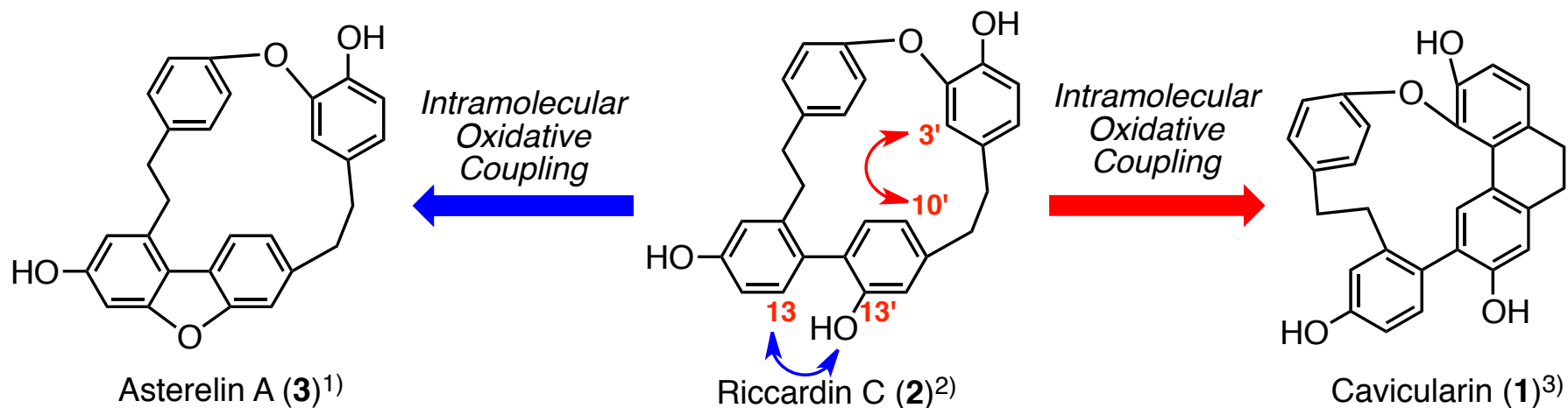
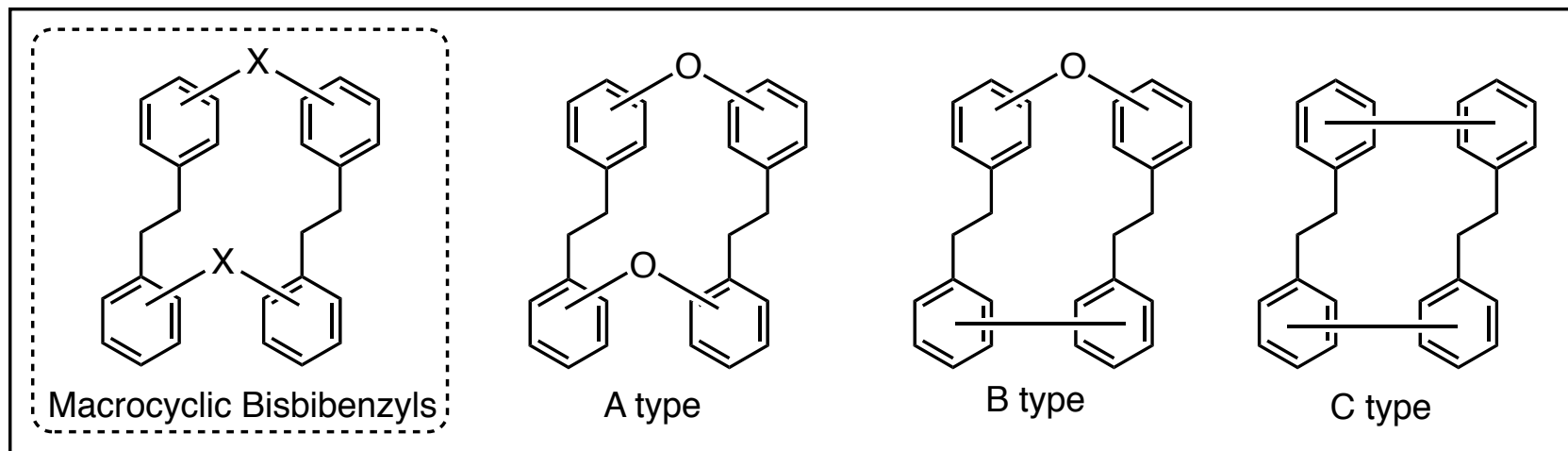


# 大環状ビスビベンジル類 Cavicularin の合成研究

徳島文理大薬

○ 牧野宏章, 久保美和, 原田研一, 福山愛保

# General Structure of Macrocyclic Bisbibenzyls

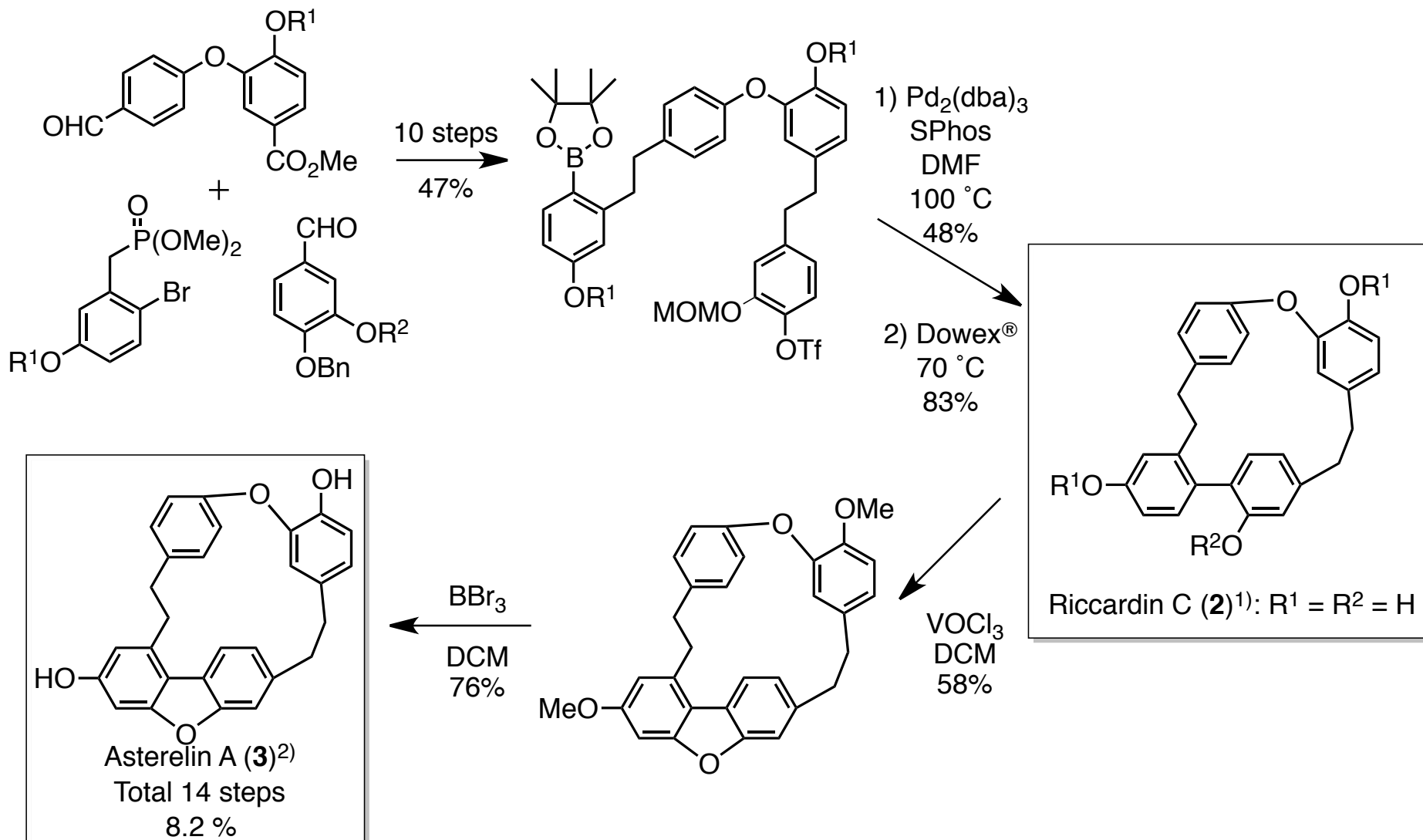


1) J. Qu, C. Xie, H. Gou, W. Yu, H. Lou, *Phytochemistry*, **2007**, *68*, 1767-1774.

2) Y. Asakawa, R. Matsuda, *Phytochemistry*, **1982**, *21*, 2143-2144.

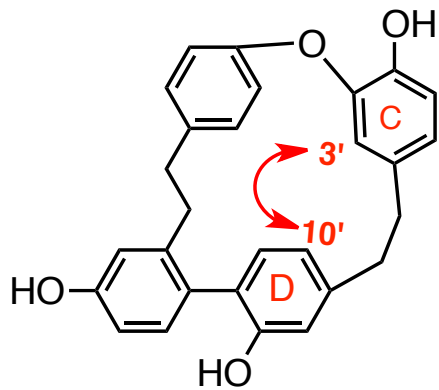
3) M. Toyota, T. Yoshida, Y. Kan, S. Takaoka, Y. Asakawa, *Tetrahedron Lett.*, **1996**, *37*, 4745-4748.

# Total Synthesis of Riccardin C and Asterelin A



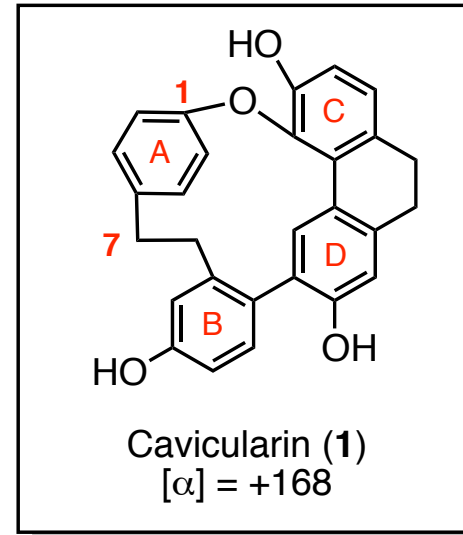
- 1) a) H. Hioki, N. Shima, K. Kawaguchi, K. Harada, M. Kubo, T. Esumi, T. Nishimaki-Mogami, J. Sawada, T. Hashimoto, Y. Asakawa, Y. Fukuyama, *Bioorg. Med. Chem. Lett.*, **2009**, *19*, 738-774. b) N. Shima, K. Kawaguchi, K. Harada, M. Kubo, H. Hioki, Y. Fukuyama, 日本薬学会第128年会, 26PW-am122.
- 2) K. Makino, M. Kubo, K. Harada, Y. Fukuyama, 日本薬学会第132年会, 30P-pm046.

# Structures of Riccardin C and Cavicularin

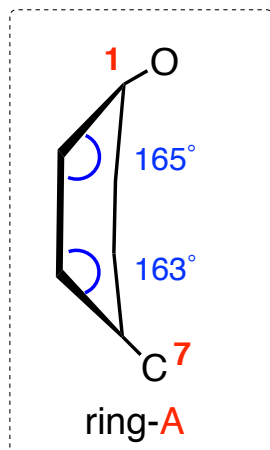


Riccardin C (2)

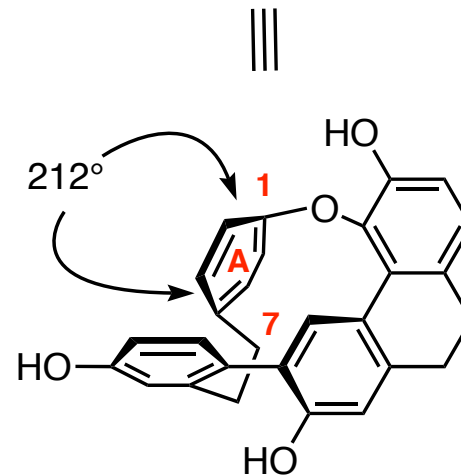
*Intramolecular  
Oxidative  
Coupling*



Cavicularin (1)  
[α] = +168

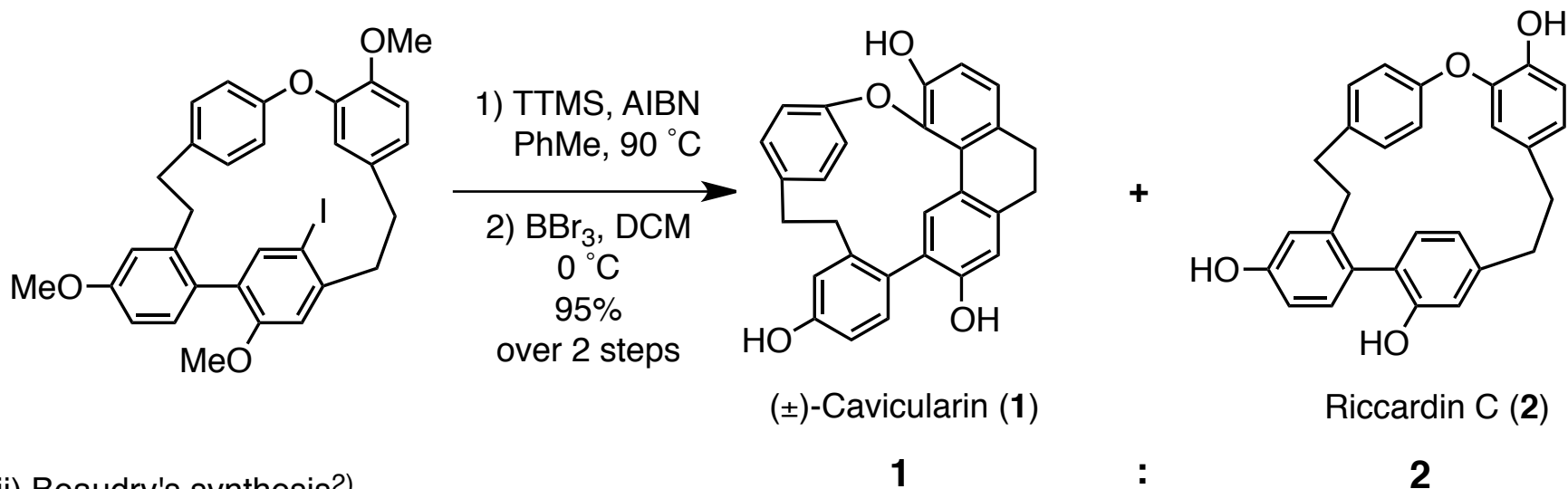


ring-A

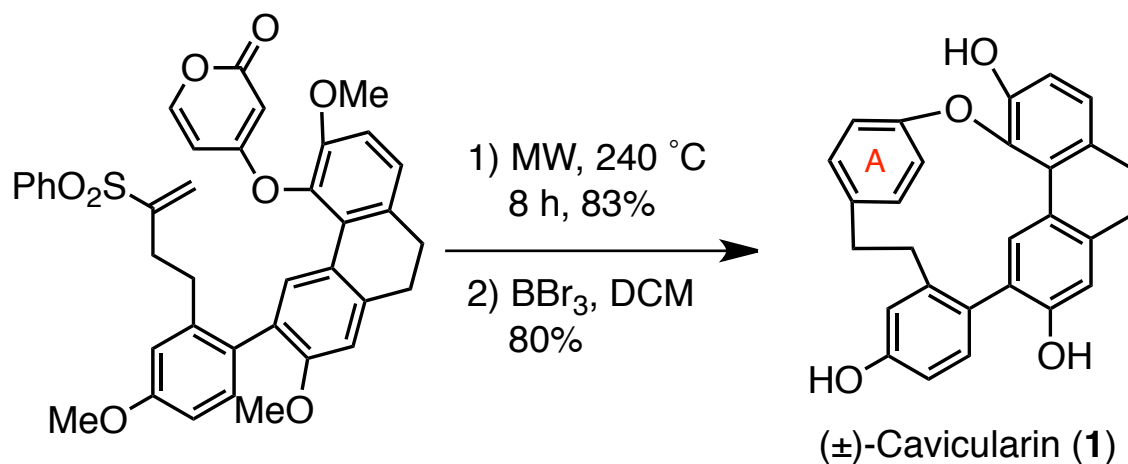


# Total Syntheses of (±)-Cavicularin by Other Groups

i) Harrowven's synthesis<sup>1)</sup>



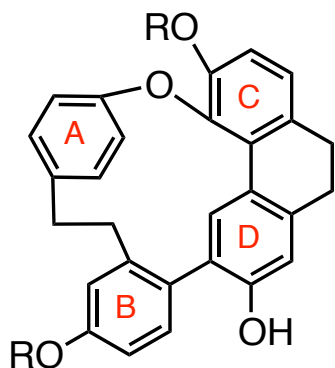
ii) Beaudry's synthesis<sup>2)</sup>



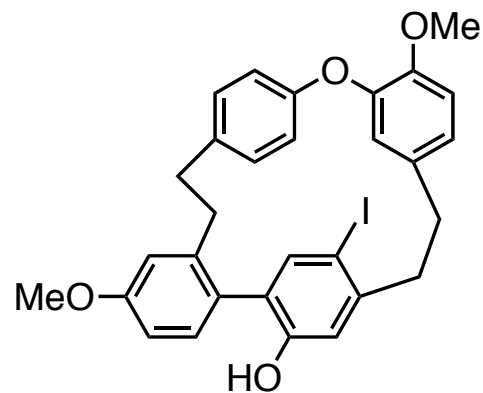
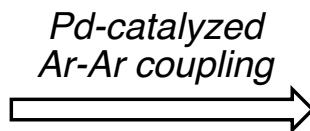
1) D. C. Harrowven, T. Woodcock, P. D. Howes, *Angew. Chem. Int. Ed.*, **2005**, *44*, 3899-3901.

2) P. Zhan, C. M. Beaudry, *Org. Lett.*, **2013**, *15*, 402-405.

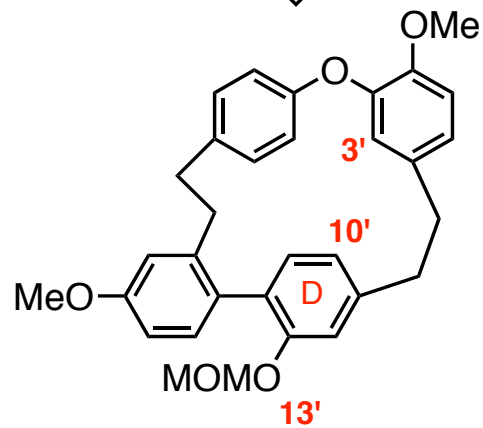
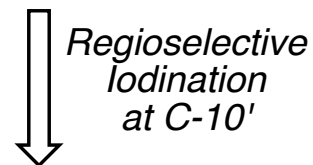
# Retrosynthetic Analysis of Cavicularin



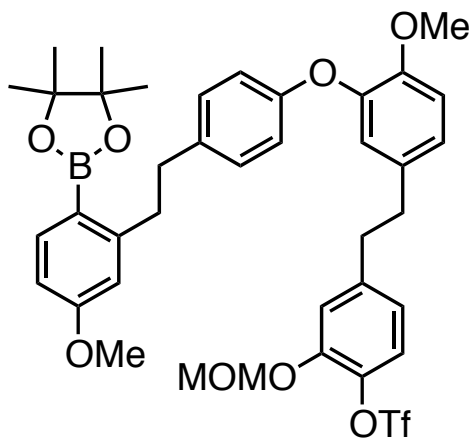
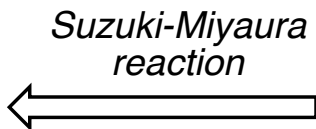
Cavicularin (1): R = H



4

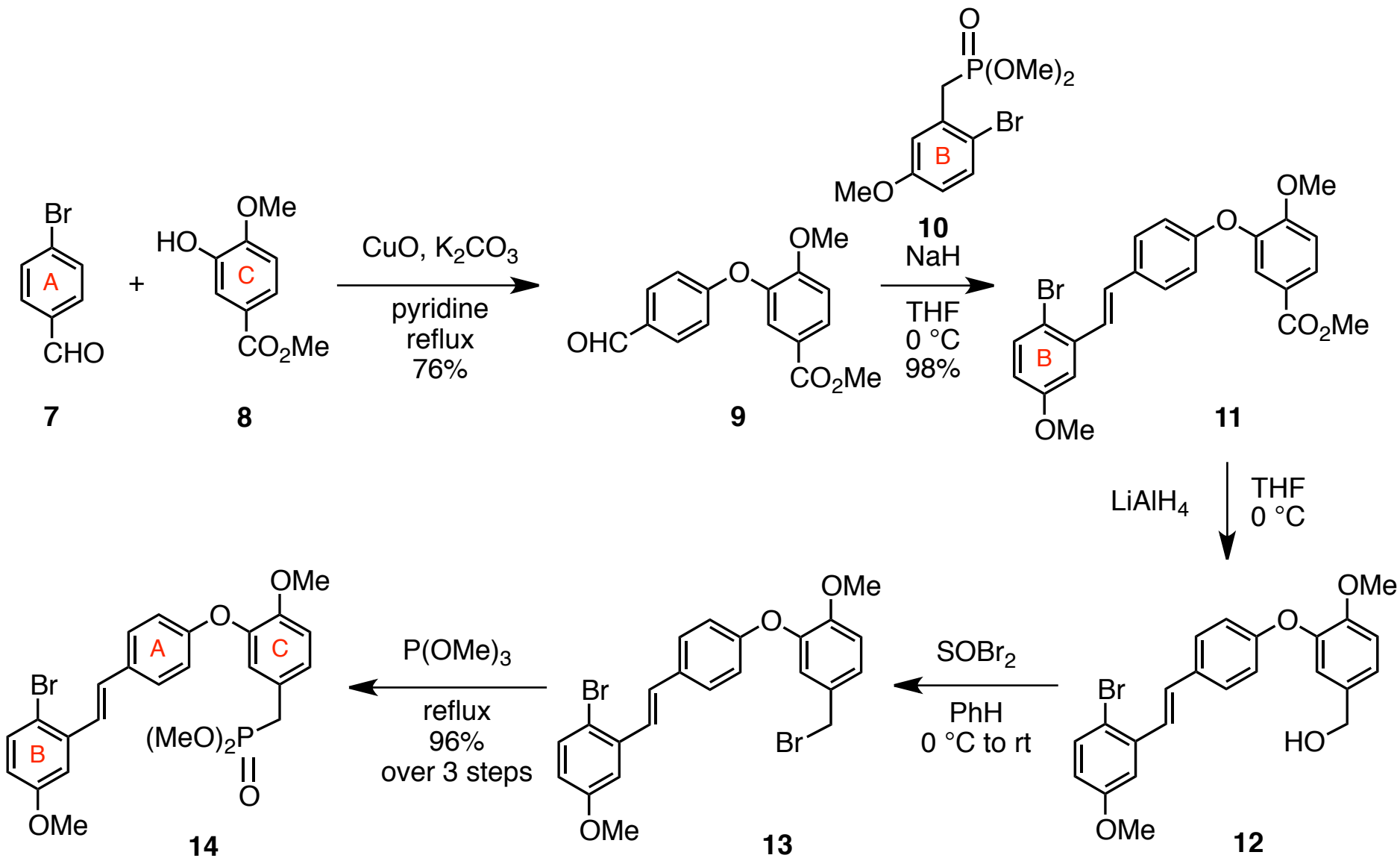


5

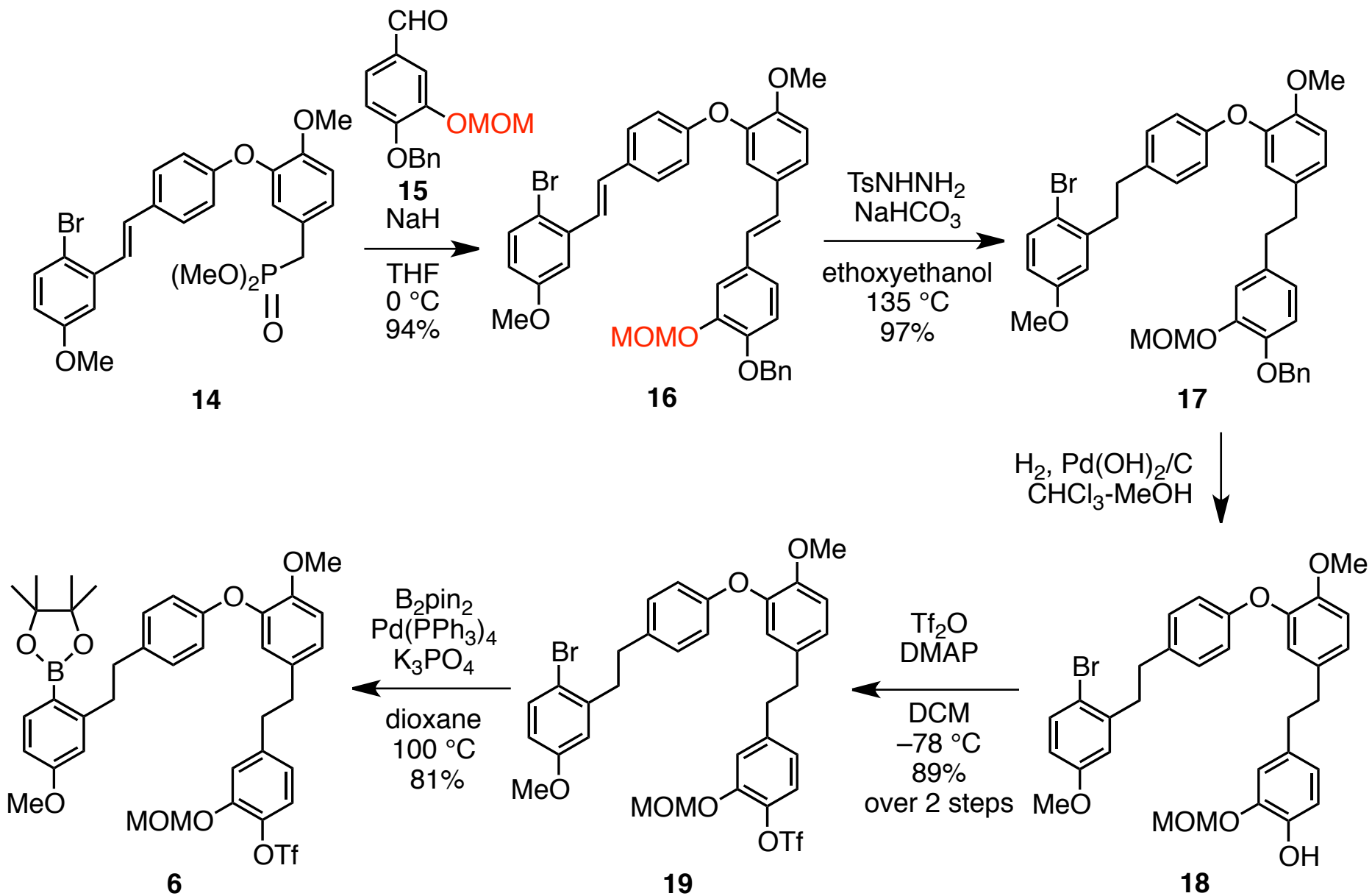


6

# Preparation of Intermediate 14

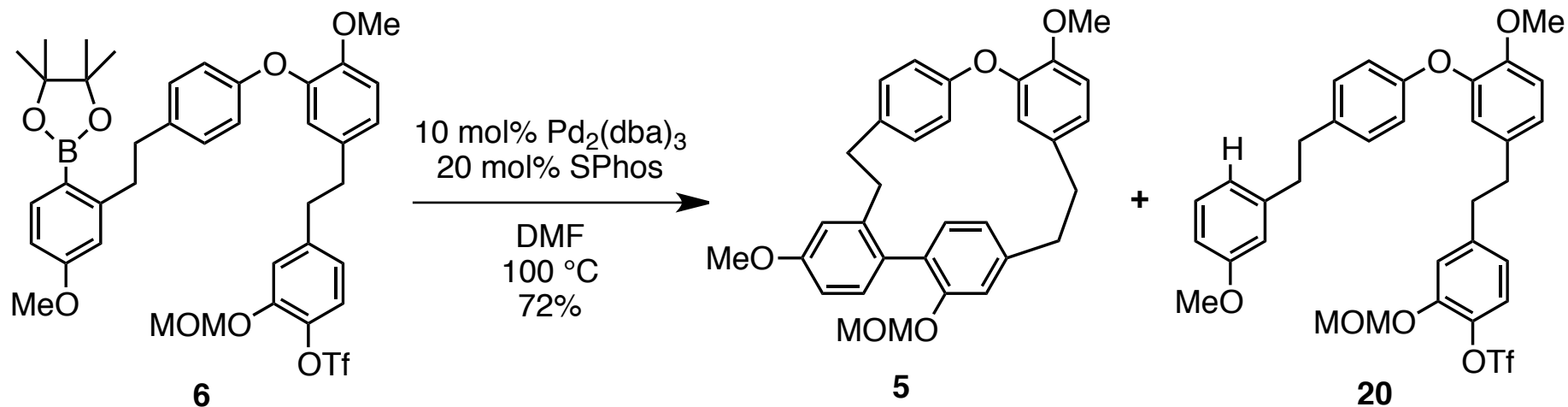


# Preparation of Intermediate 6





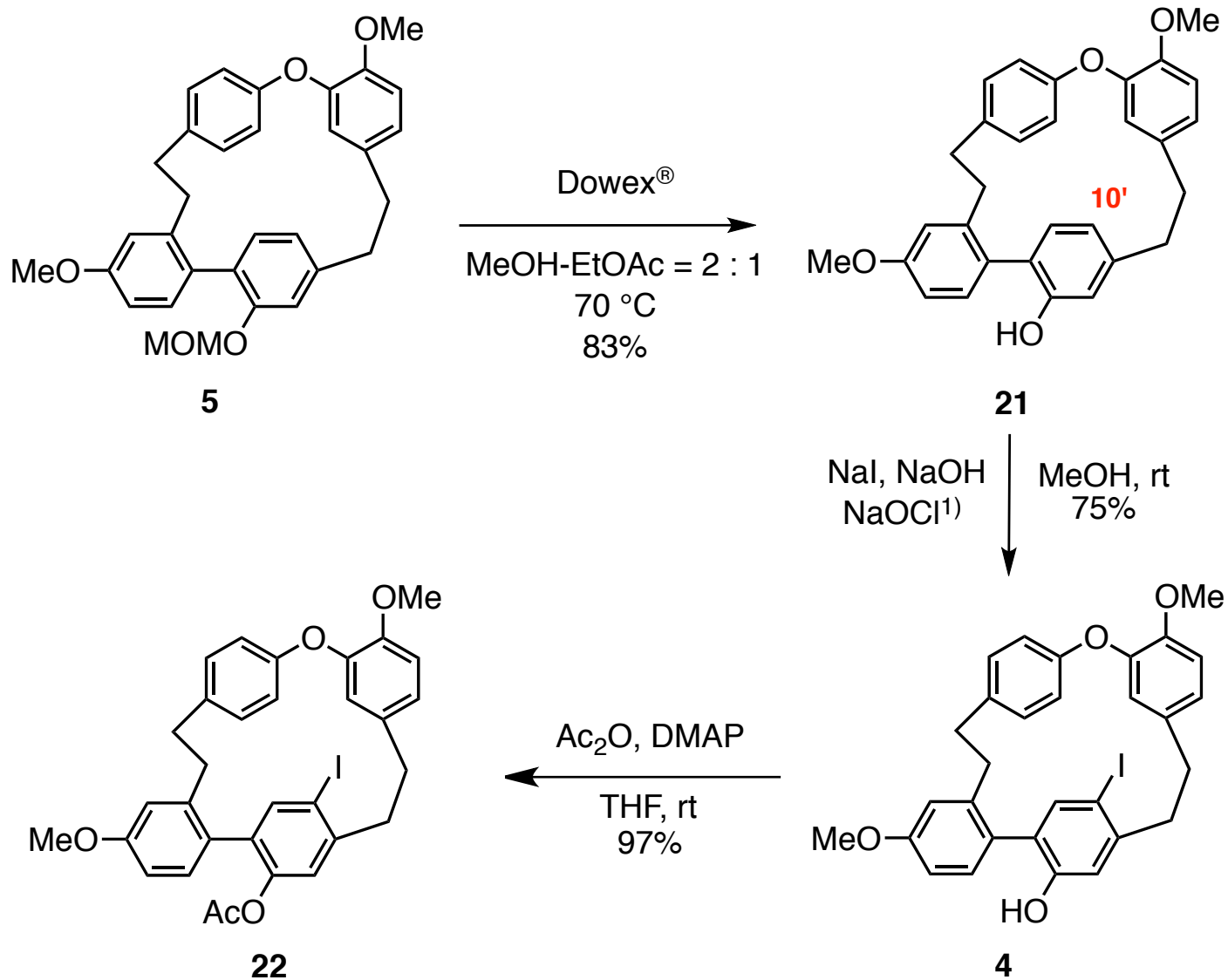
# Intramolecular Suzuki–Miyaura Reaction



| Entry | Base (3 eq)                               | Solvent          | <b>5</b> | <b>20</b> |
|-------|---|------------------|----------|-----------|
| 1     | aq. Na <sub>2</sub> CO <sub>3</sub>       | DMF              | 31       | 65        |
| 2     | anhydrous Na <sub>2</sub> CO <sub>3</sub> | DMF <sup>1</sup> | 72       | 0         |

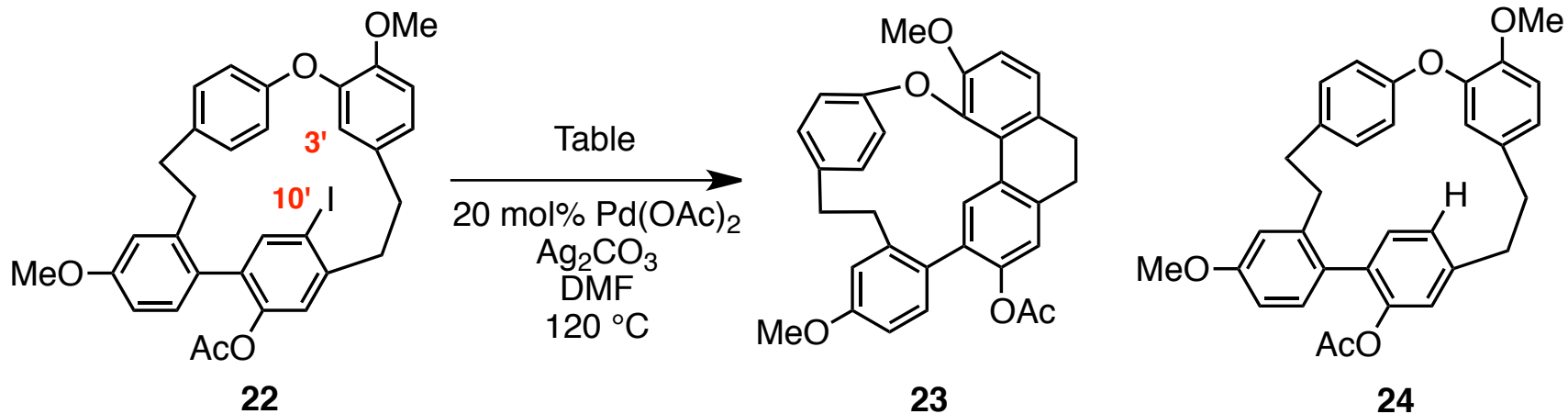
<sup>1</sup> Freshly distilled DMF was used.

# Preparation of Iodide 22



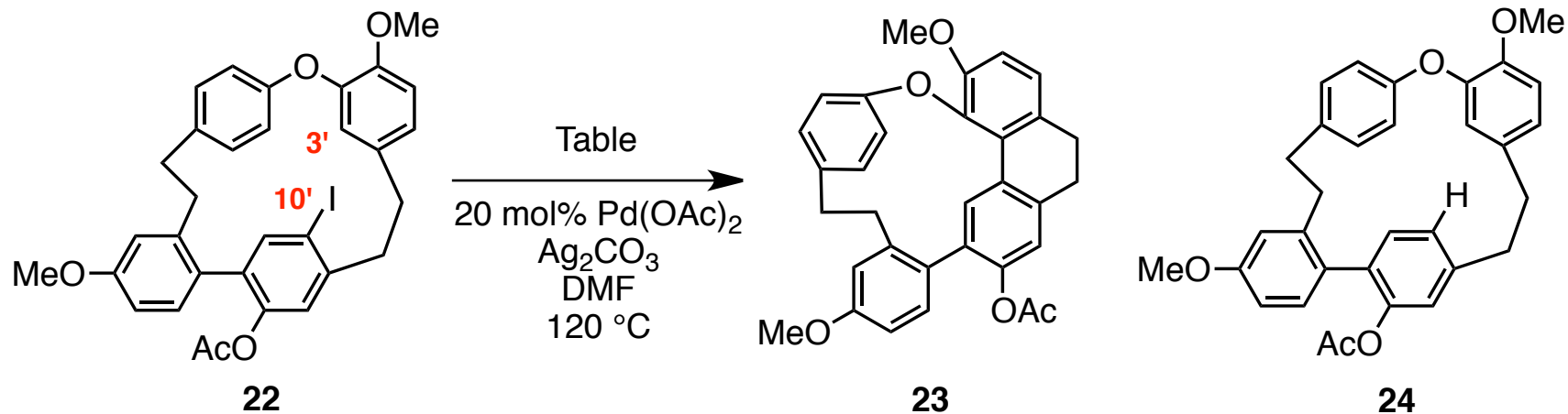
1) K. J. Edger, S. N. Falling, *J. Org. Chem.*, **1990**, *55*, 5287-5291.

# Examination of Pd-catalyzed Ar–Ar Coupling

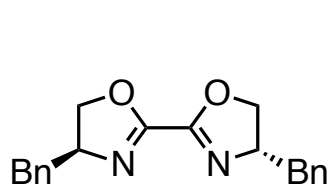


| Entry | Ligand                          | mol % of L | <b>23</b> | <b>24</b> |
|-------|---------------------------------|------------|-----------|-----------|
| 1     | ( <i>o</i> -tol) <sub>3</sub> P | 40         | 0         | 81        |
| 2     | <i>t</i> -Bu <sub>3</sub> P     | 40         | 0         | 78        |
| 3     | <i>n</i> -Bu <sub>3</sub> P     | 40         | 39        | 36        |
| 4     | Et <sub>3</sub> P               | 40         | 0         | 0         |
| 5     | -                               | -          | 0         | 74        |
| 6     | <i>n</i> -Bu <sub>3</sub> P     | 20         | 50        | 31        |

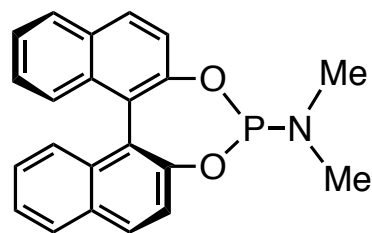
# Examination of Asymmetric Pd-catalyzed Ar–Ar Coupling



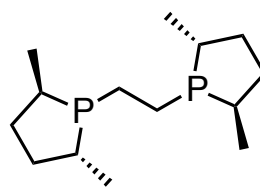
| Entry | Ligand                   | mol % of L | <b>23</b> | <b>24</b> | ee <sup>a</sup> |
|-------|--------------------------|------------|-----------|-----------|-----------------|
| 1     | dppe                     | 20         | 41        | 43        | -               |
| 2     | <b>25</b>                | 20         | 0         | 0         | -               |
| 3     | <b>26</b>                | 20         | 7         | 0         | 7               |
| 4     | ( <i>R,R</i> )-Me-BPE    | 20         | 12        | 0         | 6               |
| 5     | ( <i>S</i> )-BINAP       | 20         | 18        | 0         | 7               |
| 6     | ( <i>S,S</i> )-Chiraphos | 20         | 23        | 0         | 11              |



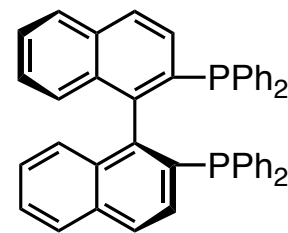
**25**



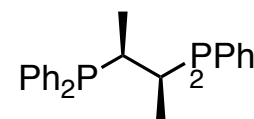
**26**



Me-BPE

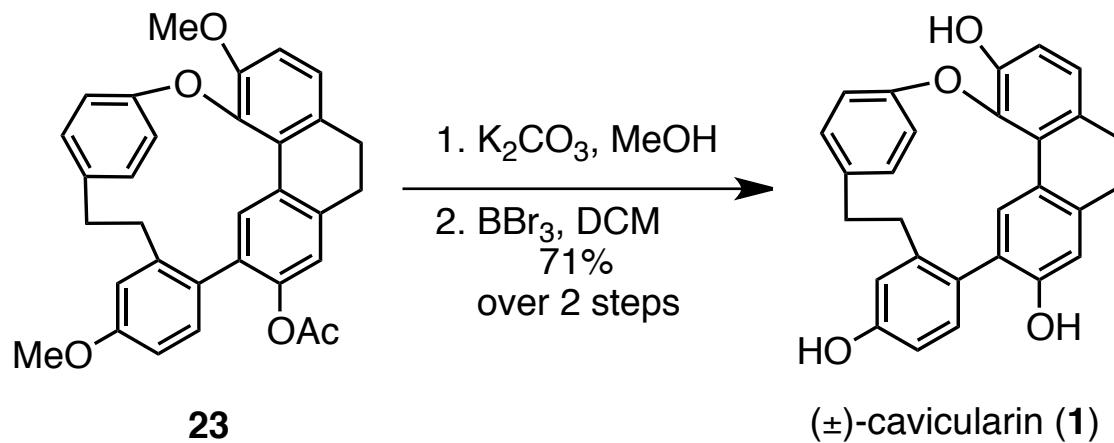


BINAP

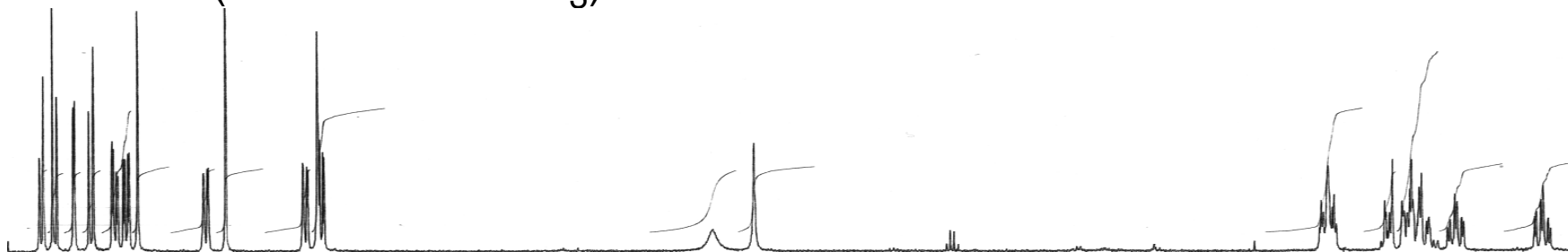


Chiraphos

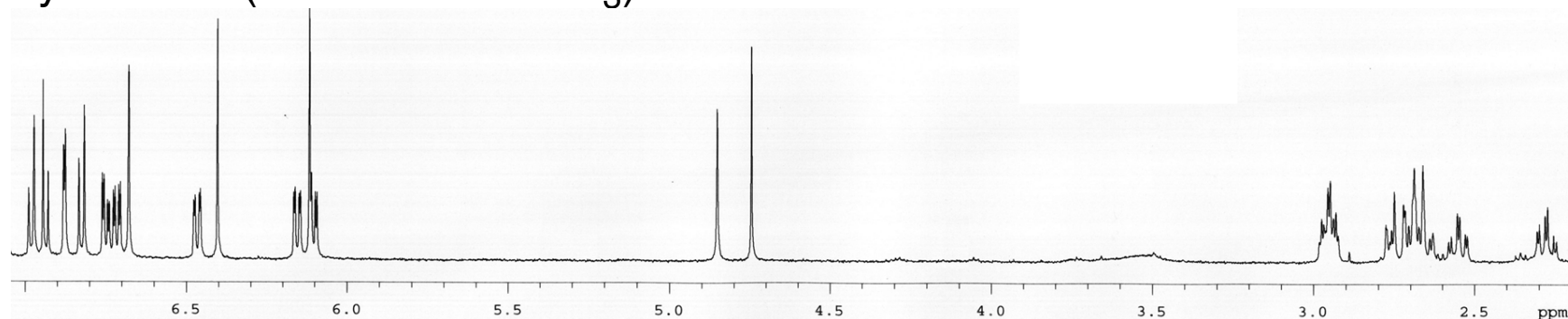
# Completion of the Synthesis of (±)-Cavicularin



Natural **1** (600 MHz in  $\text{CDCl}_3$ )



Synthetic **1** (500 MHz in  $\text{CDCl}_3$ )



# Conclusion

