Literature Report

Changbin Yu 2013-05-21 检查: 陈章培

Total Synthesis of (+)-Linoxepin by Utilizing the Catellani Reaction

Mark Lautens* *et al*. *Angew. Chem. Int. Ed*. **2013**, *52*, 5305–5308.

Education

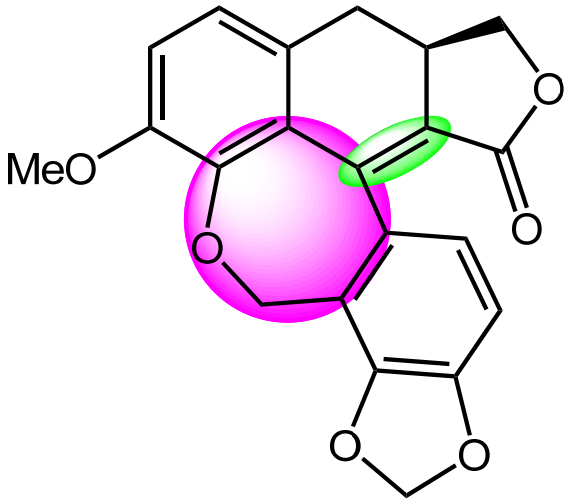
- Harvard University **NSERC PDF** with D. A. Evans 1985 - 1987
- University of Wisconsin-Madison **Ph.D**. with B. M. Trost 1985
- University of Guelph **B.Sc**. - Distinction 1981

Academic Positions

◆J. Bryan Jones Distinguished Professor	University of Toronto	1998 - present
◆Professor	University of Toronto	1995 -1998
◆Associate Professor	University of Toronto	1992 - 1995
◆Assistant Professor	University of Toronto	1987 - 1992

Research Interests

- ◆C-H Bond Activation
- ◆Heterocycles via Tandem Catalysis
- ◆Enantioselective Desymmetrization
- ◆Total Synthesis



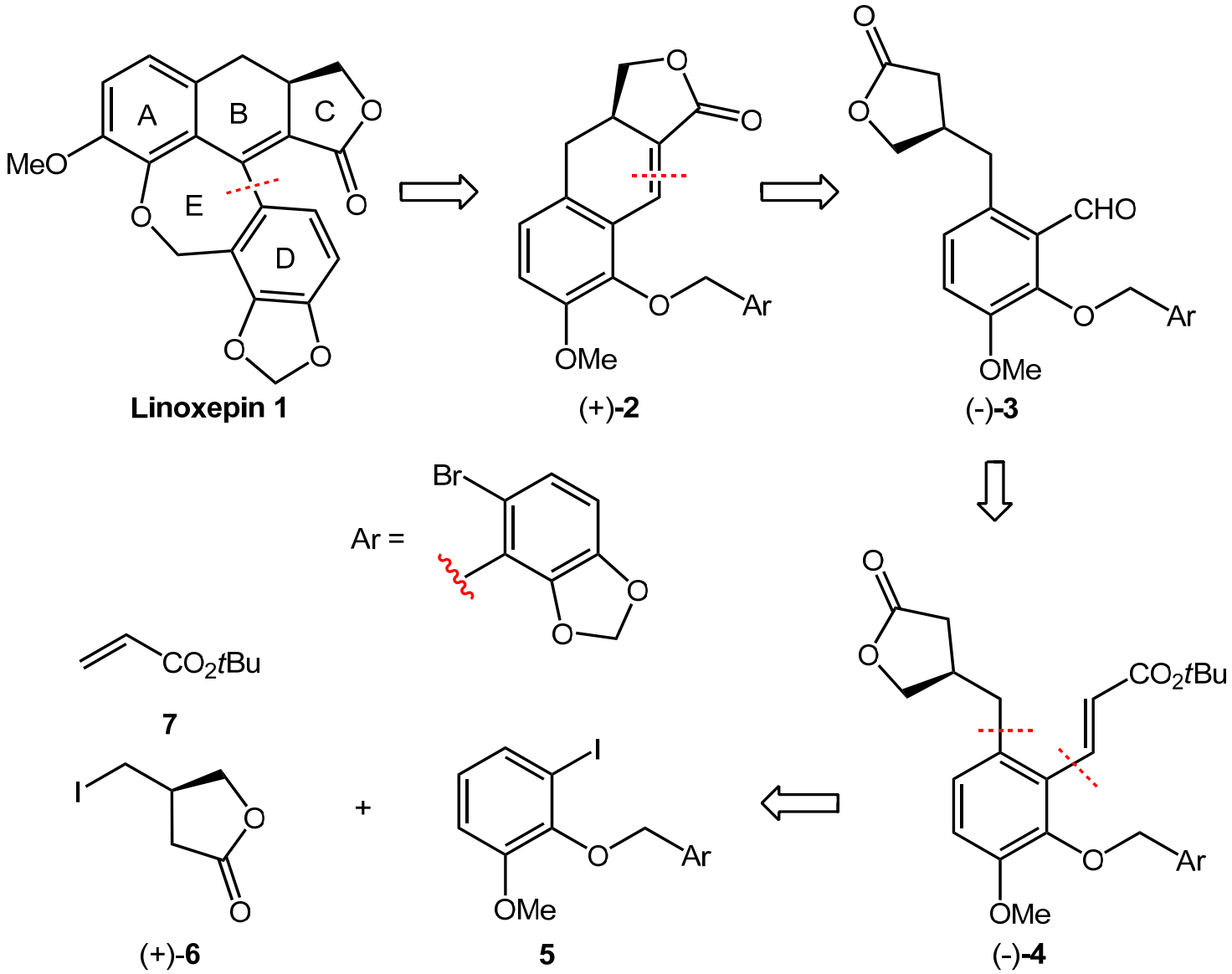
Linoxepin

Linaceae

Characters and challenges:

- Tetrasubstituted double bond embedded within a highly strained ring system.
- A dibenzo–dihydrooxepine moiety.

Retrosynthetic analysis of (+)-Linoxepin (**1**)



Linoxepin 1 (+)-**2** (-)-**3**

7

(+)-**6** **5** (-)-**4**

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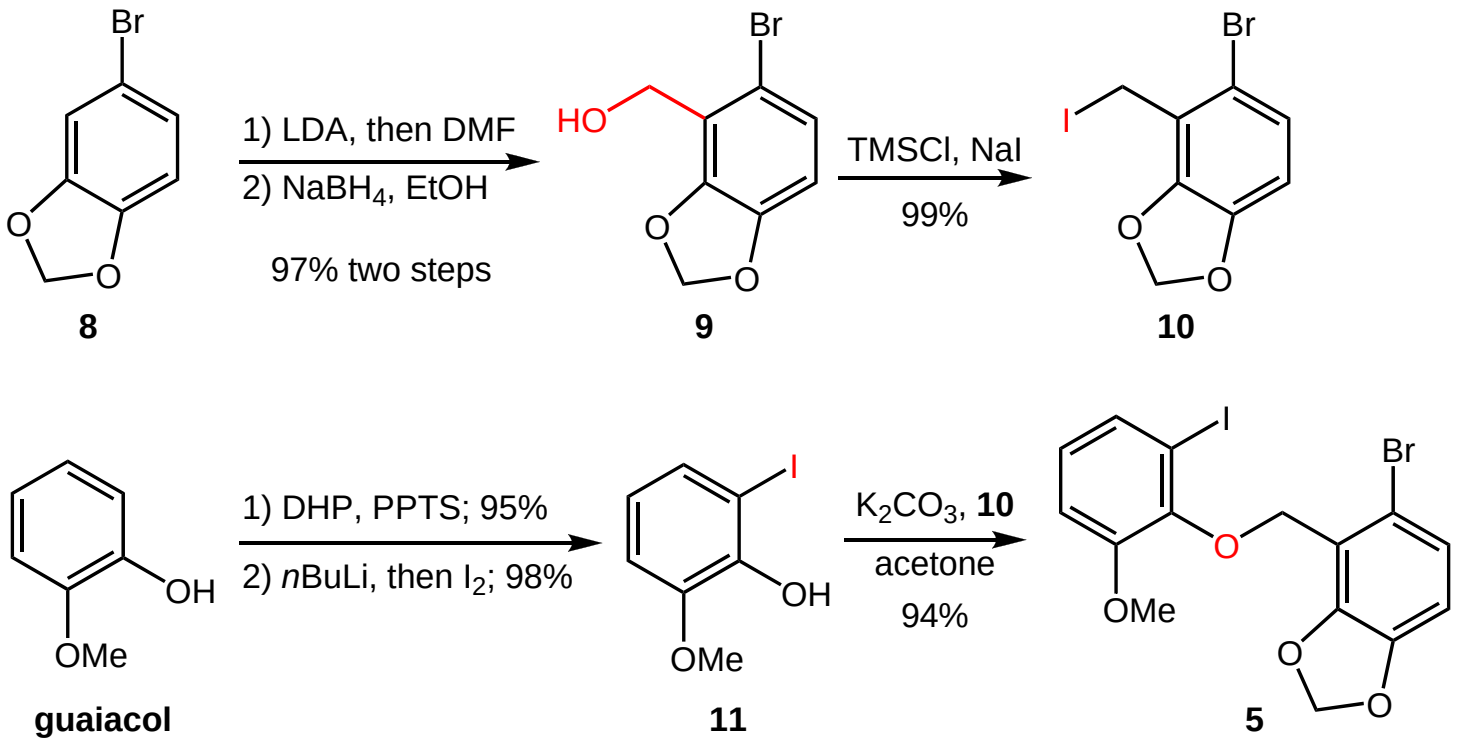

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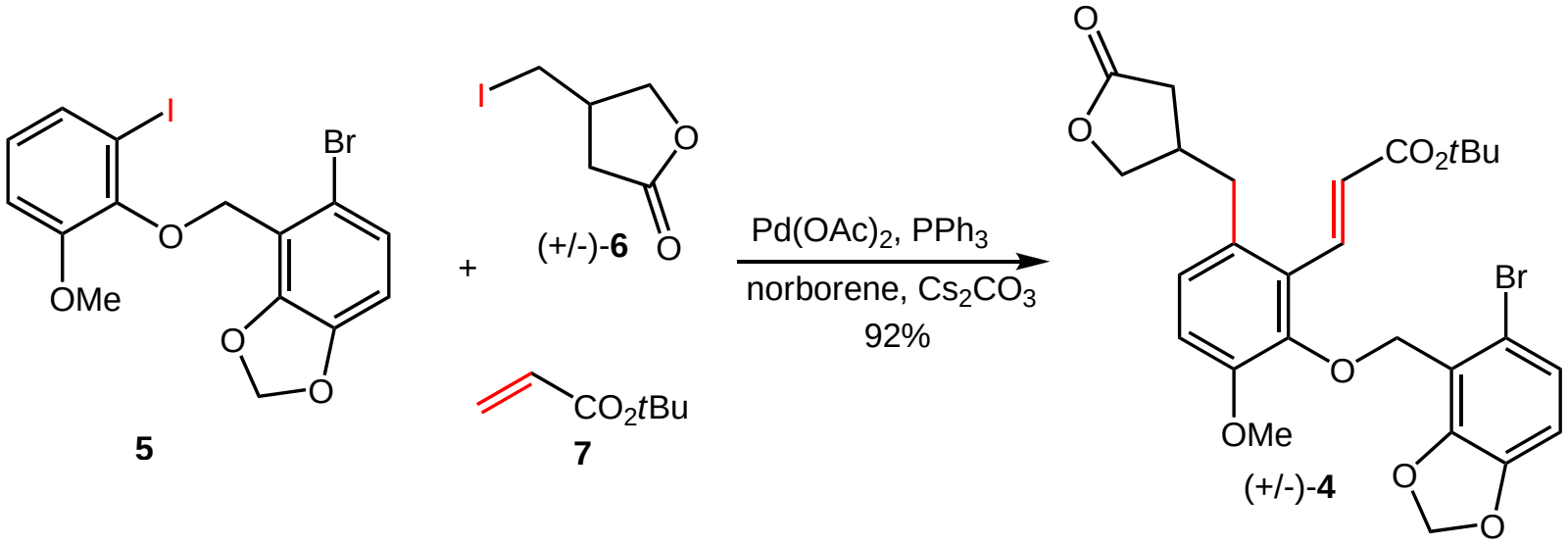

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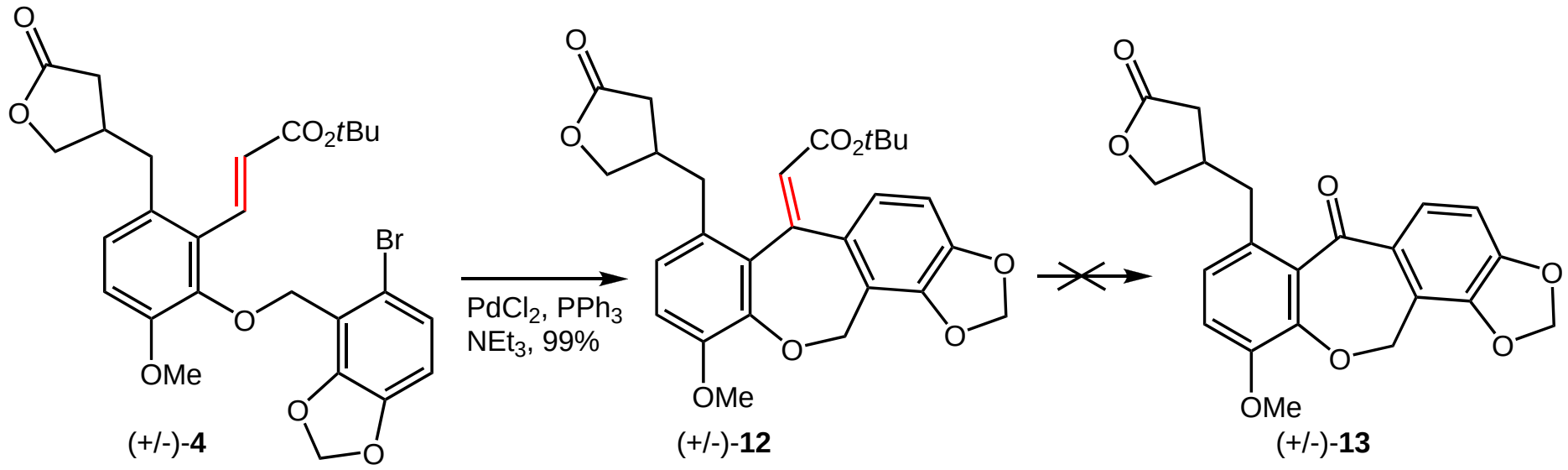

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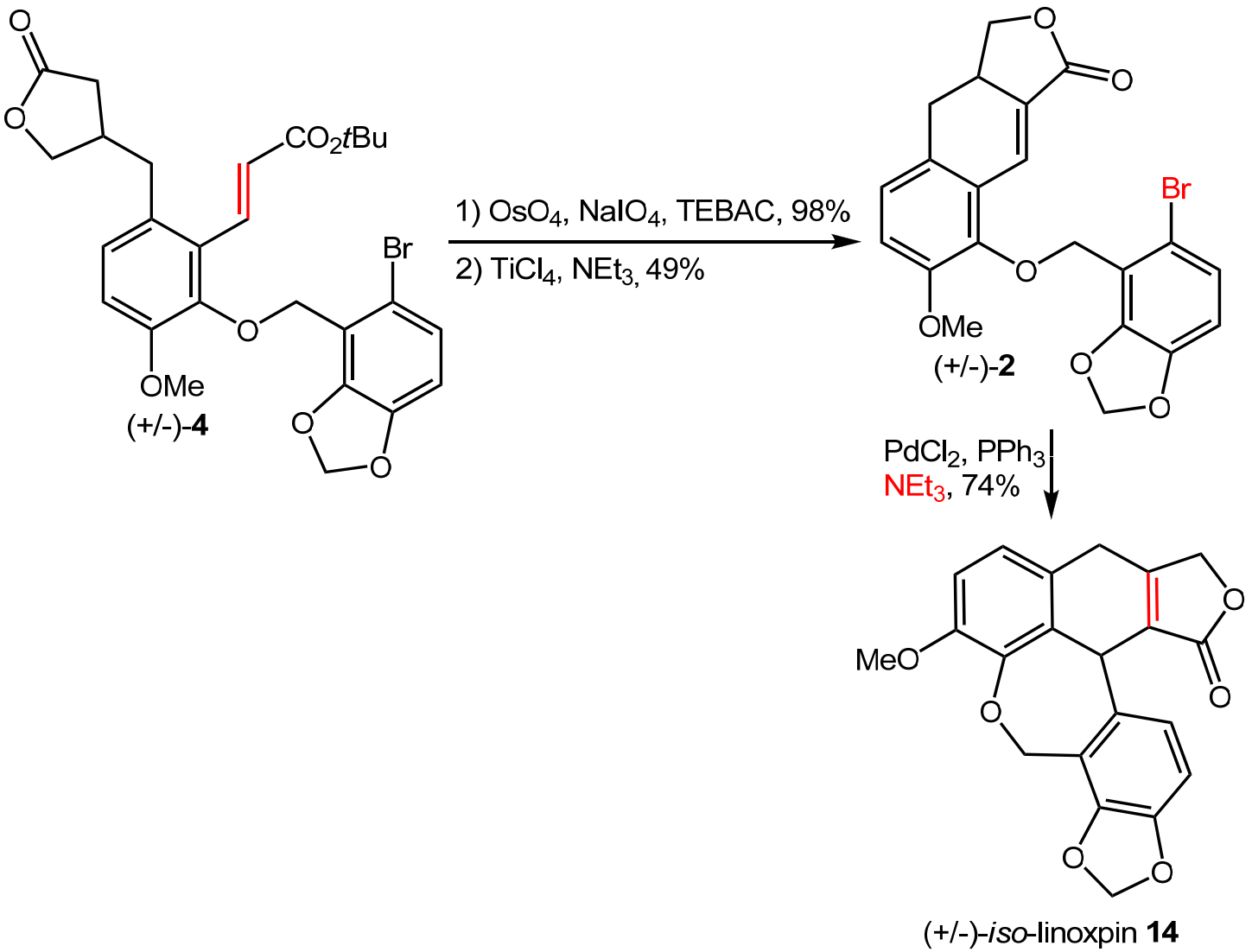

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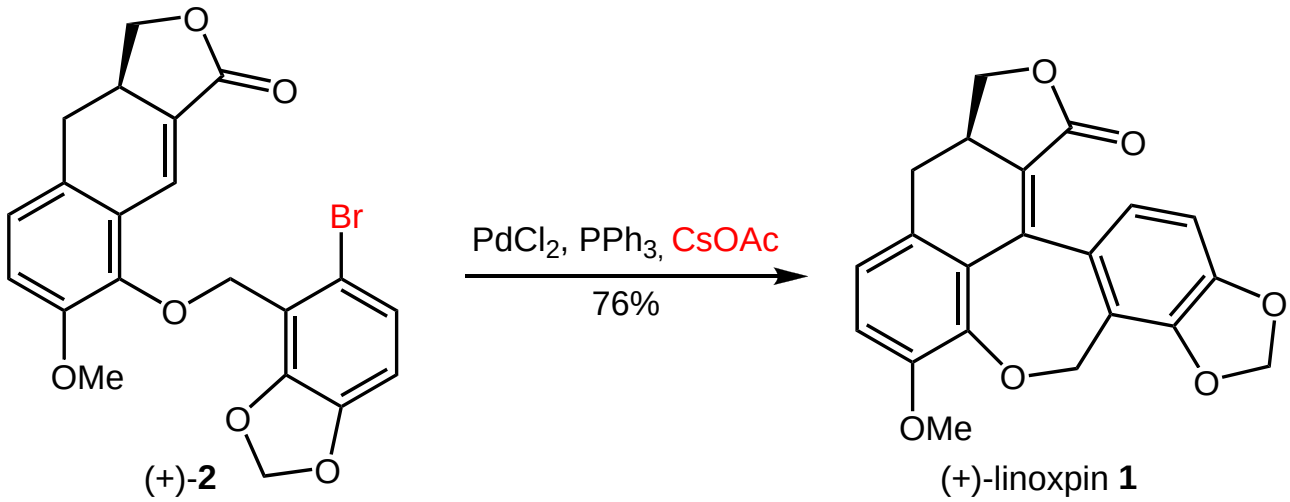

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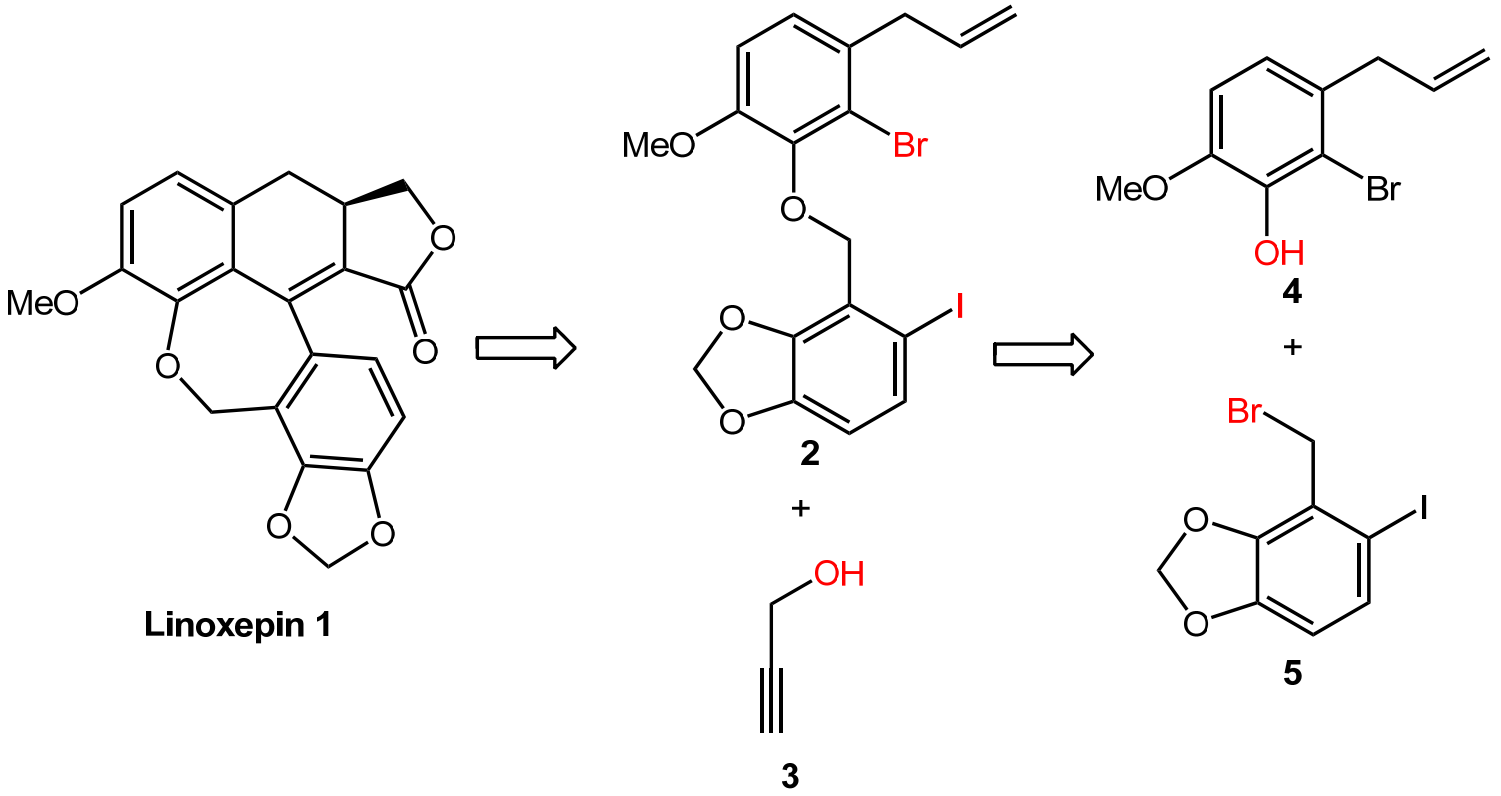
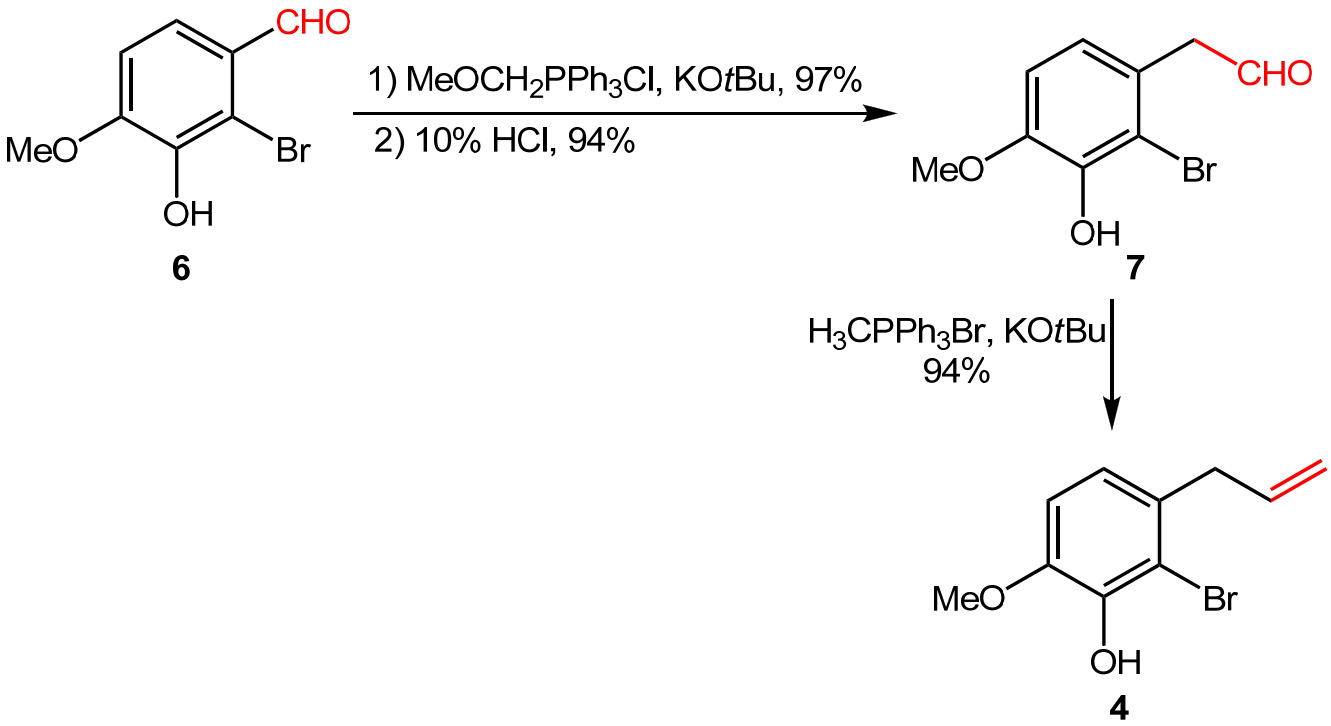
Lutz F. Tietze:



Lutz F. Tietze* *et al*. *Angew. Chem. Int. Ed*. **2013**, *52*, 3191–3194.



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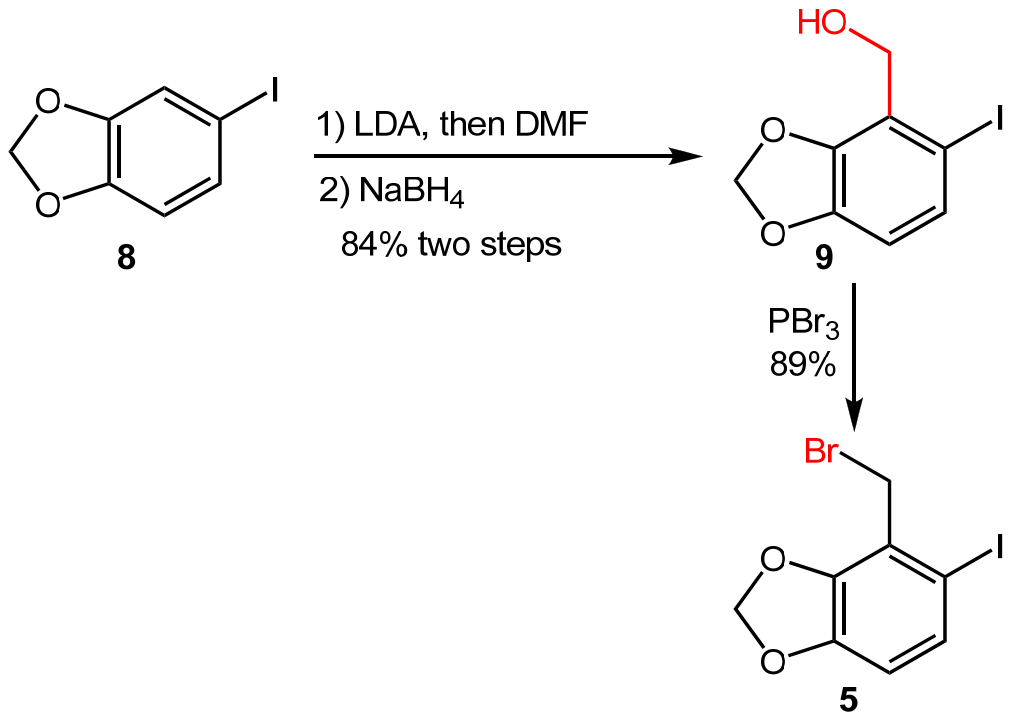

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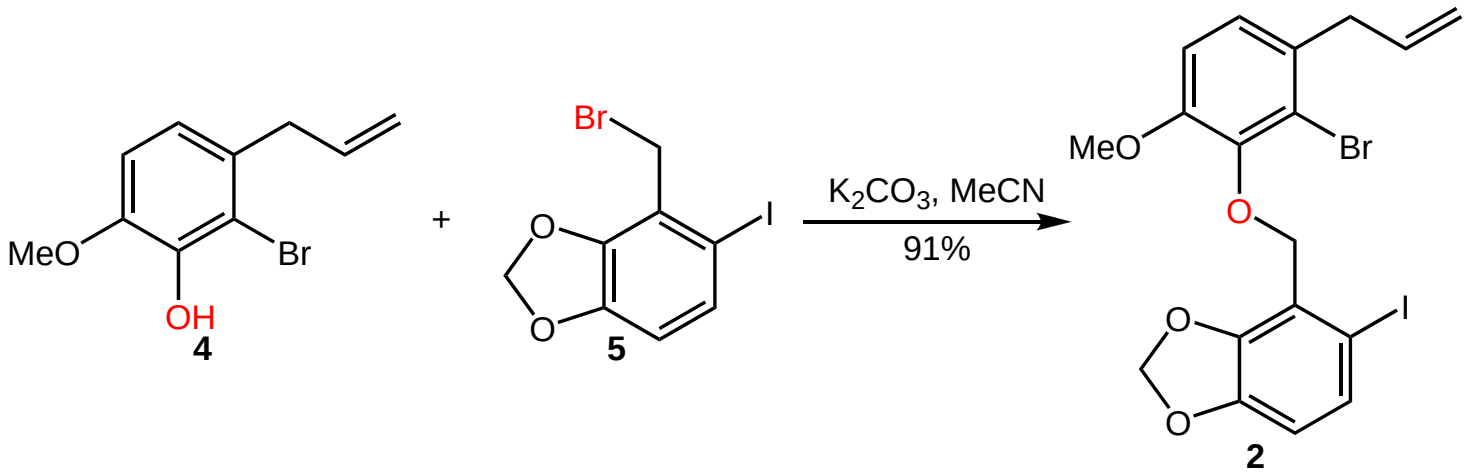

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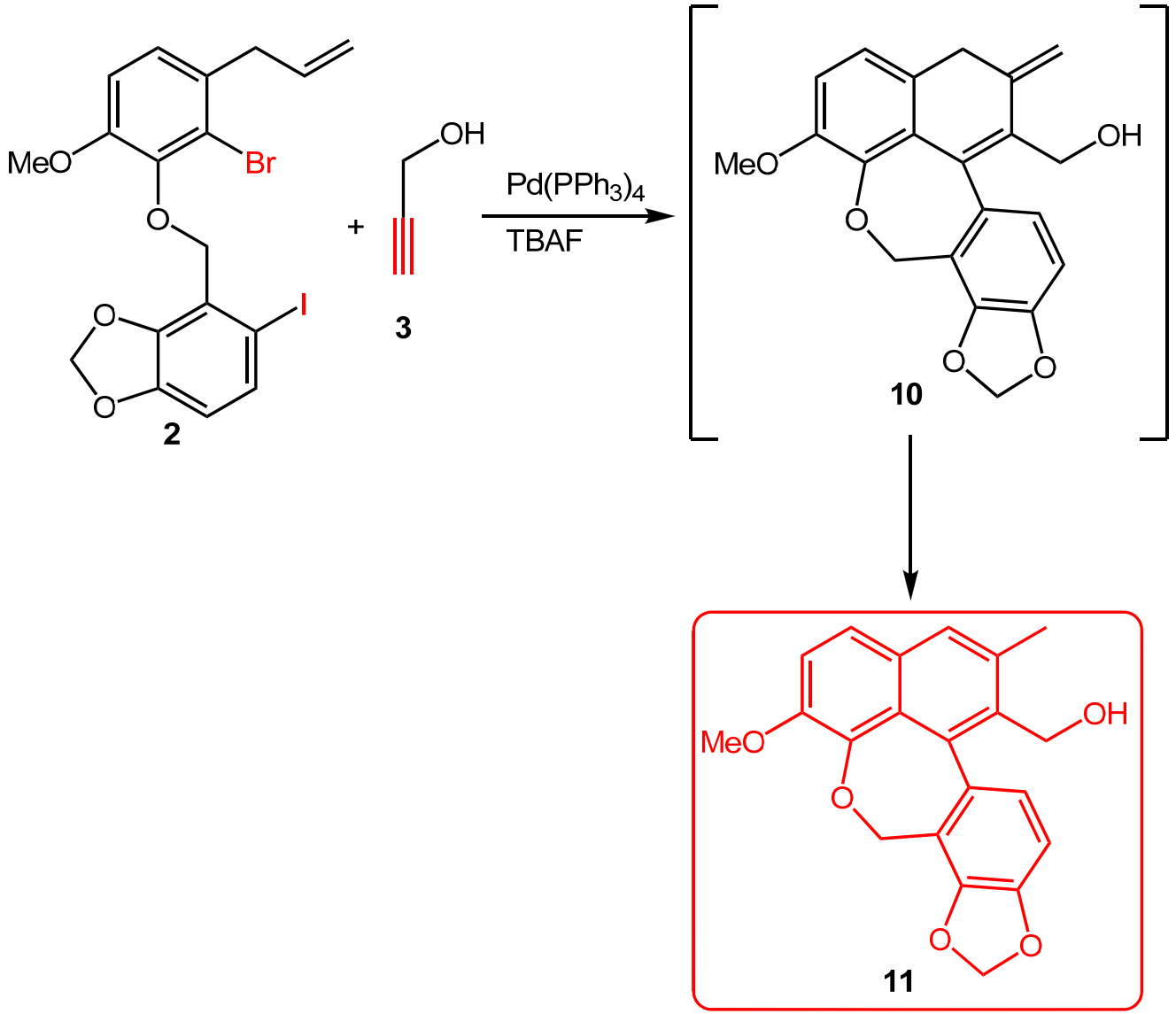

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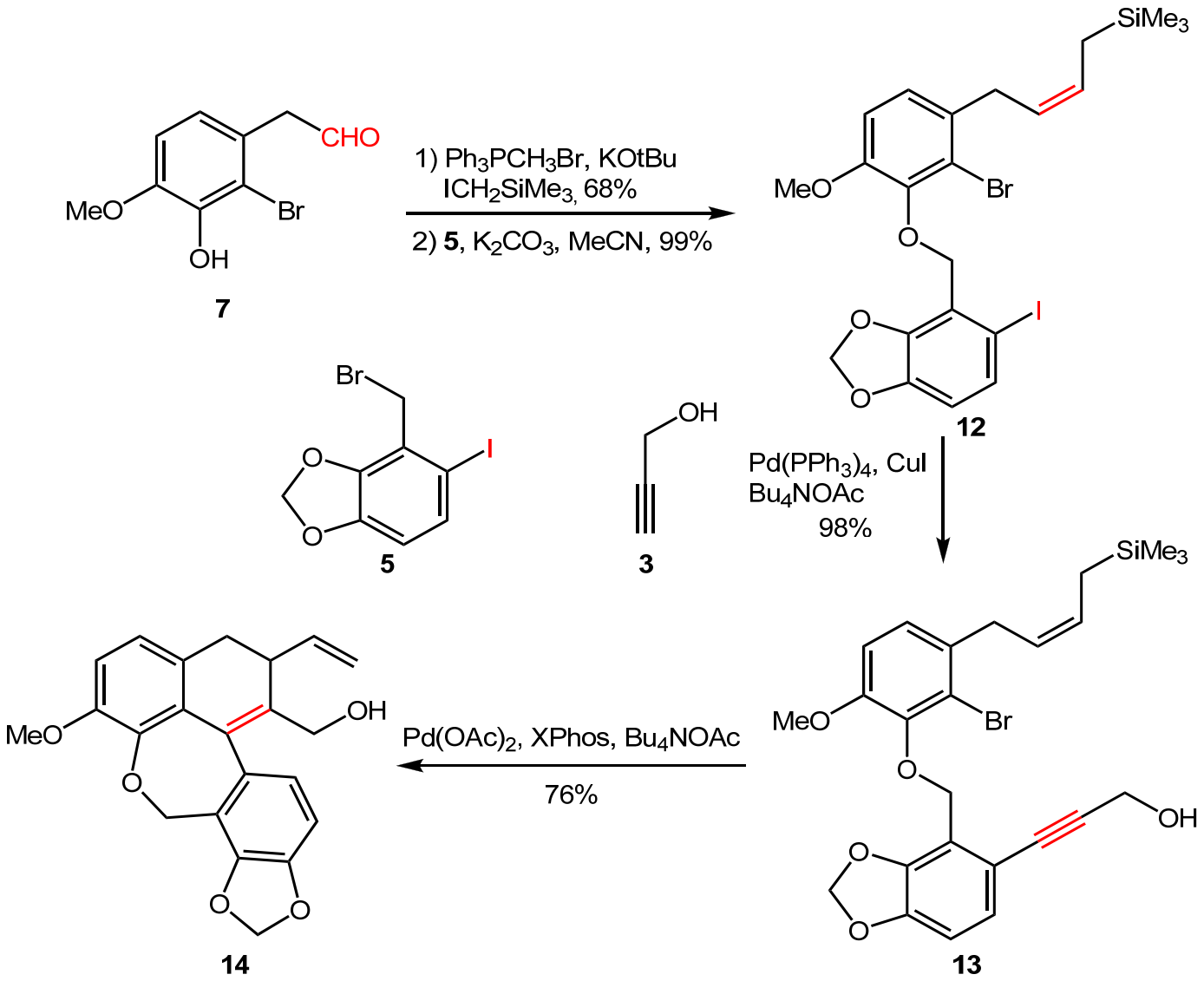

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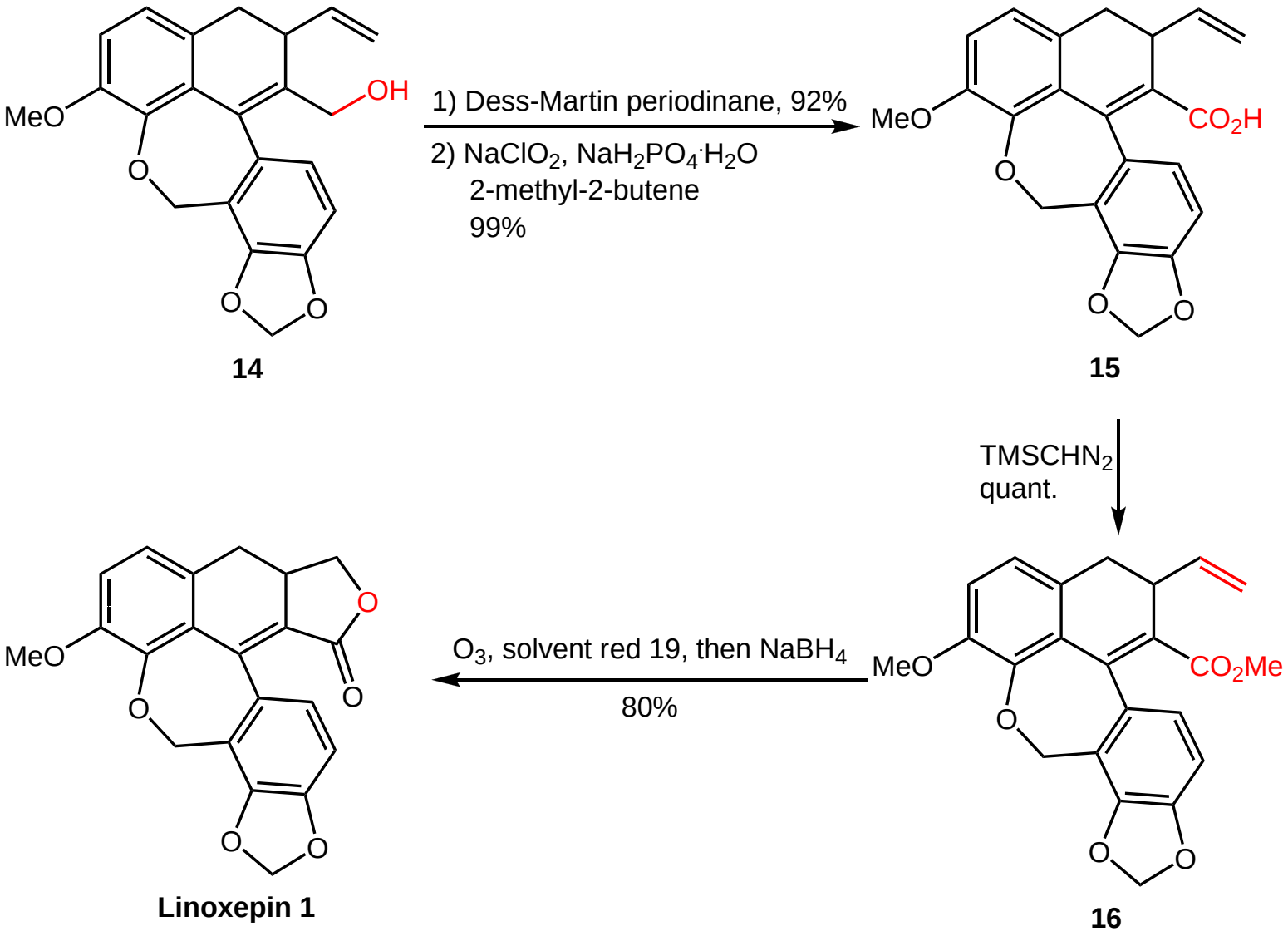
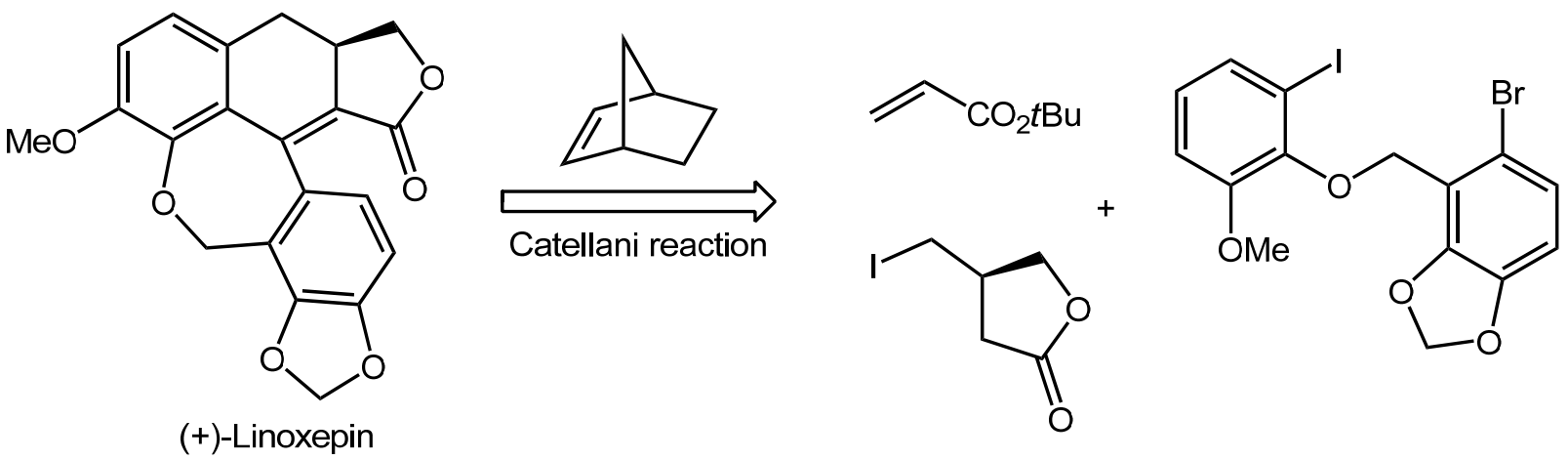


Lutz F. Tietze* *et al*. *Angew. Chem. Int. Ed*. **2013**, *52*, 3191–3194.

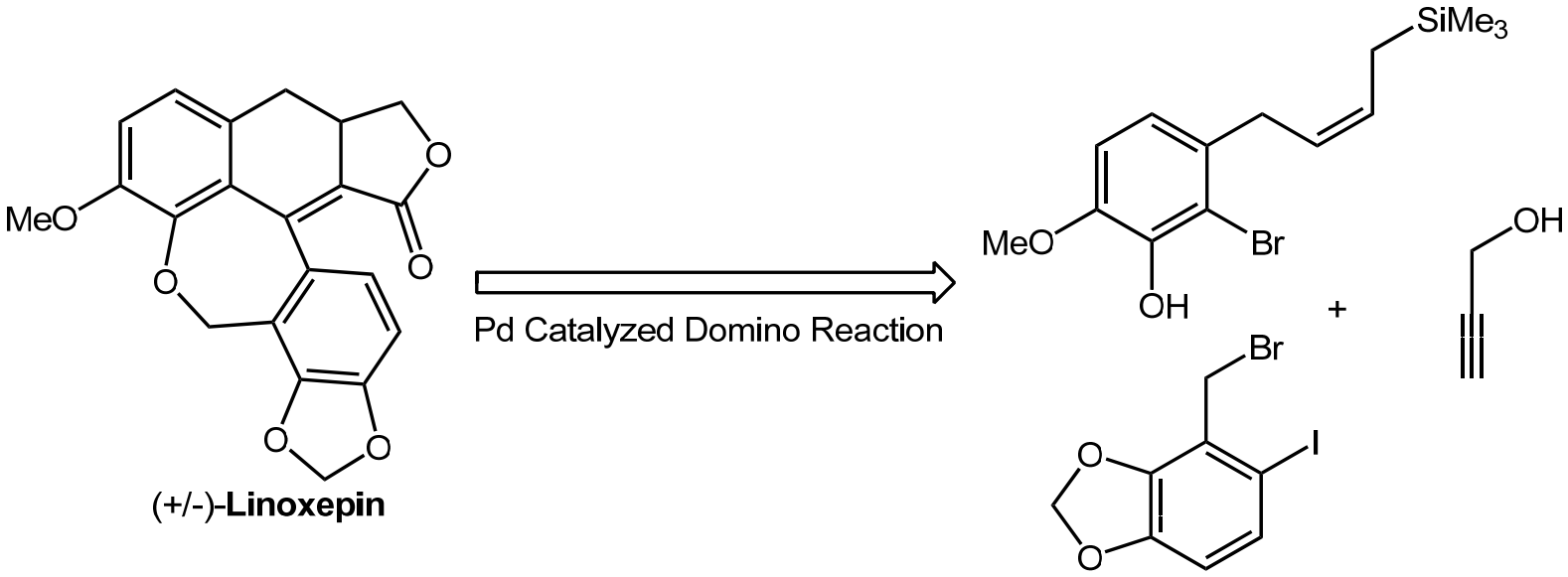
总结:

Mark Lautens:



- 8 steps (30%).
- The enantioselective, protecting-group-free total synthesis.
- A domino C-H functionalization.
- Catellani Reaction.

Lutz F. Tietze:



- The first total synthesis.
- 10 steps (30%).
- The protecting-group-free total synthesis.
- A palladium-catalyzed Sonogashira reaction/ a domino carbopalladation/Heck reaction of an allylsilane

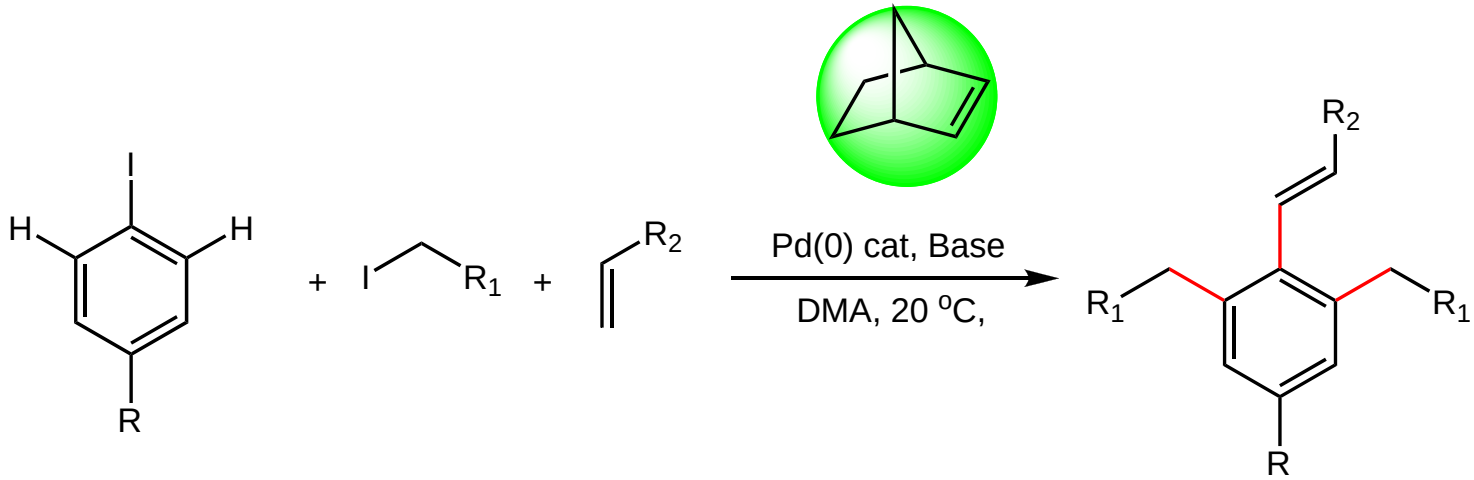
Lignans are a diverse class of plant-derived natural products belonging to the phytoestrogen family. They have long been used as herbal remedies for pain, rheumatoid arthritis, and warts. However, more recently, lignans exhibiting immunosuppressive activity, tumor growth inhibition, and anti-fungal properties have been used in disease therapy, such as the anticancer agent etoposide.

In conclusion, we have achieved the enantioselective, protecting-group-free, total synthesis of the challenging lignan (+)-linoxepin **1** using domino C-H functionalization with an overall yield of 30%. This synthesis is the first reported application of the palladium-catalyzed Catellani reaction in the synthesis of a complex natural product. We note that the optical rotation of the synthetic material is higher ([20] = + 90.0; c = 0.25, $CHCl_3$) than the reported value ([20] + 23.0; c = 0.93, $CHCl_3$). All of the spectroscopic data of the final product are in complete agreement with the published data from the isolated material. It is noteworthy that Tietze and co-workers observed a higher optical rotation in their resolved material than was found in the isolated material ([20] + 96.1; c = 0.61, $CHCl_3$). X-ray crystallographic analysis confirms the reported structure of linoxepin. We are continuing to investigate the origin of the change in regioselectivity in the final Mizoroki Heck reaction and will provide further details as they become available.

Introduction:

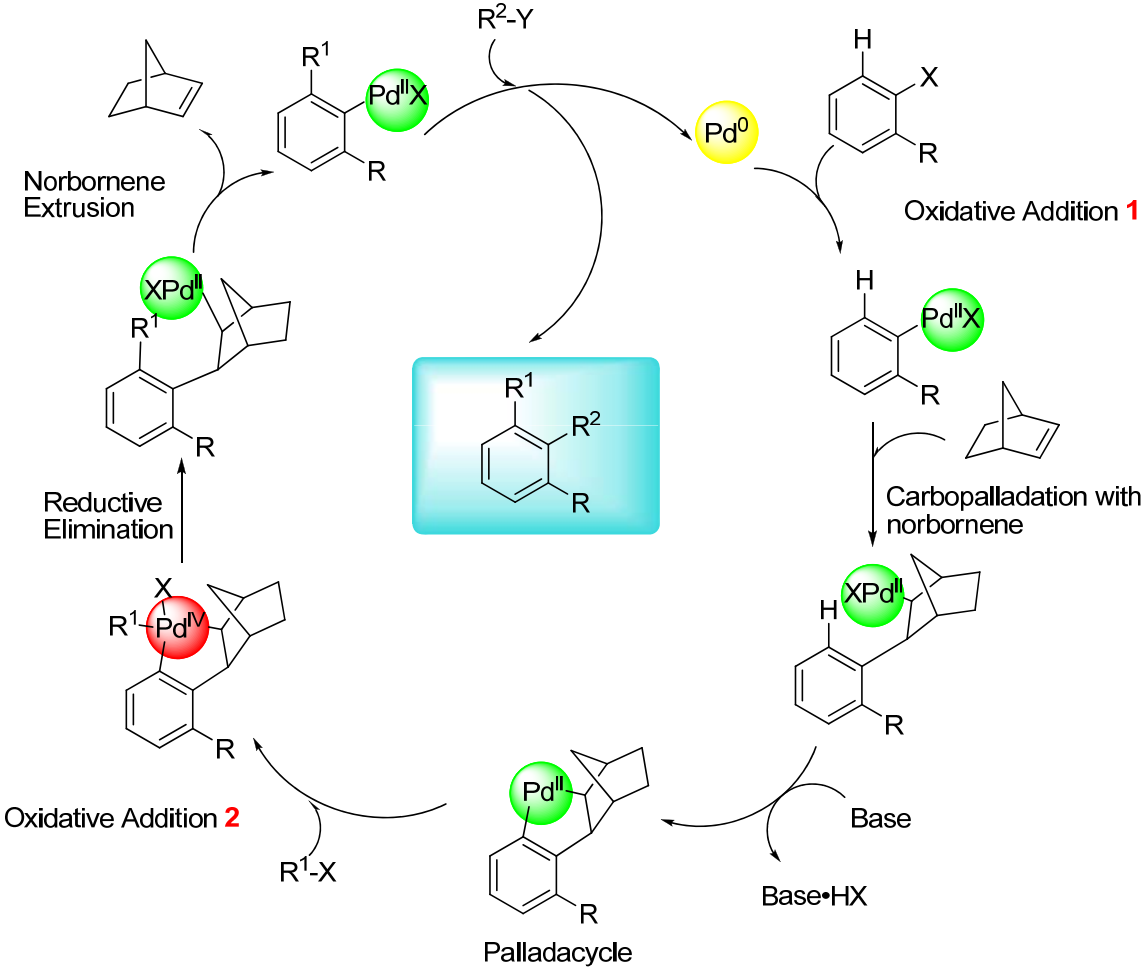
Catellani Reaction

full professor at University of Parma



M. Catellani, *Angrew. Chem. Int. Ed.* **1997**, 36, 119-122.

Mechanism:


R2-Y
Pd0
Oxidative Addition 1
Carbopalladation with norbornene
Base
Base•HX
Palladacycle
R1-X
Oxidative Addition 2
Reductive Elimination
Norbornene Extrusion