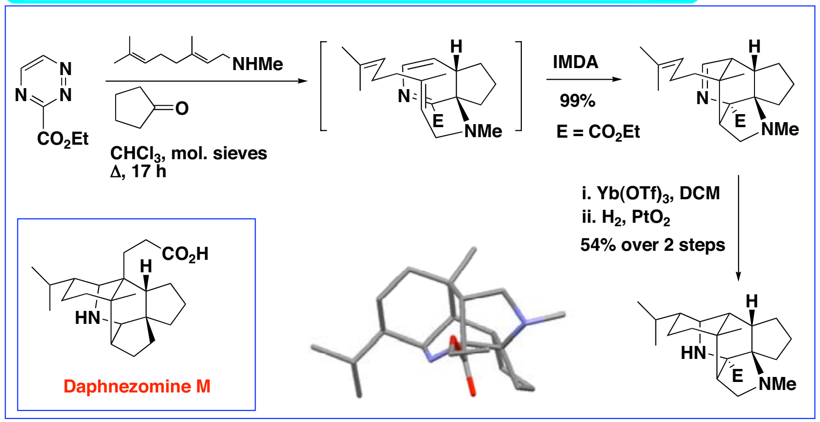
IMDA

J. Am. Chem. Soc. 2004, *126,* 12260
Tetrahedron 2007, *63,* 6004

Triple Diels-Alder Cascades for Polycycle Synthesis: Daphnezomines

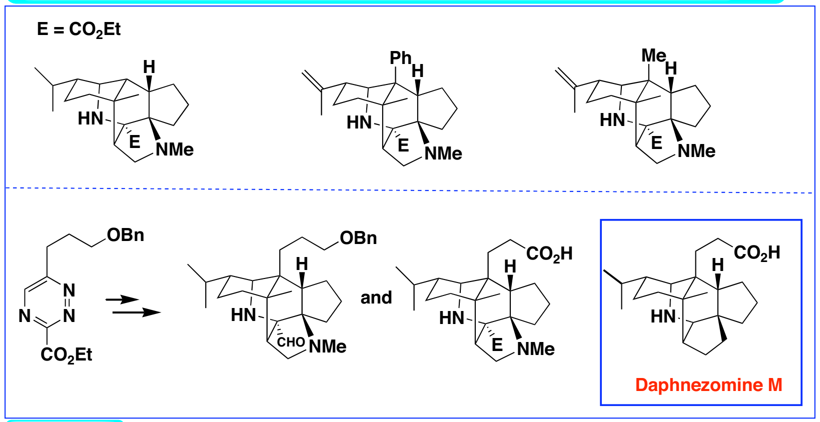


Triple Diels-Alder Cascades for Polycycle Synthesis: Daphnezomines



Steve Raw and Will Bromley

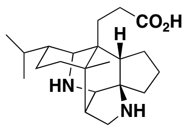
Triple Diels-Alder Cascades for Polycycle Synthesis: Daphnezomine Analogues



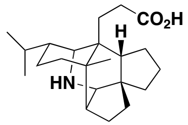
Will Bromley

Triple Diels-Alder Cascades for Polycycle Synthesis: Current Studies

1. Develop an asymmetric version of the triple Diels-Alder cascade
2. Complete synthesis of 11-Aza-daphnezomine M
3. Utilise triple Diels-Alder cascade (with a carbon linker) to prepare Daphnezomine M itself

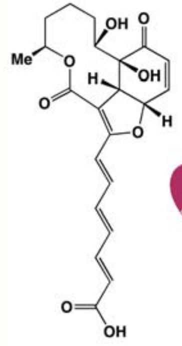


11-Aza-Daphnezomine M

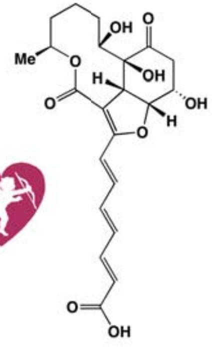


Daphnezomine M

Dictyosphaeric acid A and Dictyosphaeric acid B



Dictyosphaeric acid A



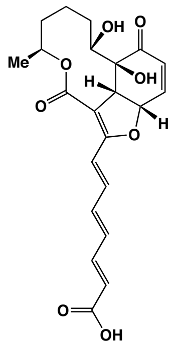
Dictyosphaeric acid B

Fermentation of a novel fungal isolate, *Penicillium dravuni* obtained from a Fijian marine algae, *Dictyosphaeria versluyii*

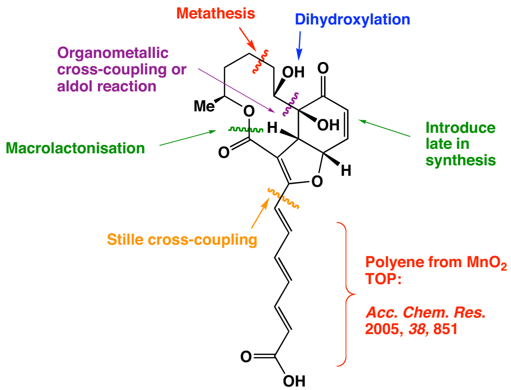
C. M. Ireland *et al. J. Nat. Prod.* 2004, *67*, 1396-1399;
C. M. Ireland *et al. Mycologia* 2005, *97*, 444-453.

Dictyosphaeric acid A inhibits methicillin-sensitive *Staph. aureus*, methicillin-resistant *Staph. aureus*, and vancomycin-resistant *Enterococcus faecium*

Dictyosphaeric acid A: Potential Approaches



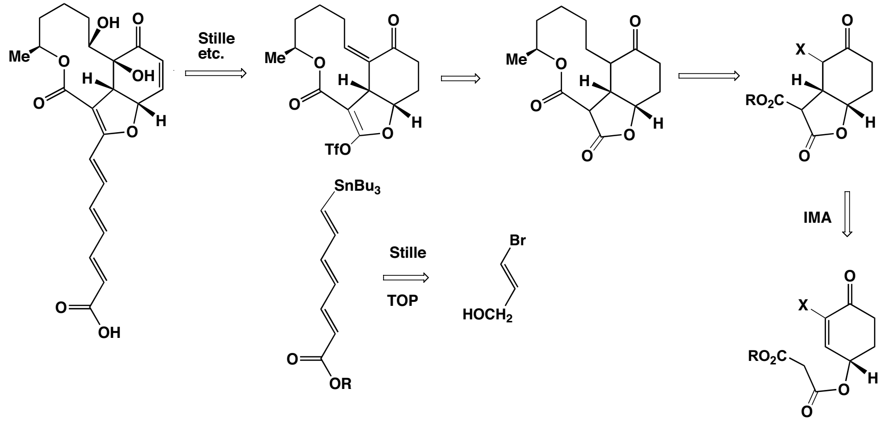
Dictyosphaeric acid A



C. M. Ireland *et al. J. Nat. Prod.* 2004, *67*, 1396-1399;
C. M. Ireland *et al. Mycologia* 2005, *97*, 444-453.

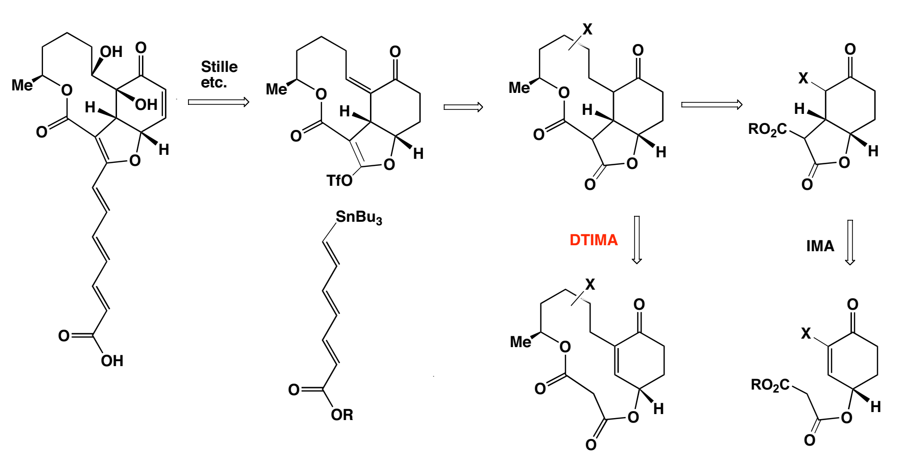
Dictyosphaeric acid A inhibits methicillin-sensitive *Staph. aureus*, methicillin-resistant *Staph. aureus*, and vancomycin-resistant *Enterococcus faecium*

Dictyosphaeric acid A: Retrosynthetic Analysis



Intramolecular Michael Addition (IMA): R. D. Little and M. R. Masjedizadeh, *Organic Reactions*, 1995, *47*, 315-552

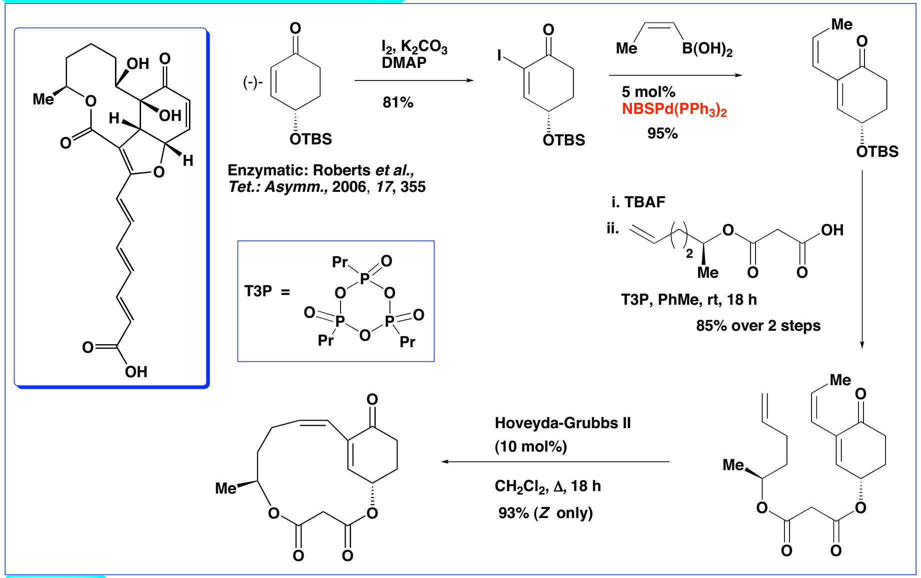
Dictyosphaeric acid A: Retrosynthetic Analysis II



Model studies: Chris Barfoot and Alan Burns, *Org. Lett.* 2008, *10*, 353

DTIMA = Doubly Tethered Intramolecular Michael Addition

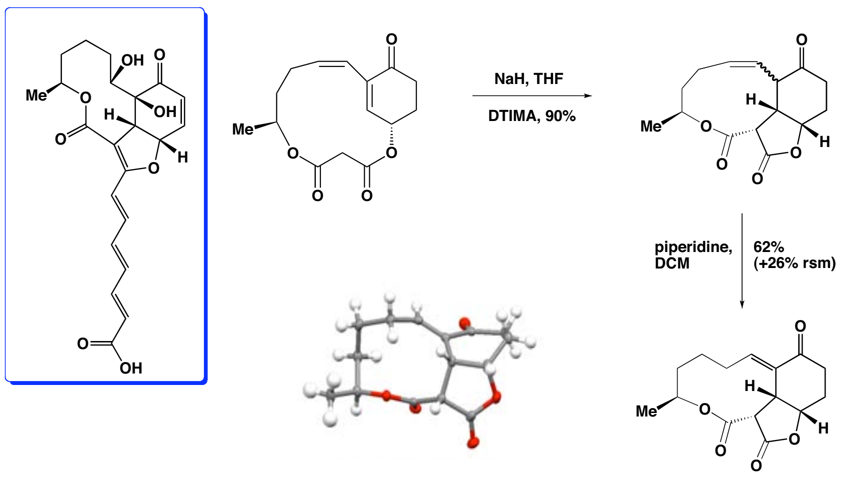
Dictyosphaeric acid A: Recent Studies 1



Alan Burns

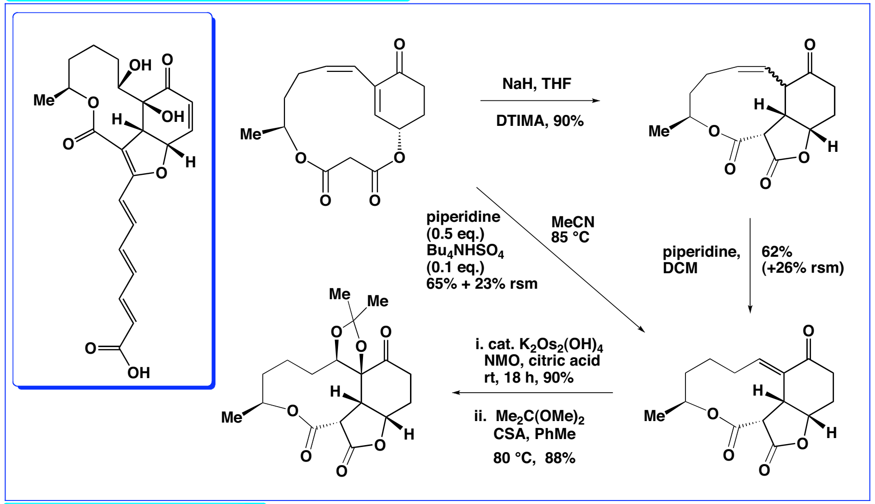
T3P: Archimica (*Angew. Chemie* 1980, *19*, 133)

Dictyosphaeric acid A: Recent Studies 2



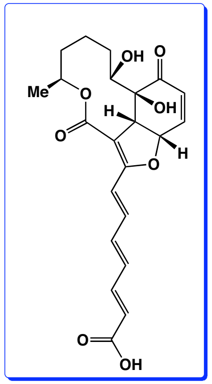
Alan Burns and Graeme McAllister

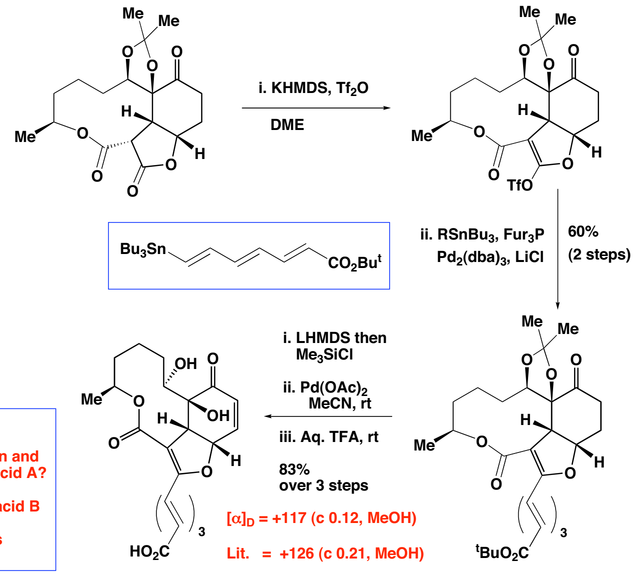
Dictyosphaeric acid A: Recent Studies 2



Alan Burns and Graeme McAllister

Dictyosphaeric acid A: Recent Studies 3





Still need to:

1. Invert alcohol configuration and complete Dictyosphaeric acid A?
2. Complete Dictyosphaeric acid B
3. Apply to Colletofragarones

Alan Burns

Dear Richard,

Thanks for sending a copy of your manuscript. I am forwarding it to Tim Bugni who is now at Wisconsin. Your synthesis provides a compelling evidence that our stereochemical assignment at C-6 is incorrect as drawn in our JNP paper.

Ironically, following up on your comment about the nOe data I pulled out Tim's thesis to look at the data. The first thing I noted on closer inspection was that we did not observe an nOe between H6 and what would be H13 in your drawing (position between 1 and 5). I should have noticed that. That lead me to re-examine the modeling that was used to evaluate stereochemistry based on nOe correlations. I am attaching the stereoview figure from Tim's thesis. It is clear from that figure that Tim had the stereochemistry correct at all centers. The hydroxy at C6 is up and the stereochemistry R.

It would appear that there was an error made in translating the stereoview to a flat drawing. I apologize for not catching this error earlier. None the less congratulations on the successful synthesis. You are certainly welcome to use this information in your conclusions if you see fit. Since this was our error, I am also comfortable with you just thanking us for providing a comparison sample.

Best Wishes

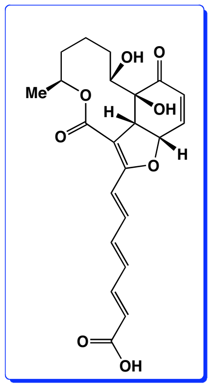
Chris

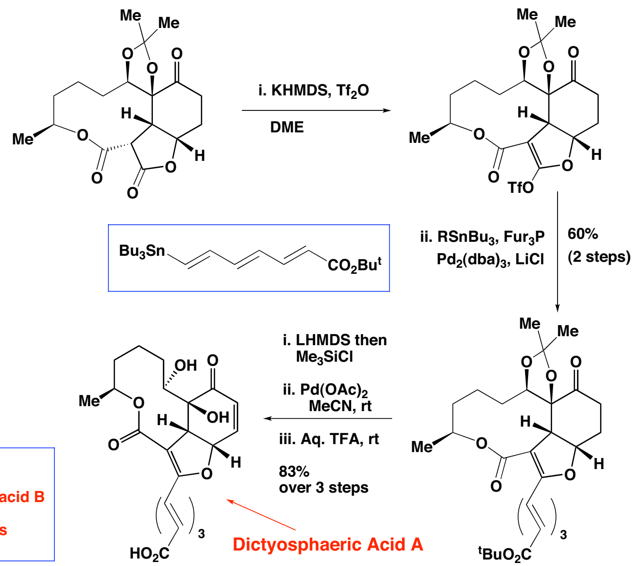
--

Chris M. Ireland

Professor and Interim Dean

Dictyosphaeric acid A: Recent Studies 3





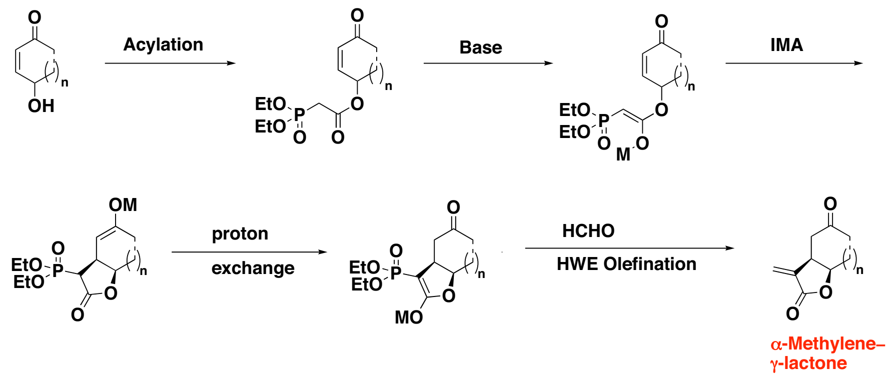
Still need to:

1. Complete Dictyosphaeric acid B
2. Apply to Colletofragarones

Alan Burns

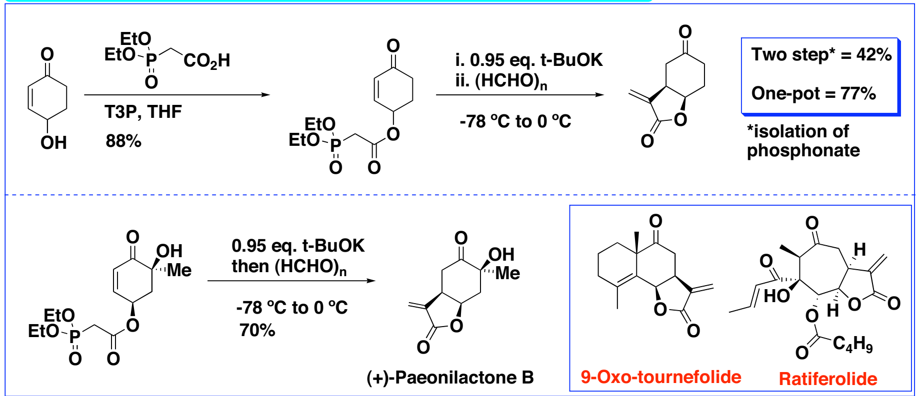
Angew. Chemie, 2010, *49,* 5574

Telescoped Intramolecular Michael / Olefination (TIMO) Sequence



For a review of α-methylene lactones (structures, biology, synthesis) see:
Kitson, Millemaggi and Taylor, *Angew. Chem. Int. Ed.* 2009, *48,* 9426

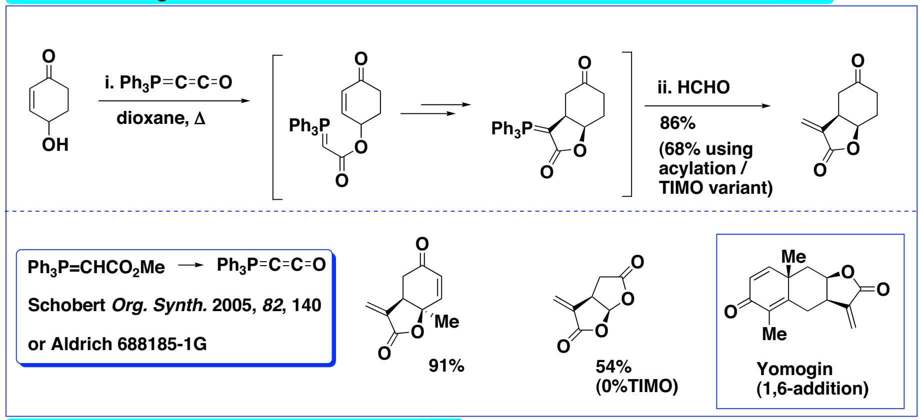
Telescoped Intramolecular Michael / Olefination (TIMO) Sequence



Mike Edwards, Russ Kitson, Martin Kenworthy, Mark Scott

Angew. Chem. Int. Ed. 2008, *47*, 1935

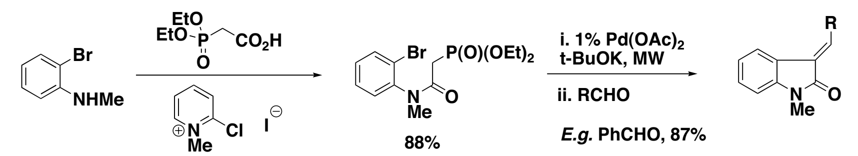
Telescoped Acylation / Intramolecular Michael / Phosphorane Olefination Sequence: Bestmann Reagent

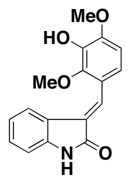


Russ Kitson
(With John Wood, Colorado) *Org. Lett.* 2009, *11*, 5338

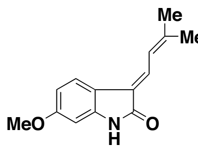
One pot annelation, base-free

Extension to Oxindole Synthesis: Telescoped Enolate Arylation / HWE Sequence





From roots of *Isatis indigotica* and a constituent of "Bai-Lan-Gen", commonly used in TCM

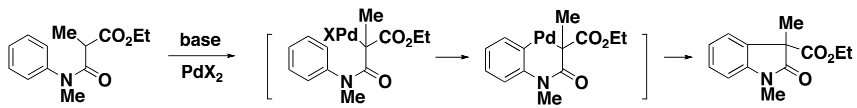


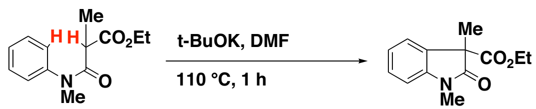
Soulieotine from *Souliea vaginata.* Anti-inflammatory analgesic used in TCM

Alexis Perry and Alessia Millemaggi

EJOC 2009, 2947

Potential C-H Activation Route for Oxindole Synthesis





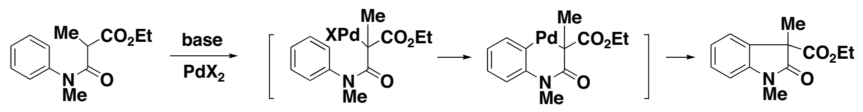
100 mol% Pd(II), 5%

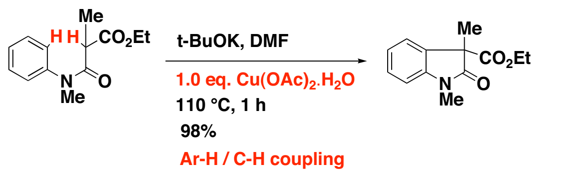
10 mol% Pd(II) *p*-BQ, 0%

10 mol% Pd(II), $Cu(OAc)_2$, 40%

Alexis Perry

Potential C-H Activation Route for Oxindole Synthesis





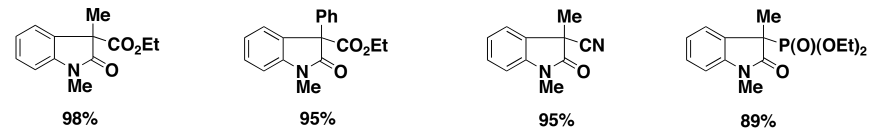
Pd not required
Note use of hydrated Cu(II)
Can use "lab" DMF
Inert atmos. not needed

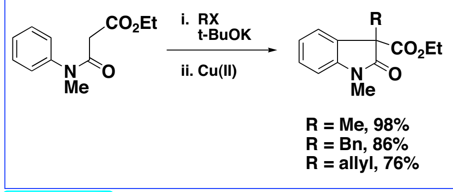
Scope / Mechanism?

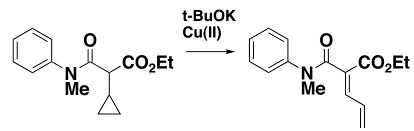
Alexis Perry

Jia, Y.-X.; Kündig, P.
Angew. Chem. Int. Ed. **2009**, *48*, 1636.

C-H Activation Route for Oxindole Synthesis: Scope





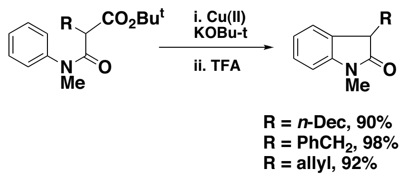


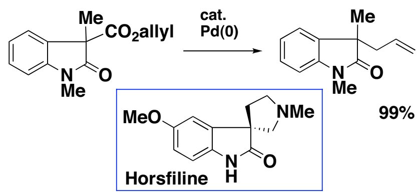
Supports radical mechanism:
homolytic aromatic substitution

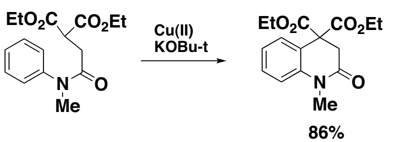
Alexis Perry

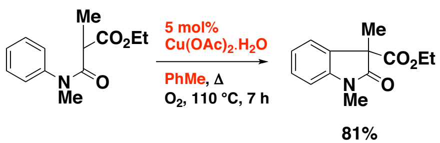
Chem. Commun., 2009, 3249

C-H Activation Route for Oxindole Synthesis: Recent Results



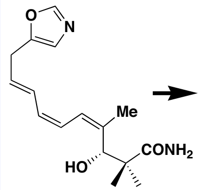




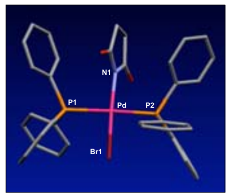


Alexis Perry, David Pugh, Johannes Klein

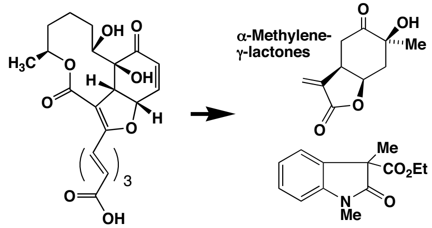
Summary and Take-Home-Message



Inthomycin A

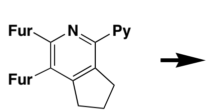


Novel Pd catalysts

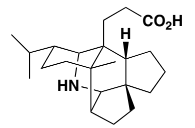


Dictyosphaeric acid A

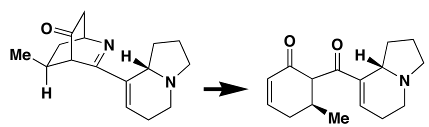
Ar-H / C-H coupling;
Oxindoles



Polysubstituted
pyridine synthesis



Triple Diels-Alder Cascades
Daphnezomine M



Grandisine B

Biosynthetic studies;
natural product
isolations