

Cephalostatin 1

Enantioselective Synthesis of (+)-Cephalostatin 1

Fortner, K. C.; Kato, D.; Tanaka, T.; Shair M. D. *J. Am. Chem. Soc.* ASAP

Tingting Mo
Wipf Group Current Lit.
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Background

1972, marine worm *Cephalodiscus gilchristi* was collected in Indian Ocean off Southeast Africa

1974, methanol and water extracts of *C. gilchristi* showed activity towards P388 leukemia
ED₅₀ = 0.01-0.001 ng/mL

1988, the active constituent, Cephalostatin 1 was isolated and its structure was elucidated.

The average GI₅₀ (Growth Inhibition of 50%) against the NCI-60 is 1.8 nM.

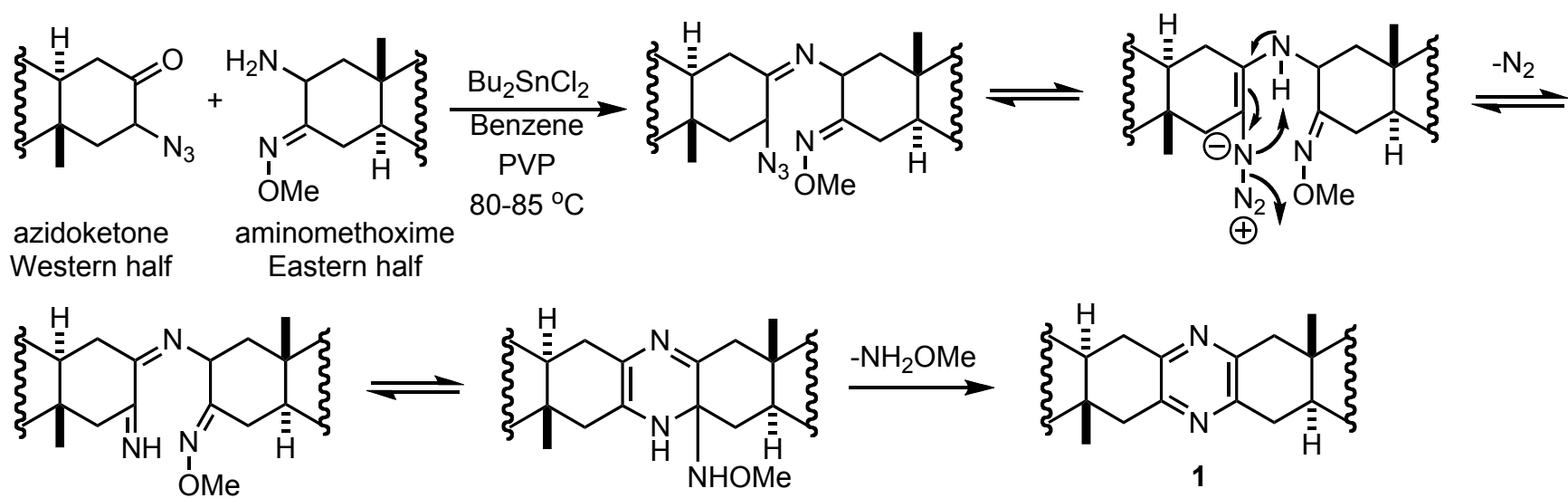
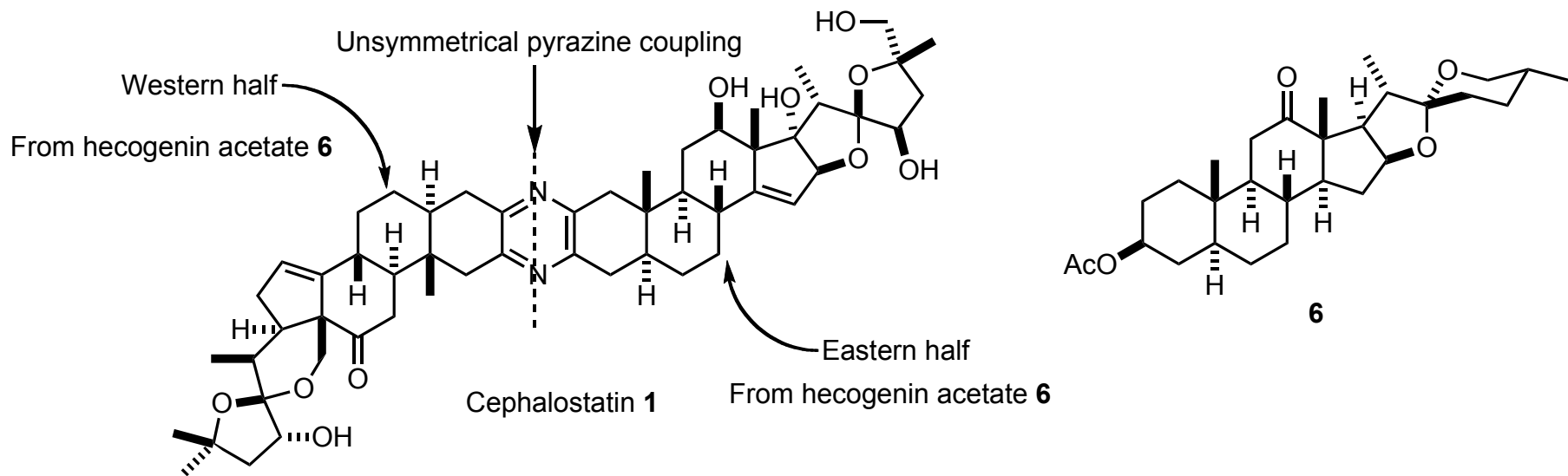
Sufficient amounts of Cephalostatin through synthesis

elucidate its cellular target

determine its efficacy *in vivo* for the treatment of cancer.

Pettit, G. R.; Inoue, M.; Kamano, Y.; Herald, D. L.; Arm, C.; Dufresne, C.; Christie, N. D.; Schmidt, J. M.; Doubek, D. L.; Krupa, T. S. *J. Am. Chem. Soc.* **1988**, *110*, 2006.
NCI-60 data are available at <http://dtp.nci.nih.gov>

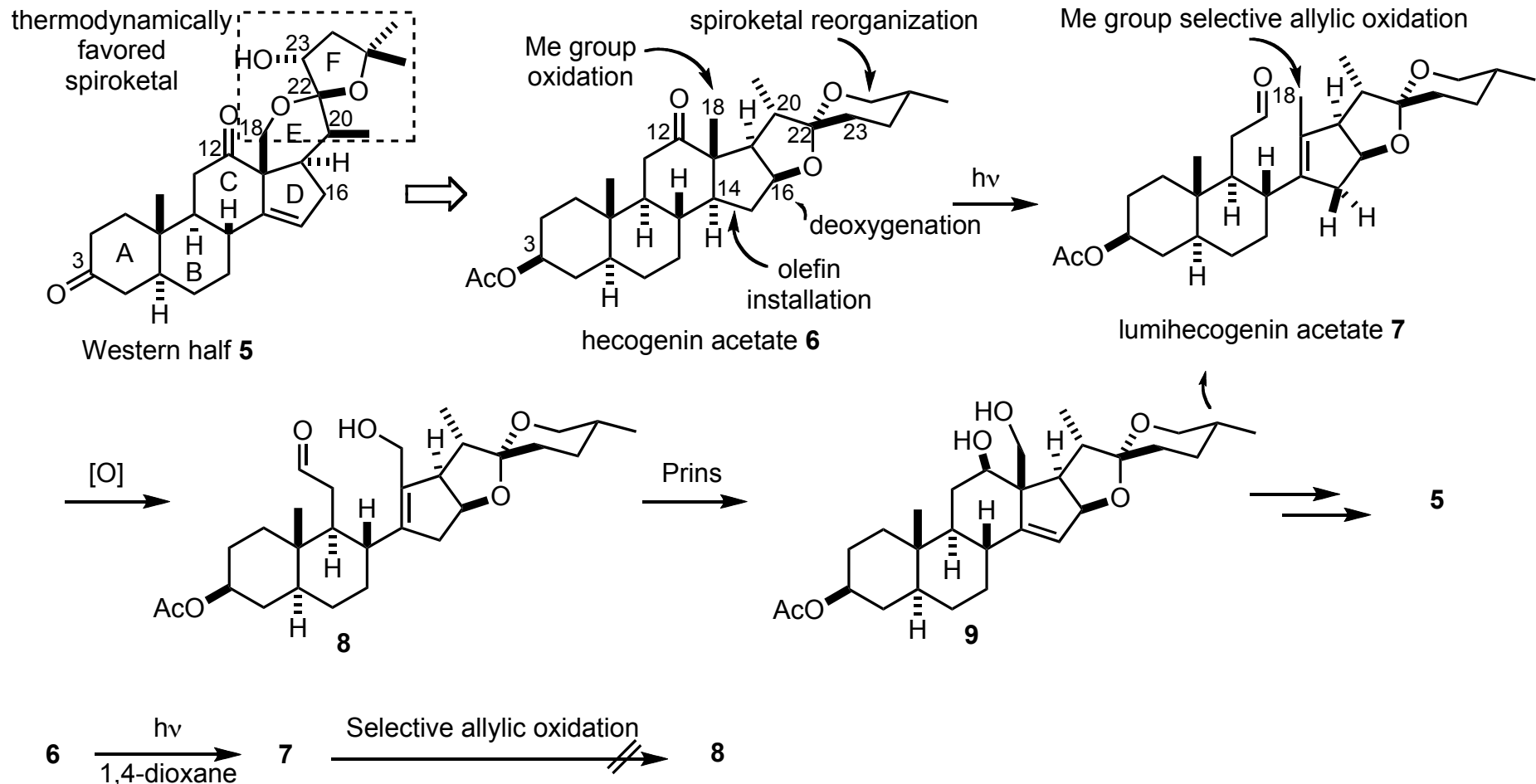
Previous Total Synthesis



LaCour, T. G.; Guo, C.; Bhandaru, S.; Boyd, M. R.; Fuchs, P. L. *J. Am. Chem. Soc.* **1998**, *120*, 692.
 Jeong, J. U.; Sutton, S. C. Kim, S.; Fuchs, P. L. *J. Am. Chem. Soc.* **1995**, *117*, 10157.

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Title paper: Synthesis of Western Half 5



Compound 7 is tetrasubstituted

Four other allylic hydrogens: two methines and one methylene

SeO₂ led to hydroxylation of the methylene

Radical halogenations were poorly regioselective

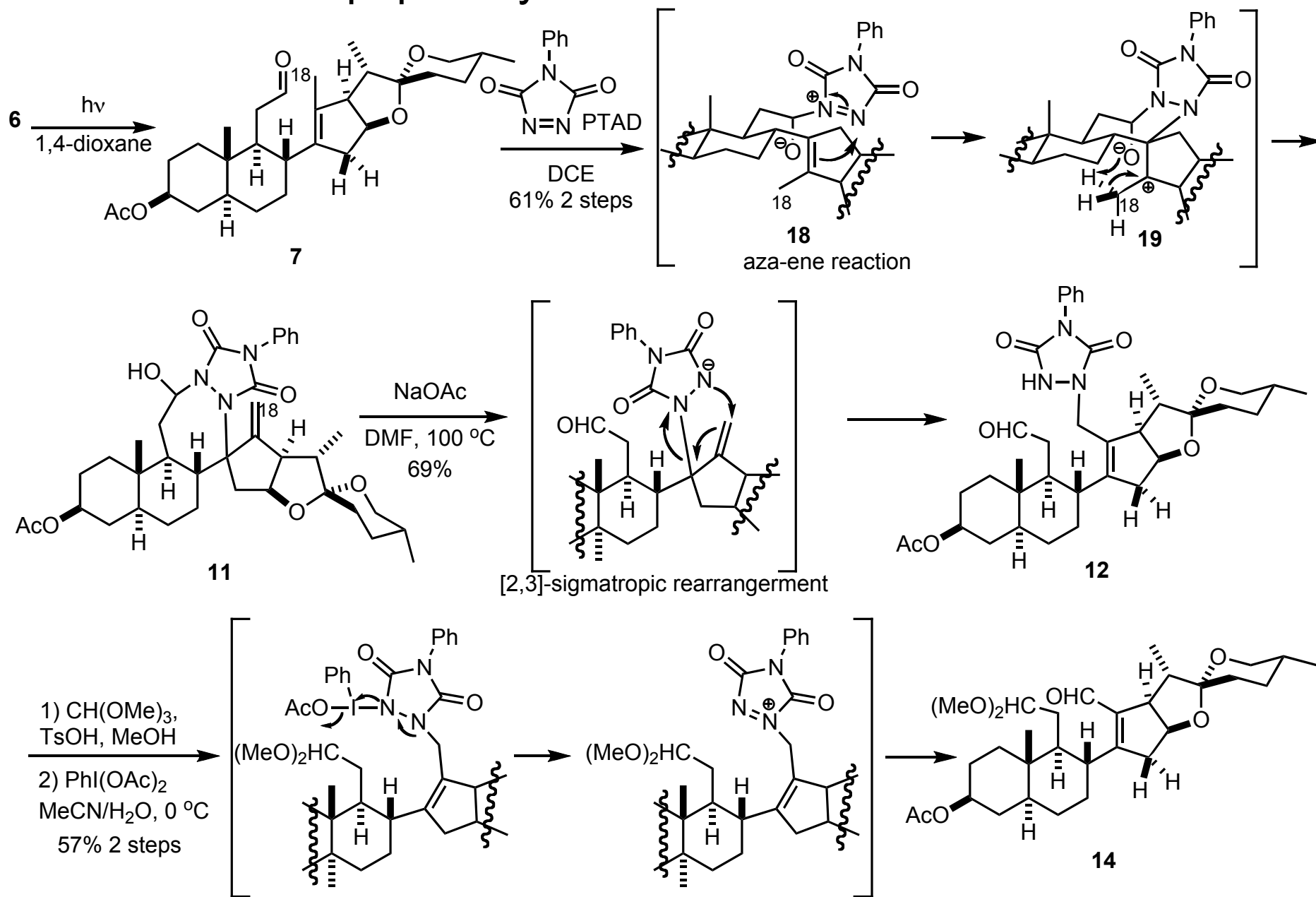
Transition metal-catalyzed allylic oxidation gave no reaction

Fortner, K. C.; Kato, D.; Tanaka, T.; Shair, M. D. *J. Am. Chem. Soc.* ASAP

Bhandaru, S.; Fuchs, P. L. *Tetrahedron Lett.* **1995**, 36, 8351.

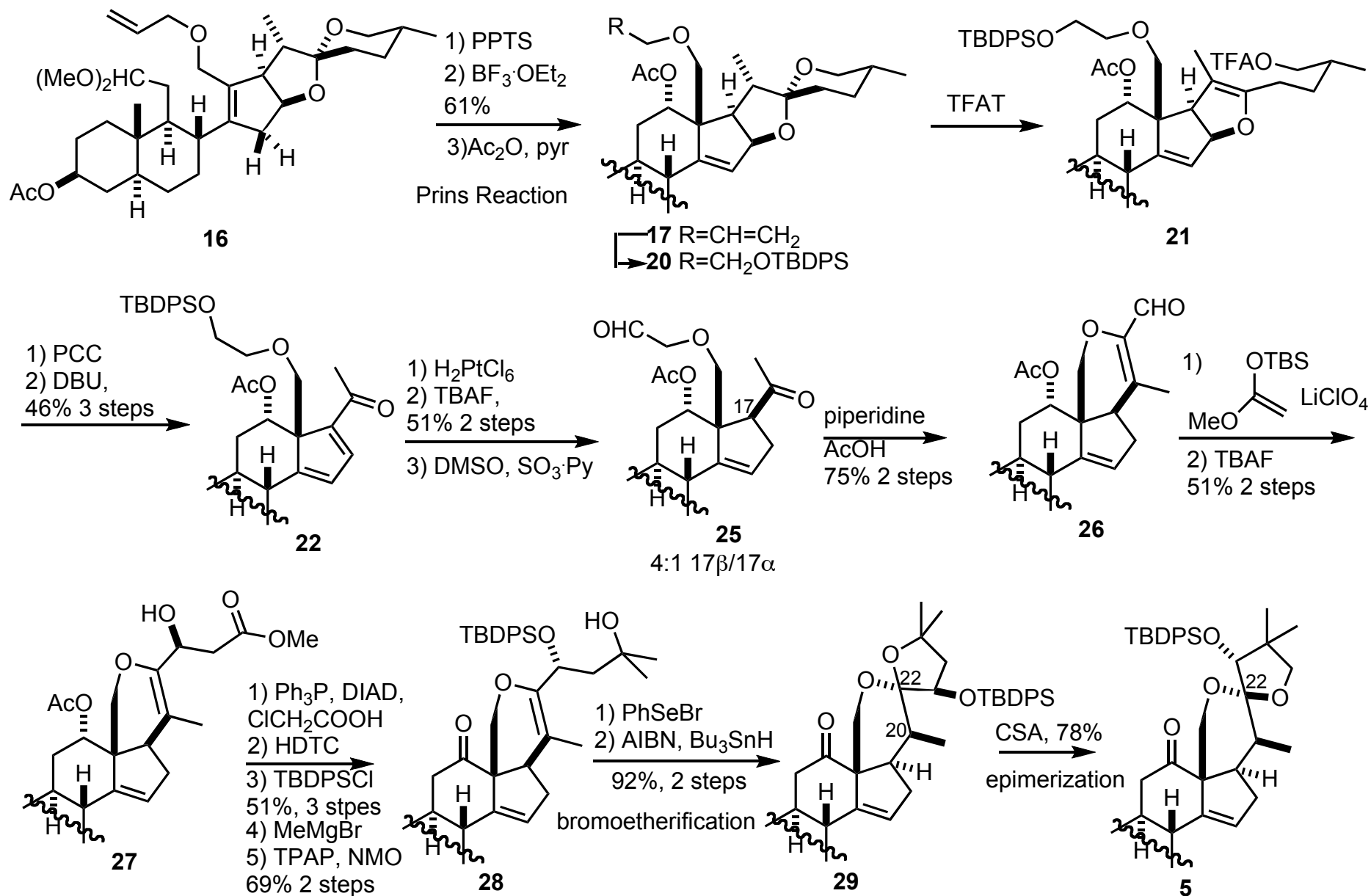
Bladon, P.; McMeekin, W.; Williams, I. A. *J. Am. Chem. Soc.* **1963**, 85, 5727.

6 Title paper: Synthesis of Western Half 5



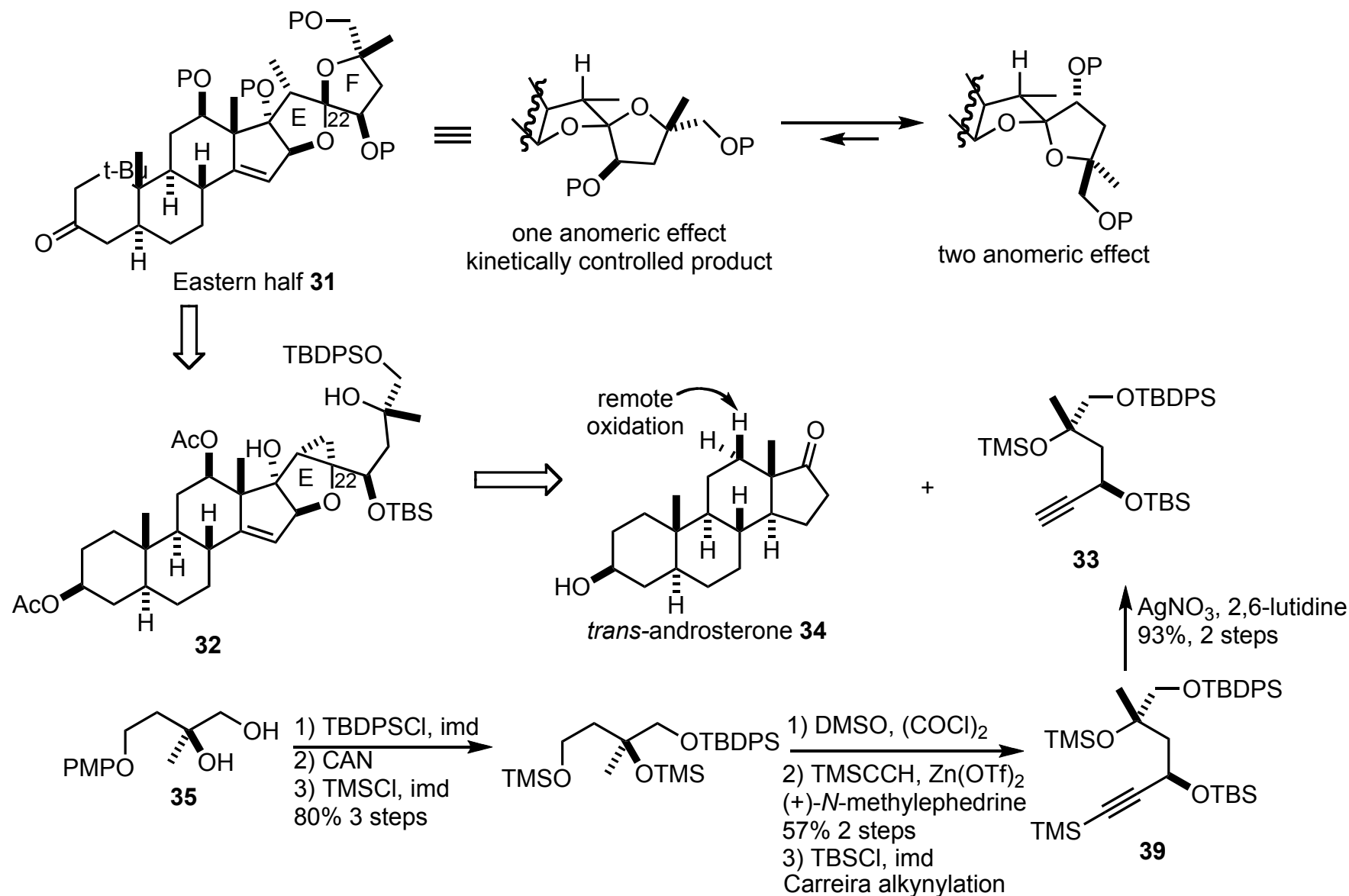
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Title paper: Synthesis of Western Half 5



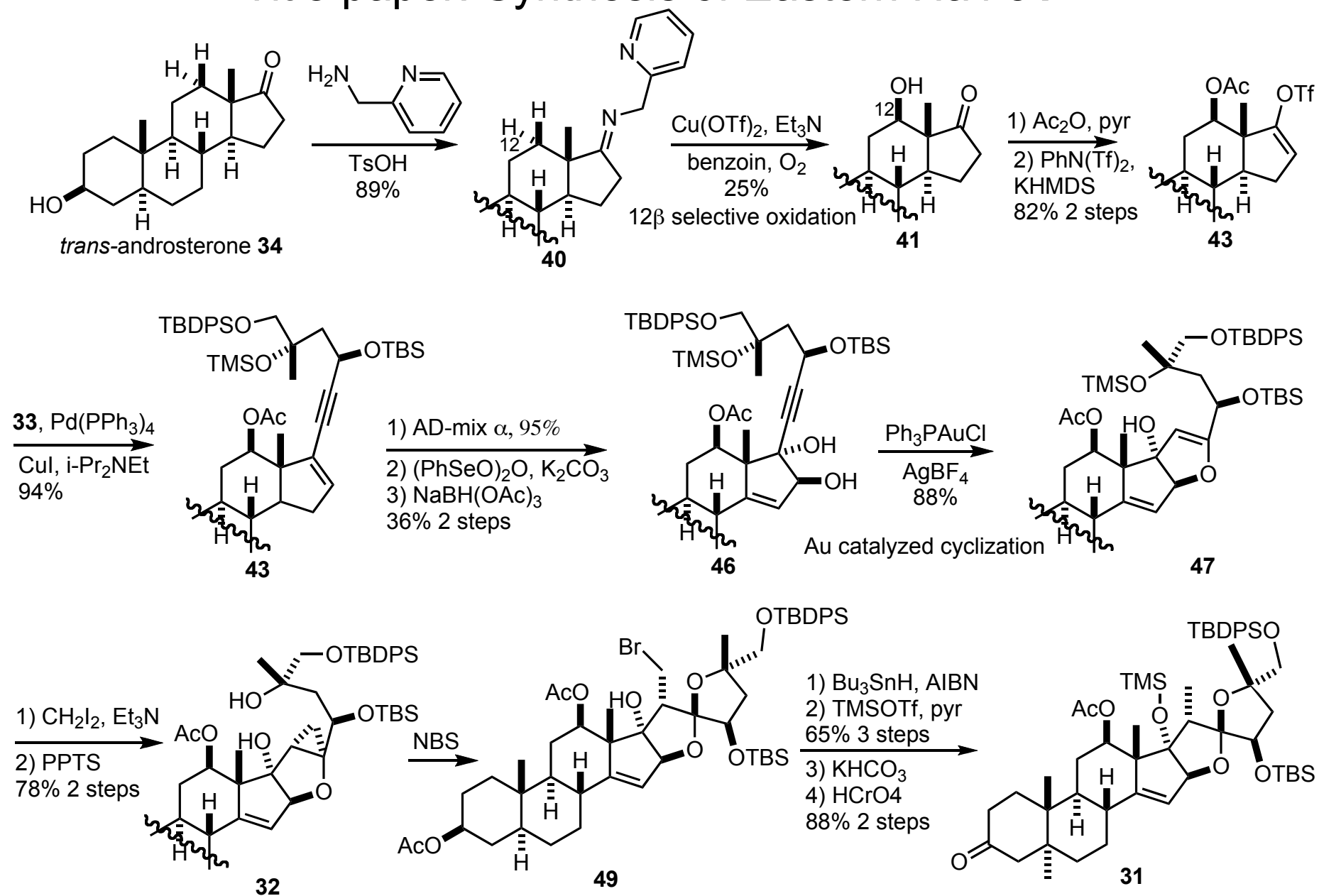
Fortner, K. C.; Kato, D.; Tanaka, T.; Shair M. D. *J. Am. Chem. Soc.* ASAP

Title paper: Synthesis of Eastern Half 31

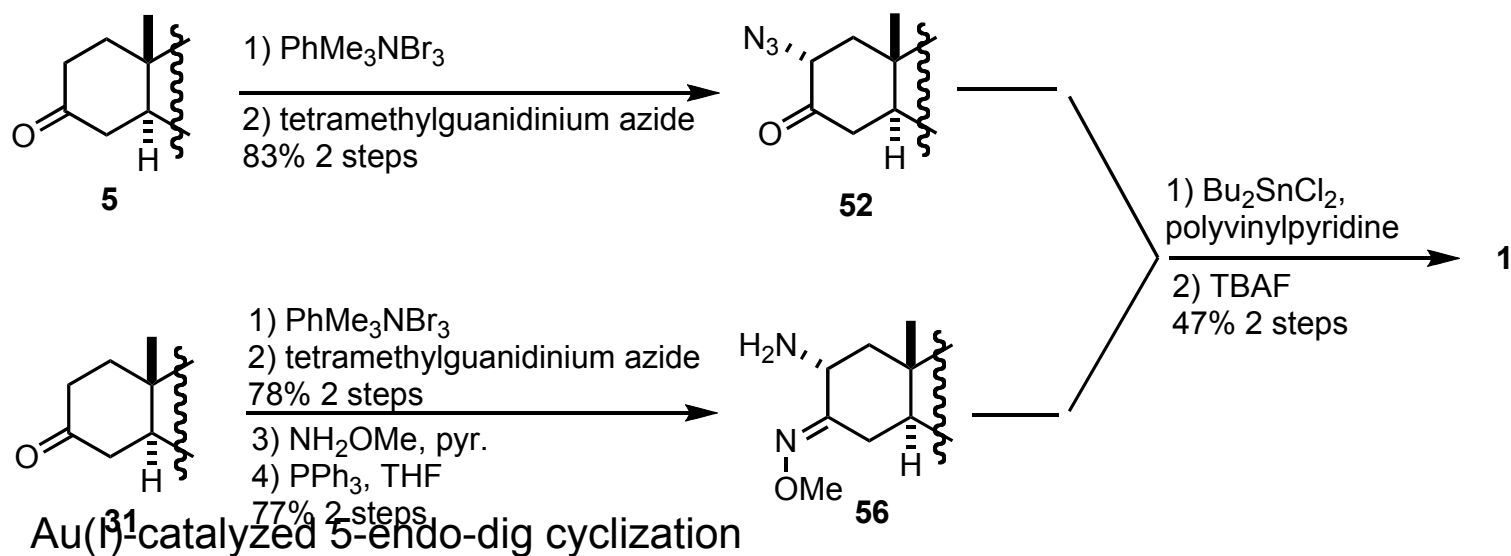


Fortner, K. C.; Kato, D.; Tanaka, T.; Shair M. D. *J. Am. Chem. Soc.* ASAP

Title paper: Synthesis of Eastern Half 31

Fortner, K. C.; Kato, D.; Tanaka, T.; Shair M. D. *J. Am. Chem. Soc.* ASAP

Completion of the synthesis of Cephalostatin 1



A unique methyl group-selective allylic oxidation: