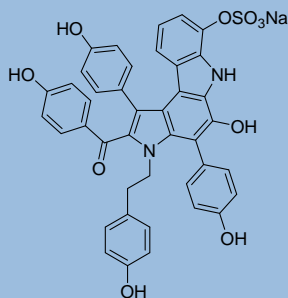


## A concise and Scalable Strategy for the Total Synthesis of Dictyodendrin B Based on Sequential C-H Functionalization

M. J. Gaunt et al., Angew. Chem. Int. Ed. **2015**, *54*, 5451.

Daniel Meyer  
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06.08.2015, Journal Club



### Content

- > Matthew J. Gaunt
- > Dictyodendrin B: Isolation, mode of action
- > Retrosynthetic Analysis
  - Fürstner
  - Iwoa and Ishibashi
  - Tokuyama
  - Jia
  - Gaunt
- > Forward Synthesis
- > Conclusion

## Matthew J. Gaunt

- > Fellow of University of Birmingham
- > PhD at Dr. Jonathan B. Spencer (Cambridge)
- > Postdoc Prof. Amos B. Smith (University of Pennsylvania)
- > Junior research Fellow at Prof. Steven Ley
- > Since 2003 independent research carrier (Cambridge)
  
- > Synthesis of complex molecules and natural products
  - Metal catalyzed C-H bond functionalization
  - Catalytic asymmetric synthesis using small molecule catalysts
  - Cascade strategies for natural product synthesis



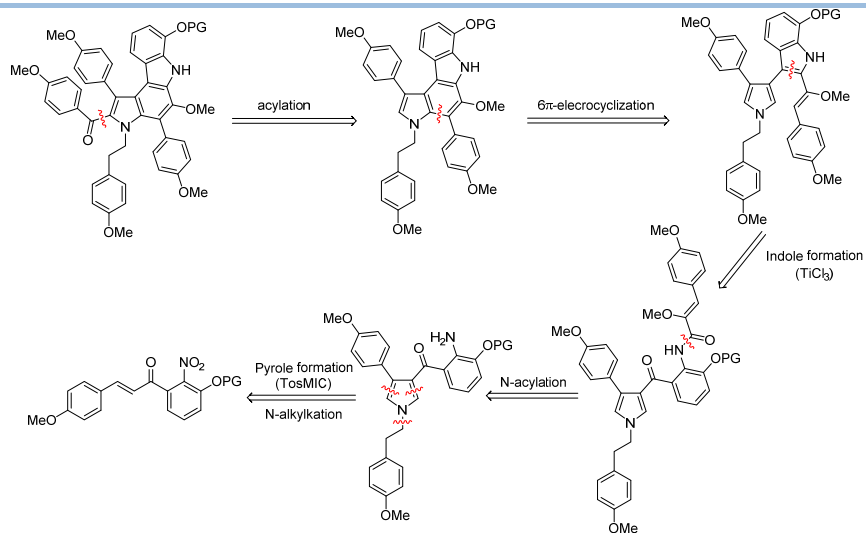
3

## Dictyodendrin B

- > Dictyodendrin A-E isolated from sponge *dictyodendrilla verongiformis*
  
- > Inhibitory activities towards telomerases and BACE1
  - Telomerases help by the cell division
  - BACE1 cause early-onset in Alzheimer's disease
  
- > Potential as chemotherapy agents and neurodegenerative probes

4

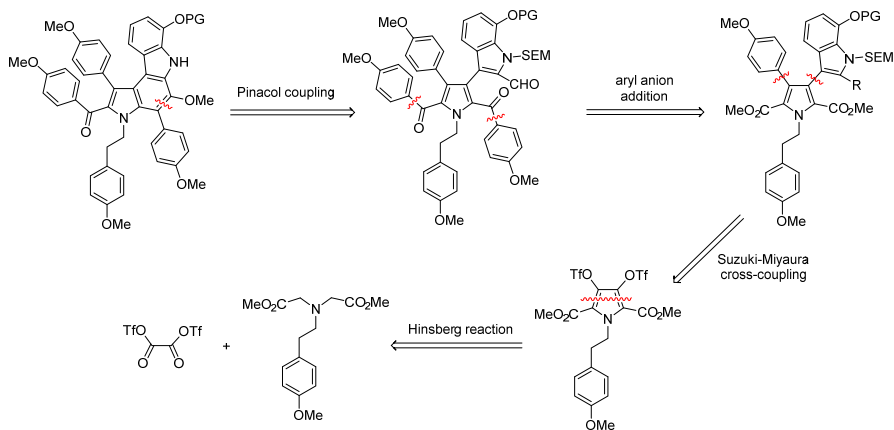
## Retrosynthetic Analysis: Fürstner



J. Am. Chem. Soc. **2005**, 127, 11620. J. Am. Chem. Soc. **2006**, 128, 8087.

5

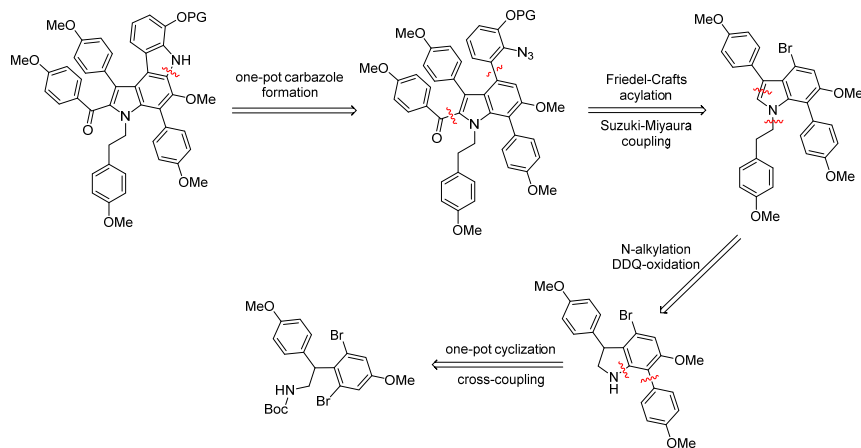
## Retrosynthetic Analysis: Iwoa/Ishibashi



Tetrahedron Lett. **2010**, 51, 533.

6

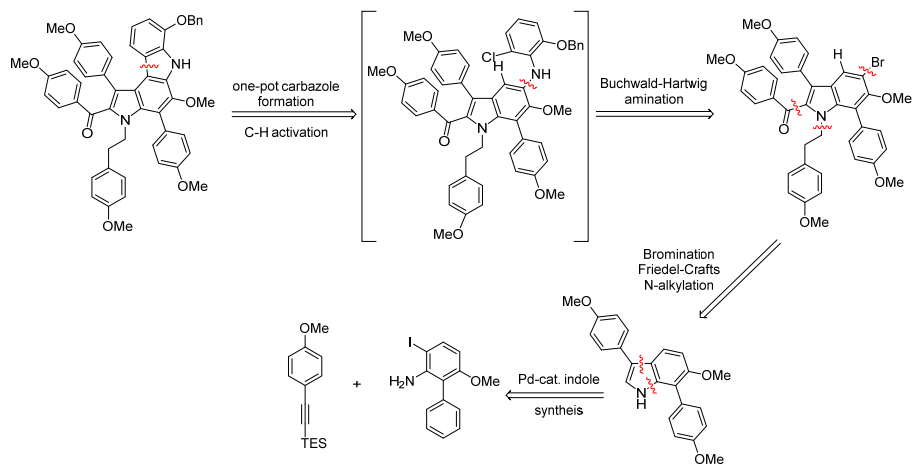
## Retrosynthetic Analysis: Tokuyama



Angew. Chem. Int. Ed. **2010**, 49, 5925.

7

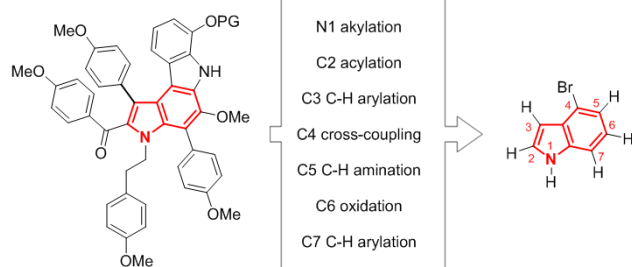
## Retrosynthetic Analysis: Jia



J. Org. Chem. **2013**, 78, 5810.

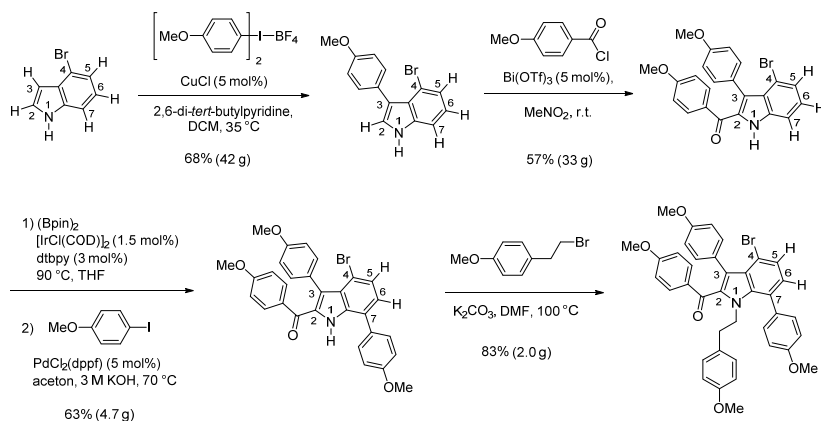
8

## Retrosynthetic Analysis: Gaunt



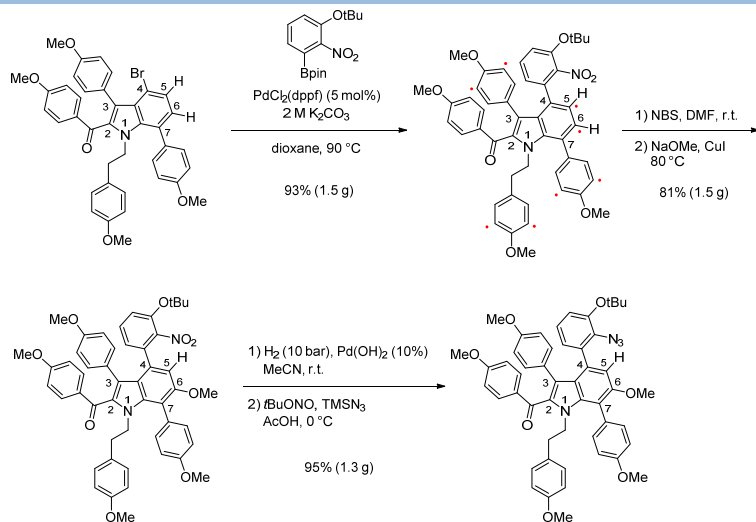
9

## Forward Synthesis



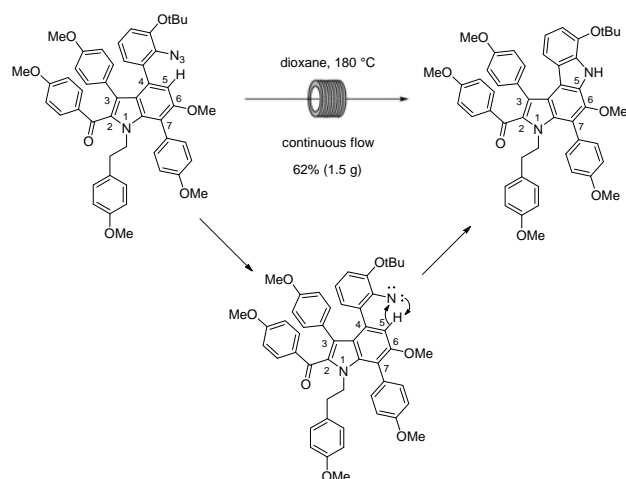
10

## Forward Synthesis



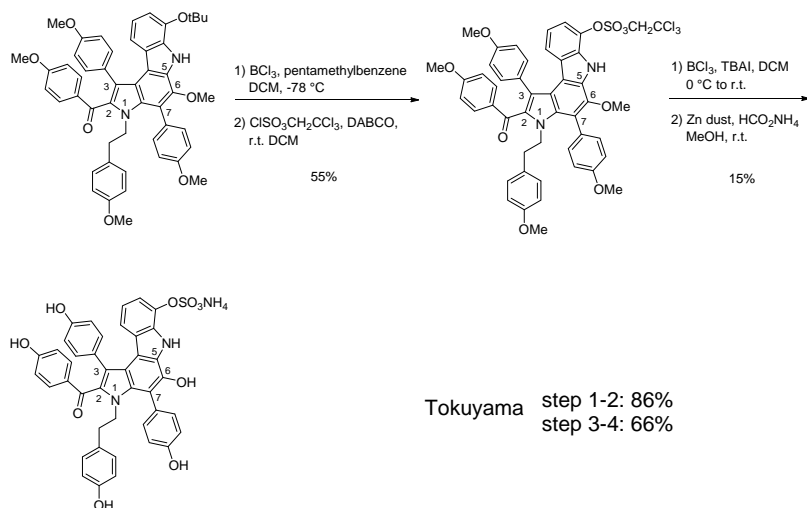
11

## Forward Synthesis



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## Deprotection and sulfonation



13

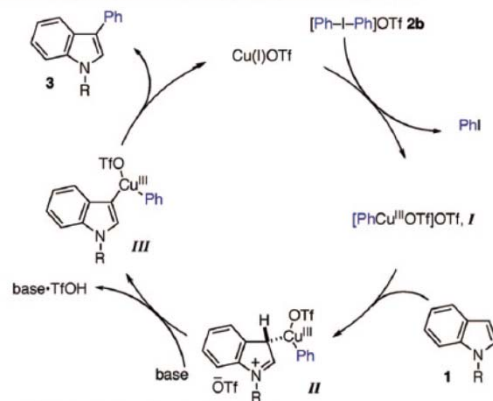
## Conclusion

- > Protected Dictyodendrin B: 9% yield over 11 steps
  - Sequential direct functionalization
- > Deprotection and sulfonation: 8% yield over 4 steps

14

## Cu-catalyzed C-H arylation

a. Proposed catalytic cycle for the Cu(II) catalyzed C-H arylation



J. Am. Chem. Soc. **2008**, 130, 8172.

15

## Ir-catalyzed C-H borylation



J. Am. Chem. Soc. **2006**, 128, 15552.

16



# Cu-mediated etherification

