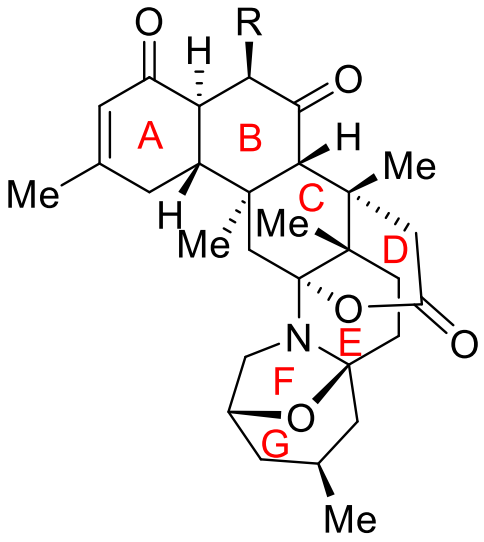
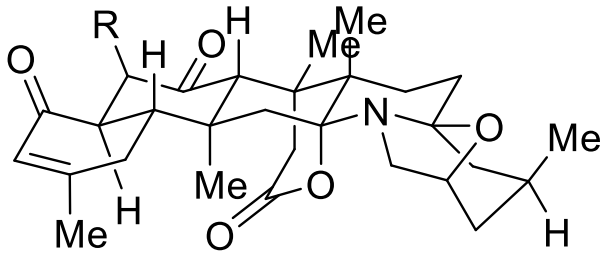
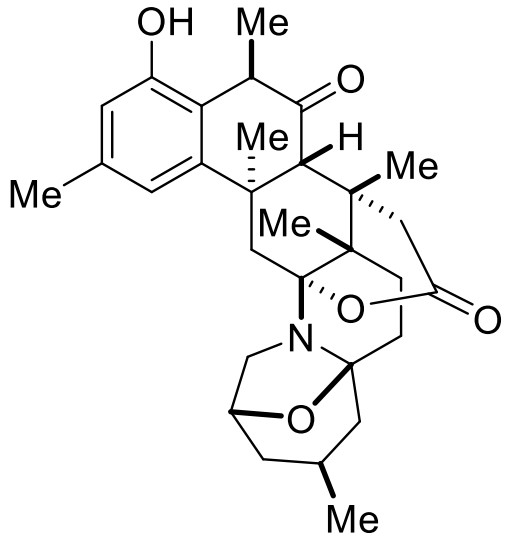
Total Synthesis of the Zoanthamine Alkaloids





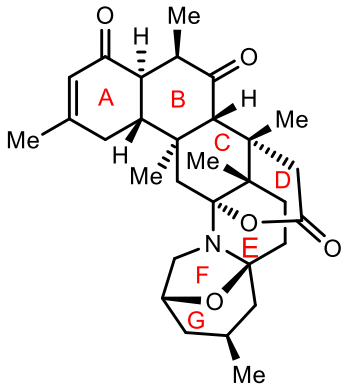
R=Me, Zoanthamine(**1**)
R=H, Noezoanthamine(**2**)
R=CH_2OH, Oxyzoanthamine(**3**)



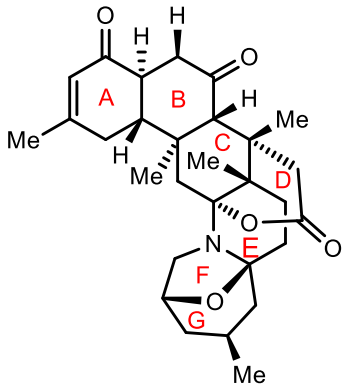
Zoanthenol(**4**)

汇报人：章振宇
时间：2024.05.15

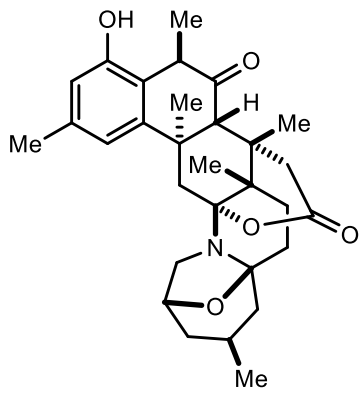
实验室安全问题



Zoanthamine(**1**)



Noezoanthamine(**2**)

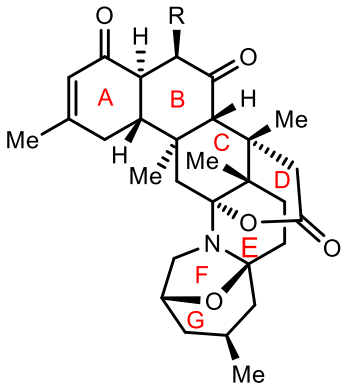


Zoanthenol(**4**)

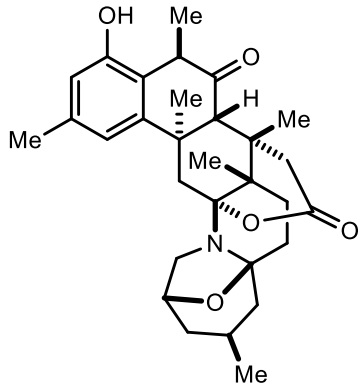
Zoanthamine(**1**)于1984年从印度维沙卡帕特南海岸的Zoanthus物种中发现，是该家族的第一个分离的生物碱。该物质可以抑制卵巢切除小鼠的骨重量和强度的损失，被认为是抗骨质疏松药物的候选物。除了强有力的镇痛作用外，还表现出对佛波醇肉豆蔻酸酯诱导的炎症的有效抑制活性

Norzoanthamine(**2**)于1995年分离，可以抑制卵巢切除小鼠的骨重量和强度的损失，被认为是抗骨质疏松药物的有希望的候选物。最近，除对人血小板聚集的强效抗血小板活性外，已证明去甲虫胺衍生物可强烈抑制P-388鼠白血病细胞系的生长

Zoanthenol(4)于1999年分离，是该家族生物碱中唯一含有芳环的成员



R=Me, Zoanthamine(**1**)
R=H, Noezoanthamine(**2**)
R=CH_2OH, Oxyzoanthamine(**3**)

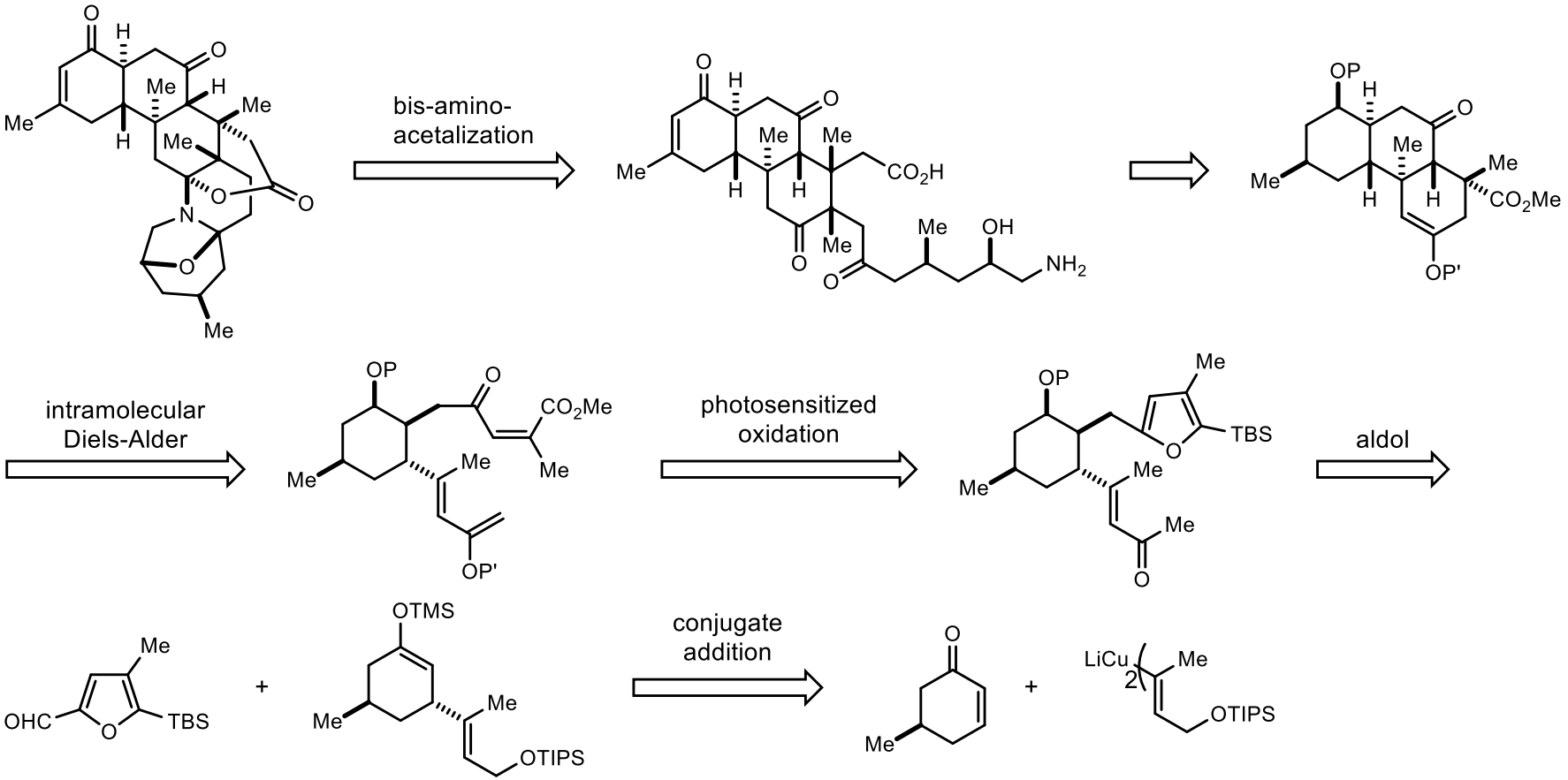


Zoanthenol(**4**)

Synthetic challenges:
• a topographically intricate heptacyclic skeleton bearing the trans-anti-trans-fused perhydrophenanthrene A-B-C ring, the bridged δ-lactone D ring, and the bis-amino acetal E-F-G ring
• ten stereocenters, among them seven contiguous stereogenic centers located on the B and C rings, which also include three quaternary centers
•densely functionalized and highly oxidized skeleton with two ketones, one lactone and bis-amino acetal.

♦**Miyashita课题组的工作**（*science,* **2004**, *305*, 495–499.）

♦**Total Synthesis of Norzoanthamine**



♦**Miyashita课题组的工作**（*science,* **2004**, *305*, 495–499.）

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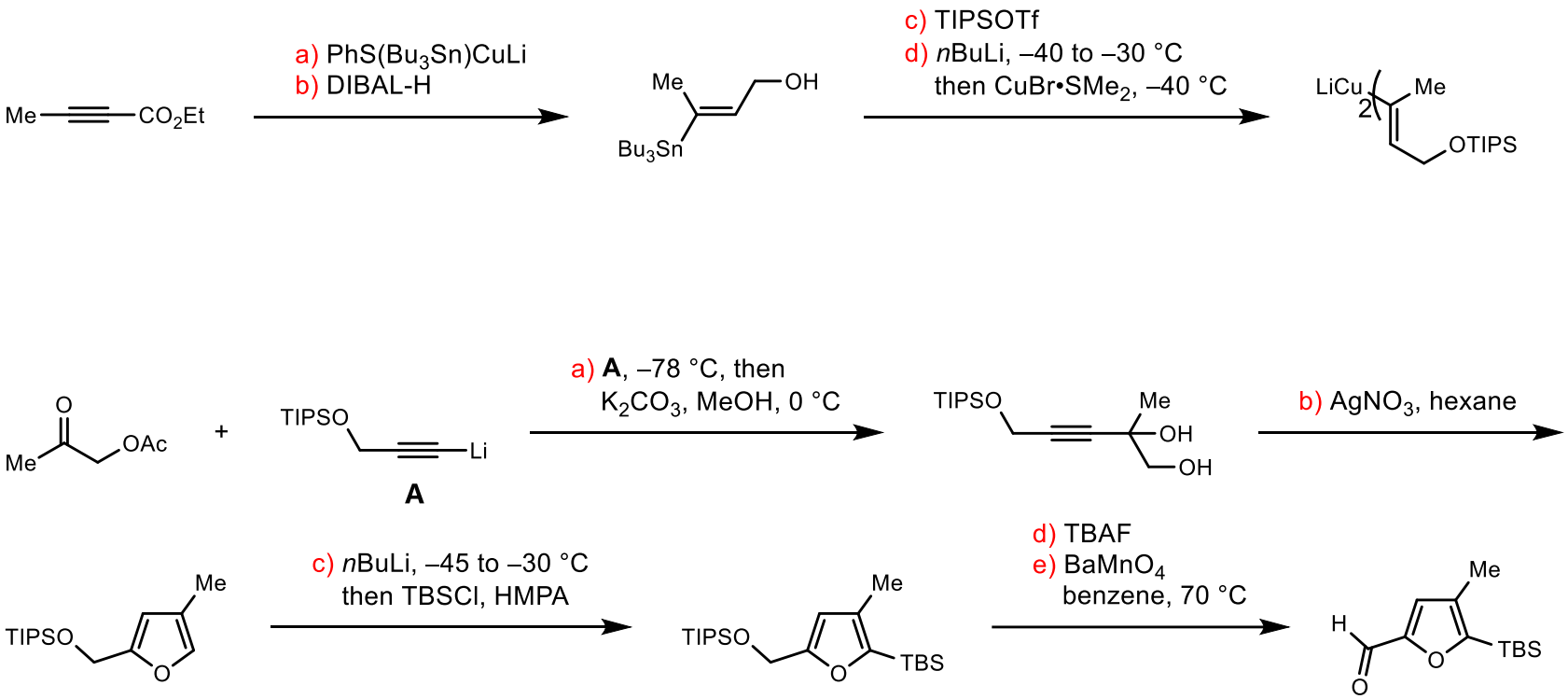
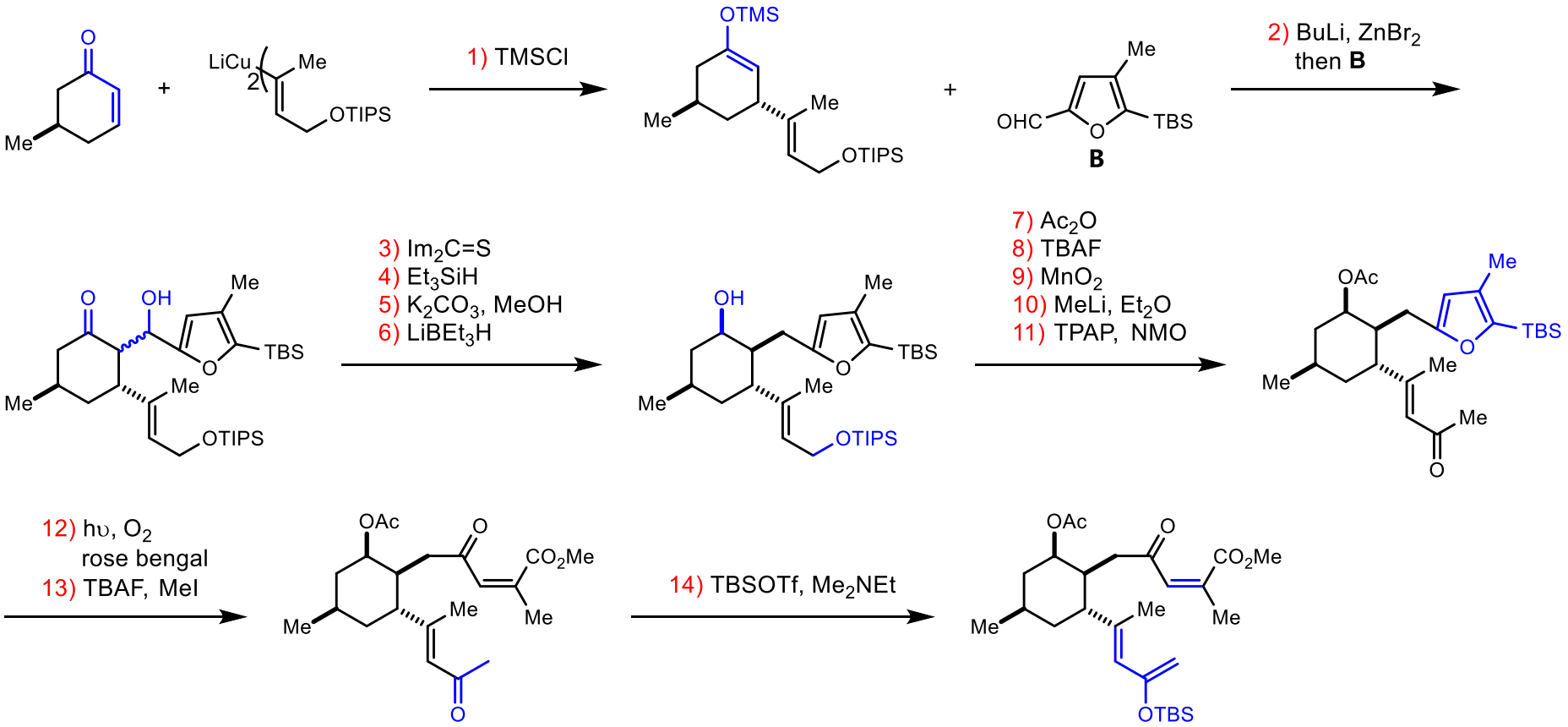


♦**Miyashita课题组的工作**（*science*, **2004**, *305*, 495–499.）

♦**Total Synthesis of Norzoanthamine**



♦**Miyashita课题组的工作**（*science,* **2004**, *305*, 495–499.）

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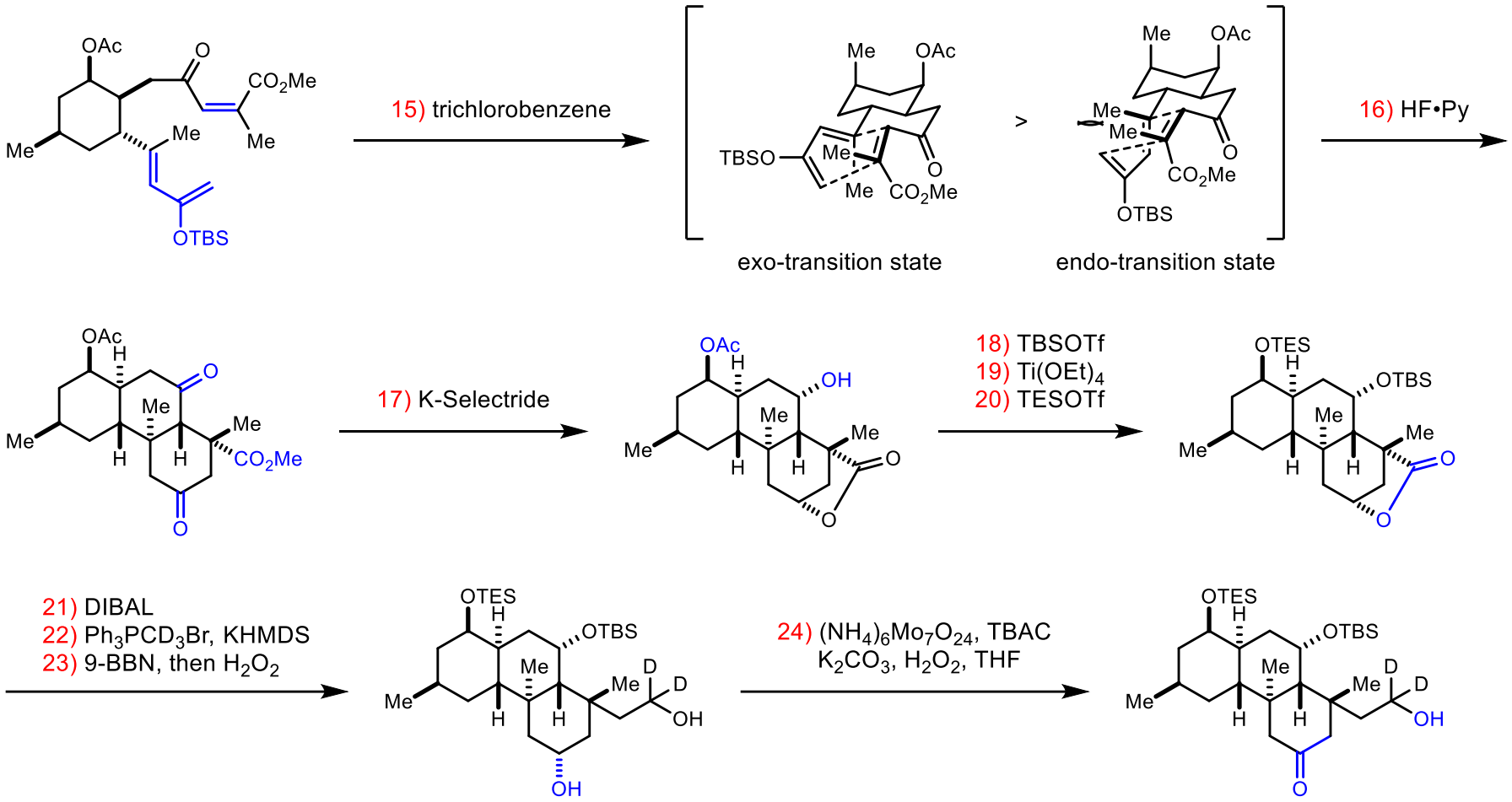
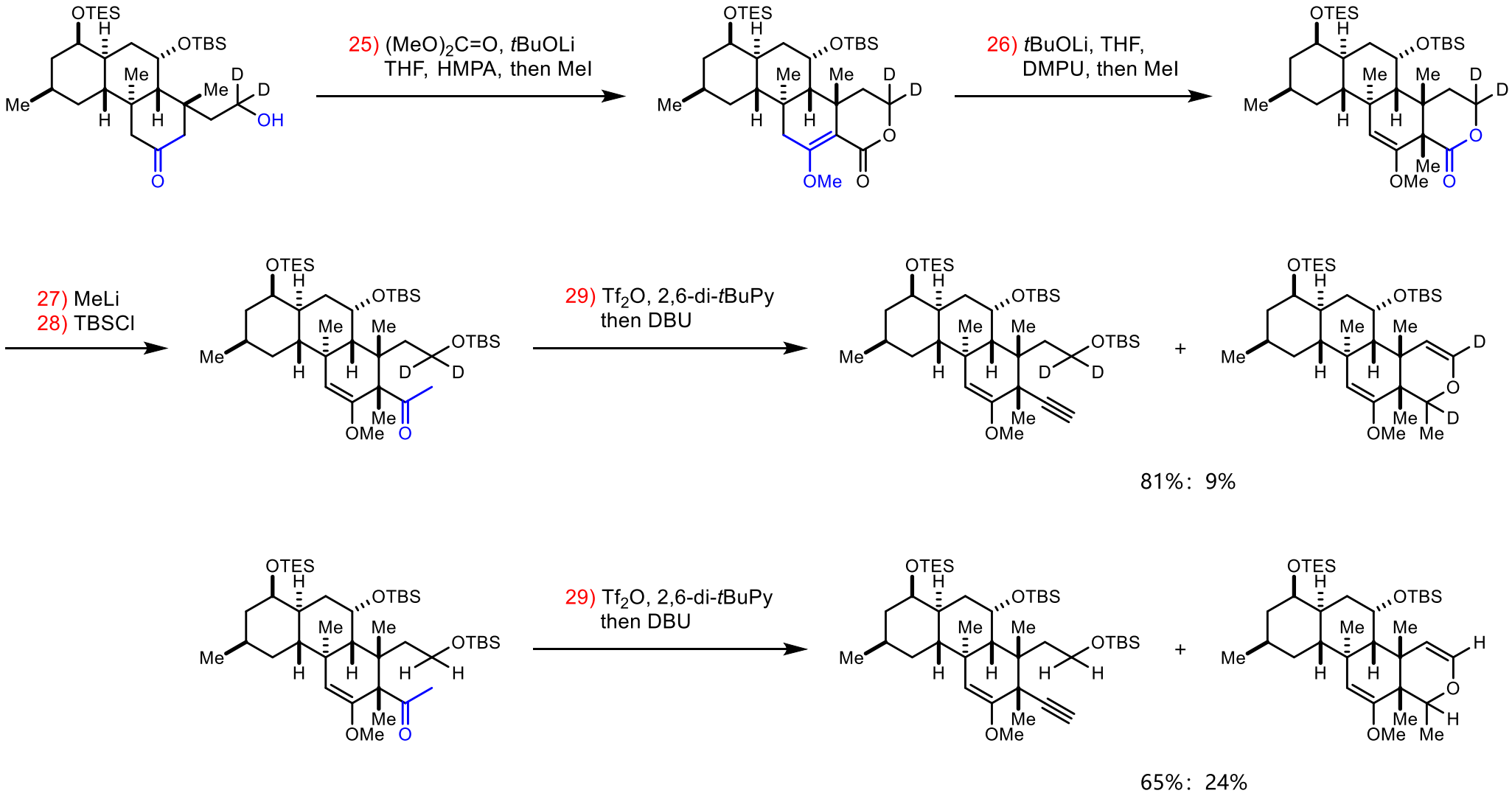


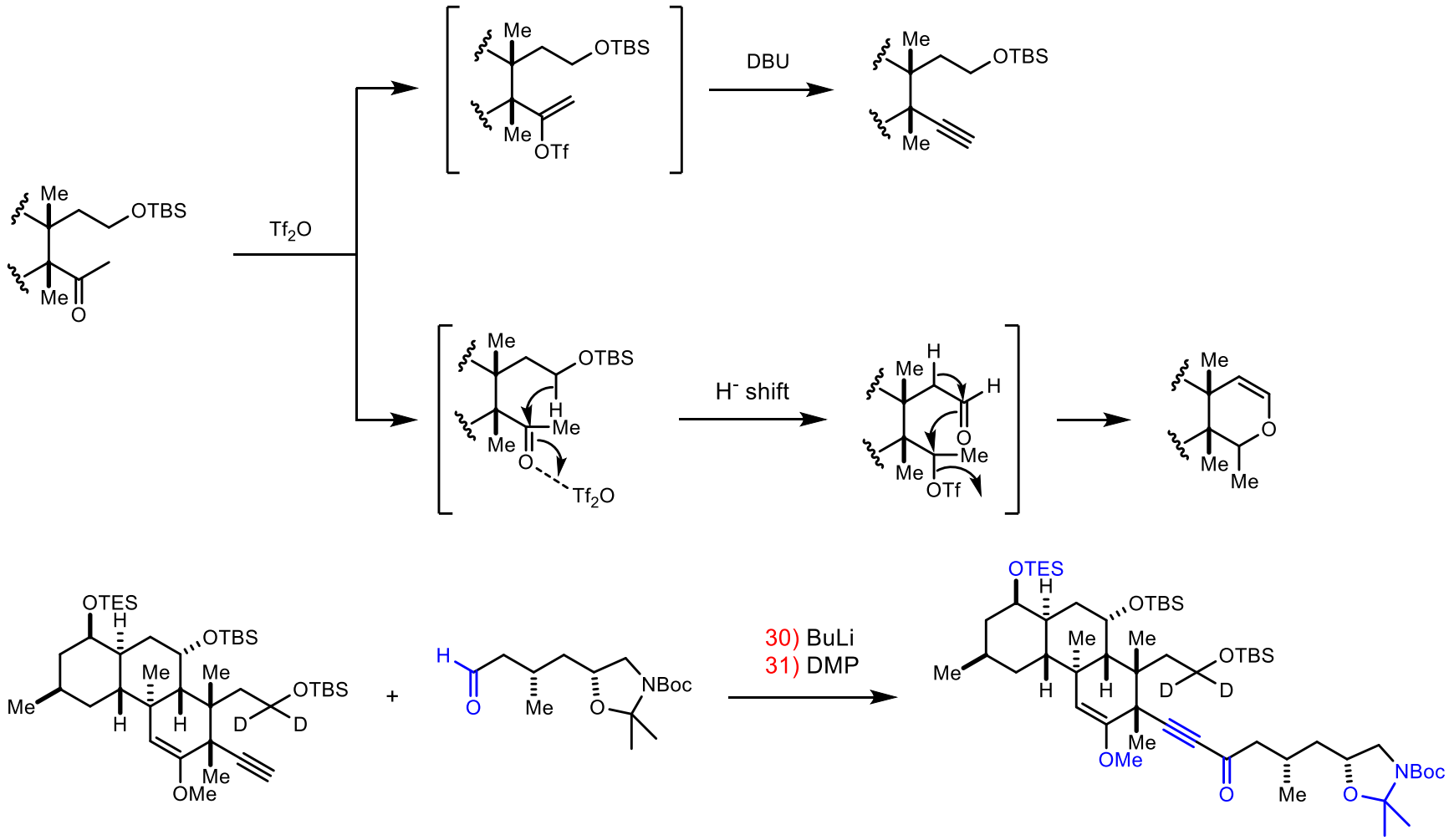
♦**Miyashita课题组的工作**（*science,* **2004**, *305*, 495–499.）

♦**Total Synthesis of Norzoanthamine**



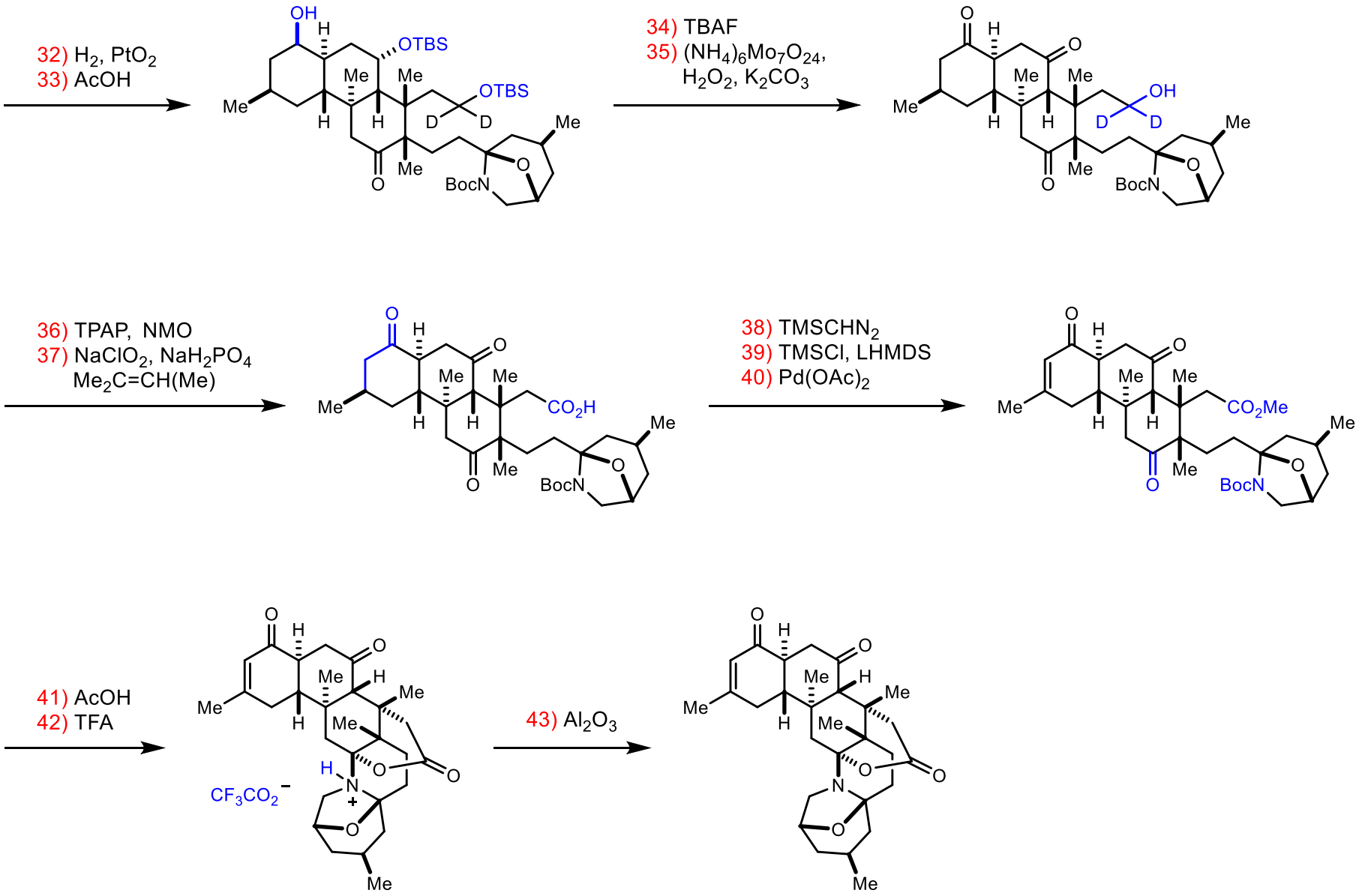
♦**Miyashita课题组的工作**（*science*, **2004**, *305*, 495–499.）

♦**Total Synthesis of Norzoanthamine**



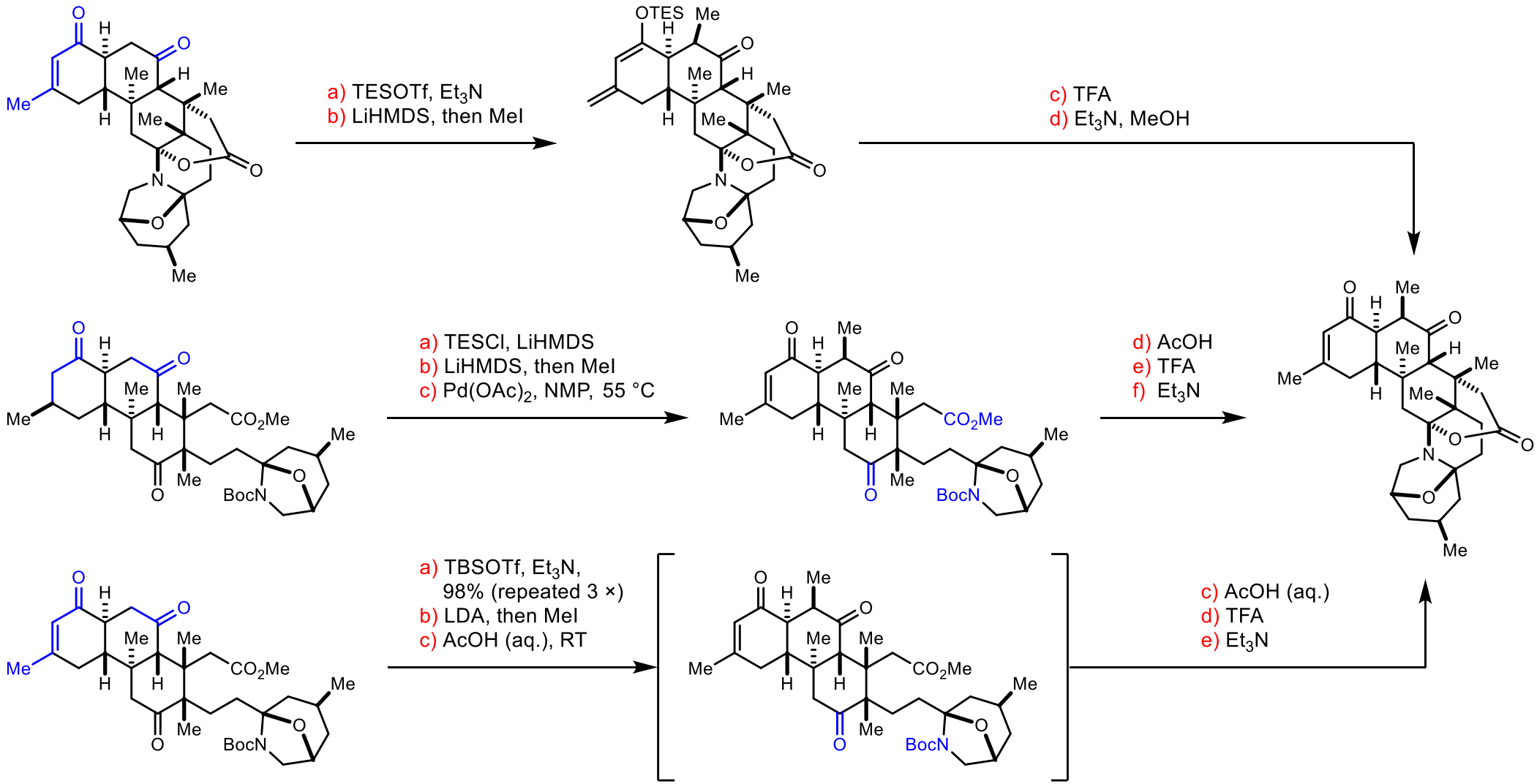
♦**Miyashita课题组的工作**（*science,* **2004**, *305*, 495–499.)

♦**Total Synthesis of Norzoanthamine**



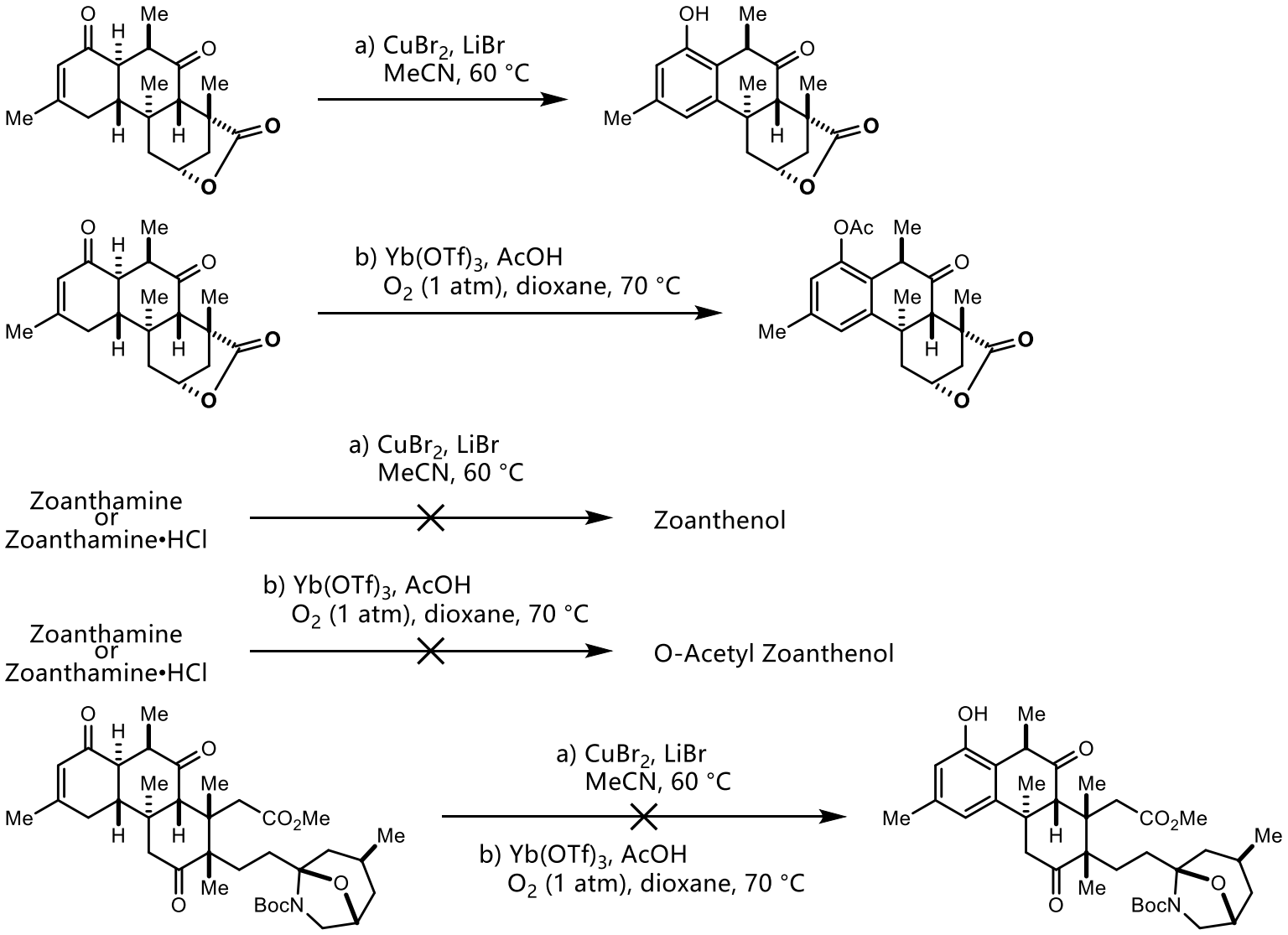
♦**Miyashita课题组的工作**（*Chem. Eur. J.*, **2009**, *15*, 6626–6644.）

♦**Synthetic Studies of the Zoanthamine Alkaloids: The Total Syntheses of Norzoanthamine and Zoanthamine**



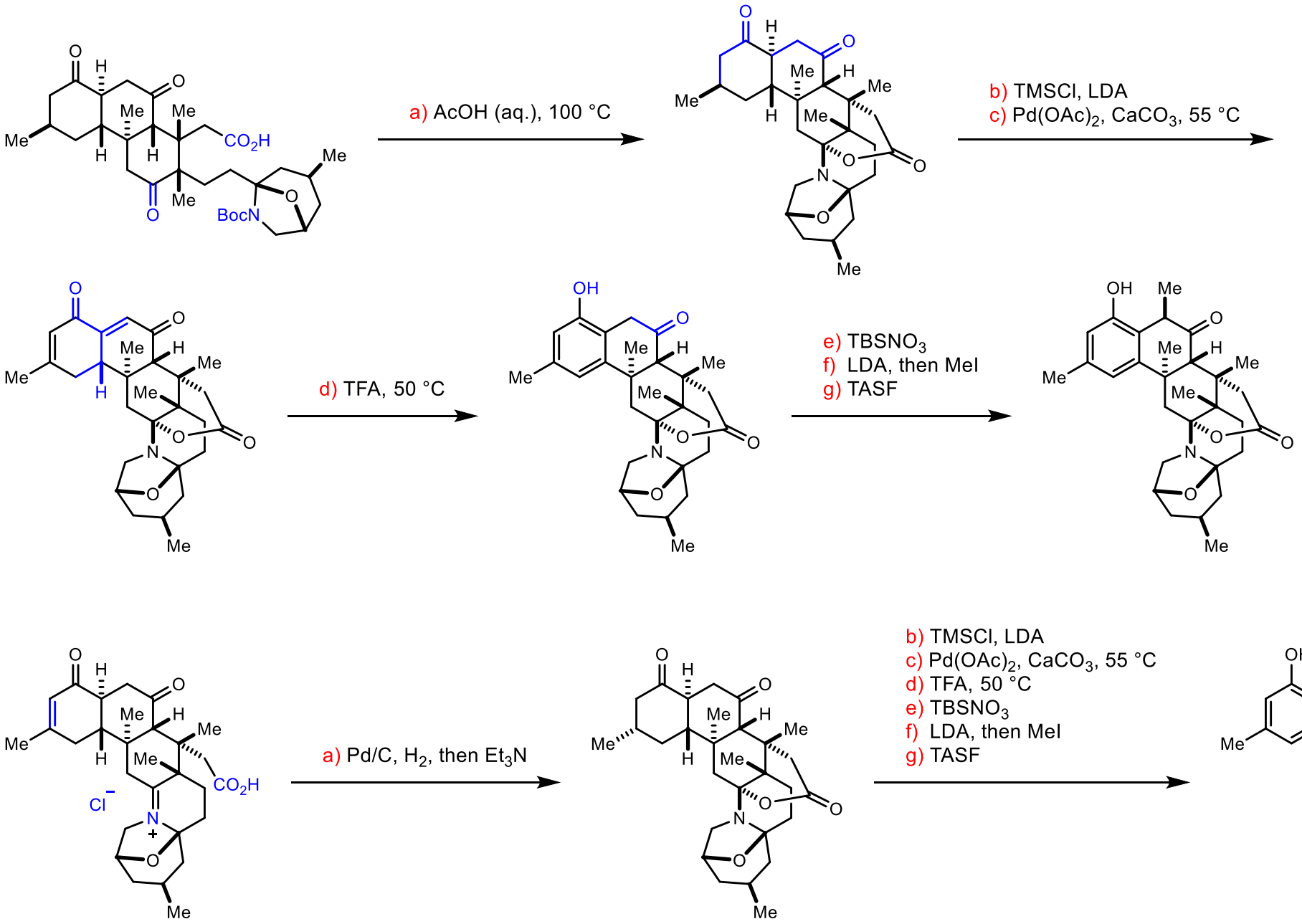
♦**Miyashita课题组的工作**（*Angew. Chem. Int. Ed.*, **2009**, *48*, 8905–8909.）

♦**Total Synthesis of Zoanthenol**



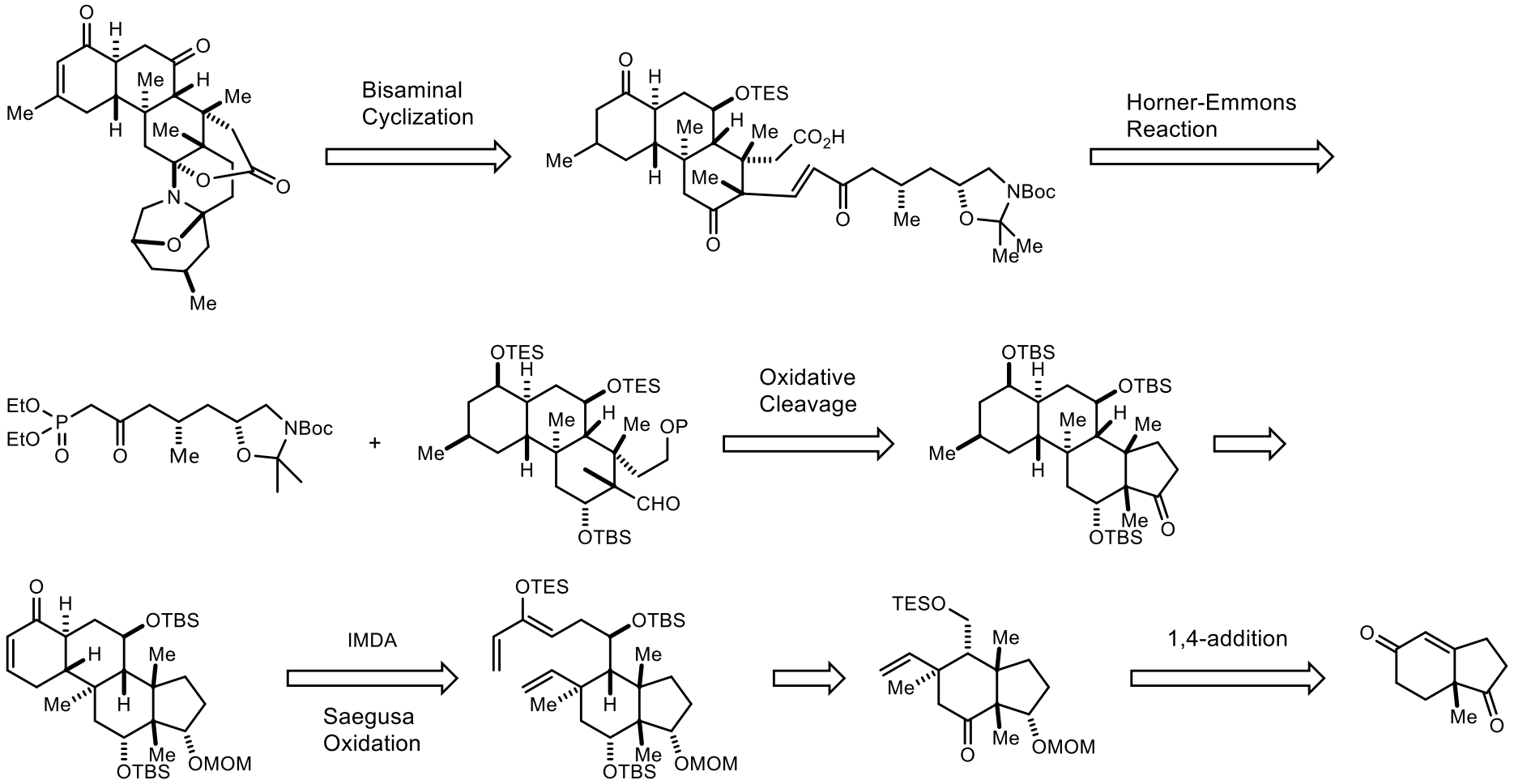
♦**Miyashita课题组的工作**（*Angew. Chem. Int. Ed.*, **2009**, *48*, 8905–8909.)

♦**Total Synthesis of Zoanthenol**



♦**Kobayashi课题组的工作**（*Angew. Chem. Int. Ed.*, **2009**, *48*, 1400–1403.）

♦**Synthetic Study of (–)-Norzoanthamine: Construction of the ABC Ring Moiety**



♦**Kobayashi课题组的工作**（*Angew. Chem. Int. Ed.*, **2009**, *48*, 1400–1403.)

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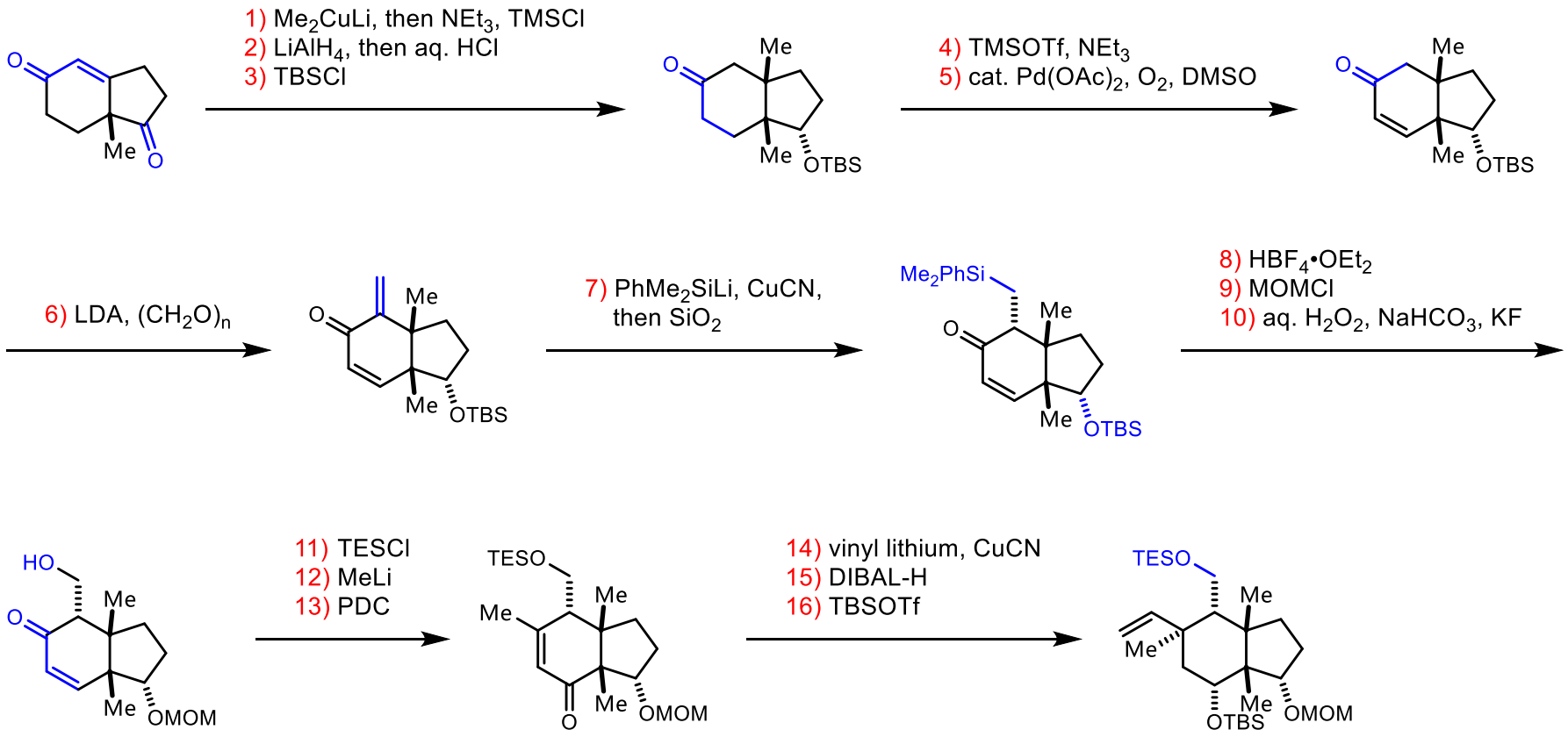

♦**Kobayashi课题组的工作**（*Angew. Chem. Int. Ed.*, **2009**, *48*, 1400–1403.）

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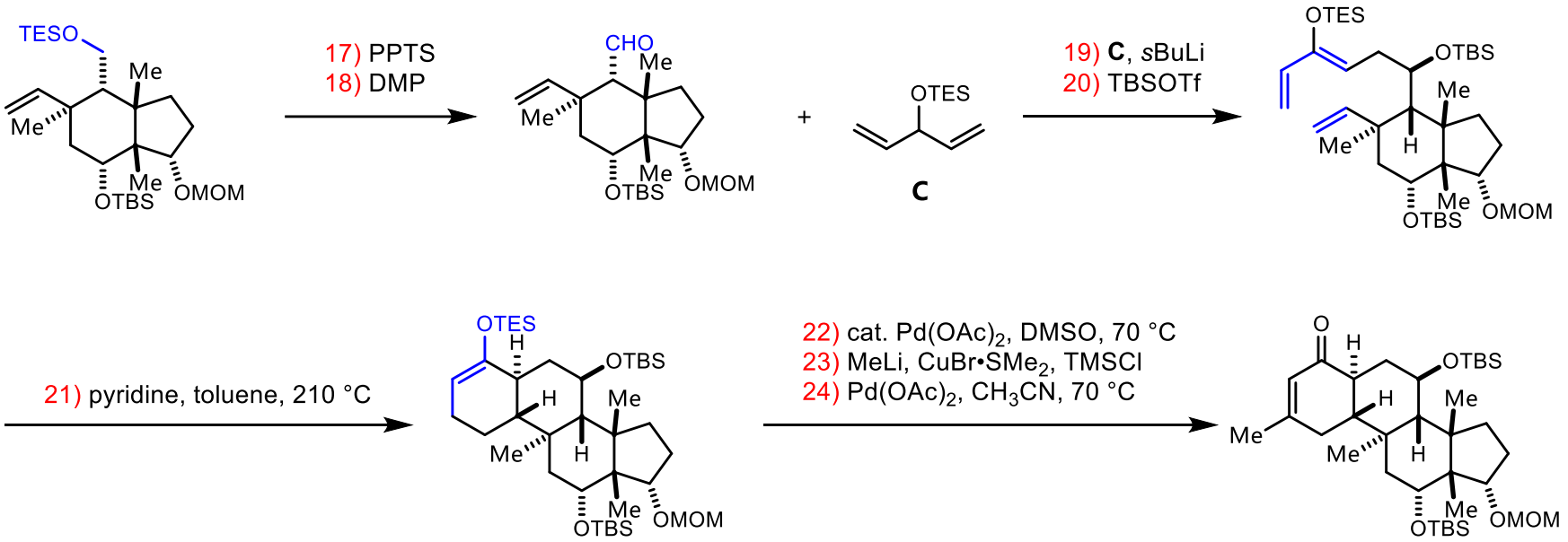

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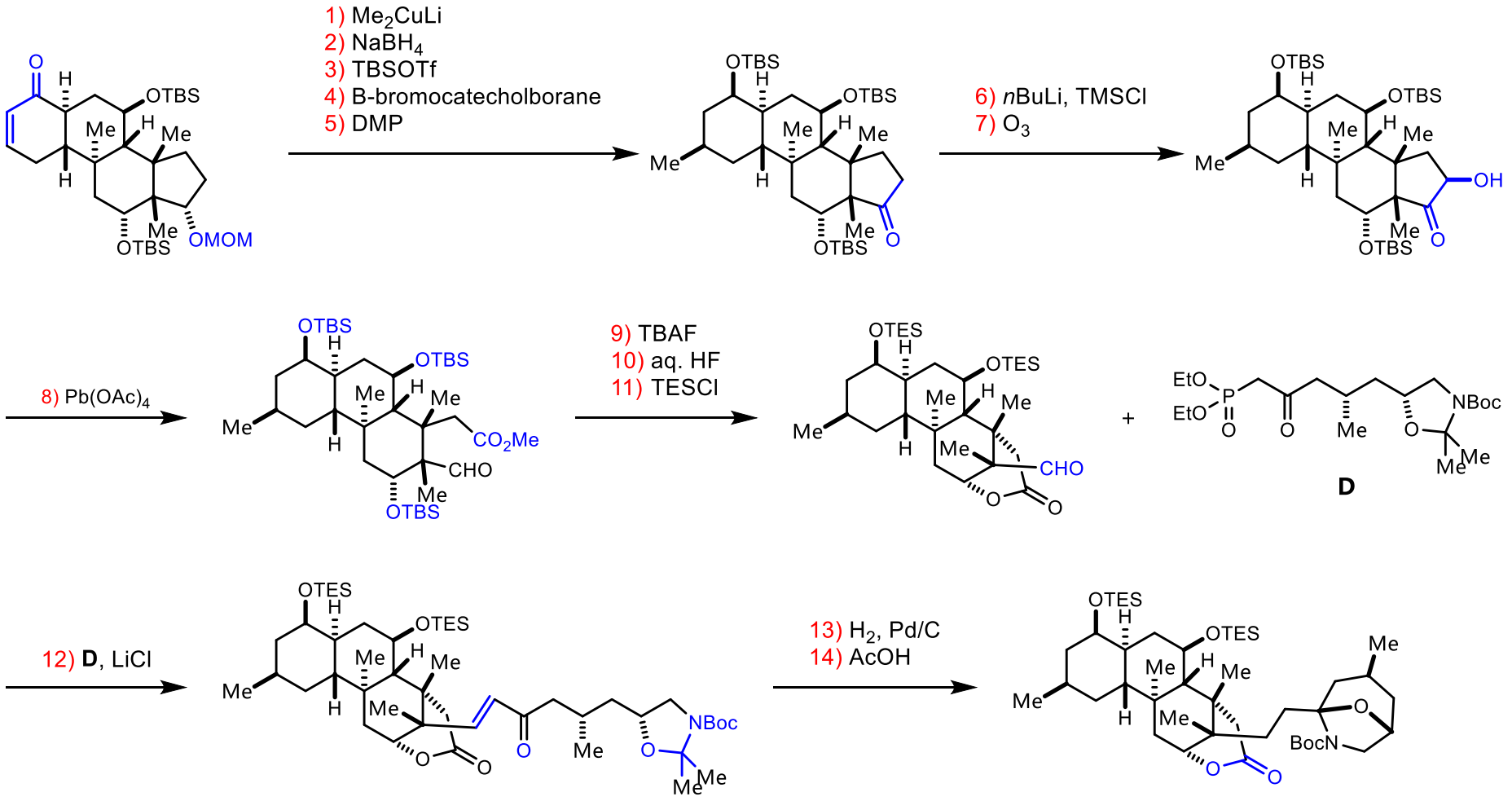
♦**Total Synthesis of （–）-Norzoanthamine**



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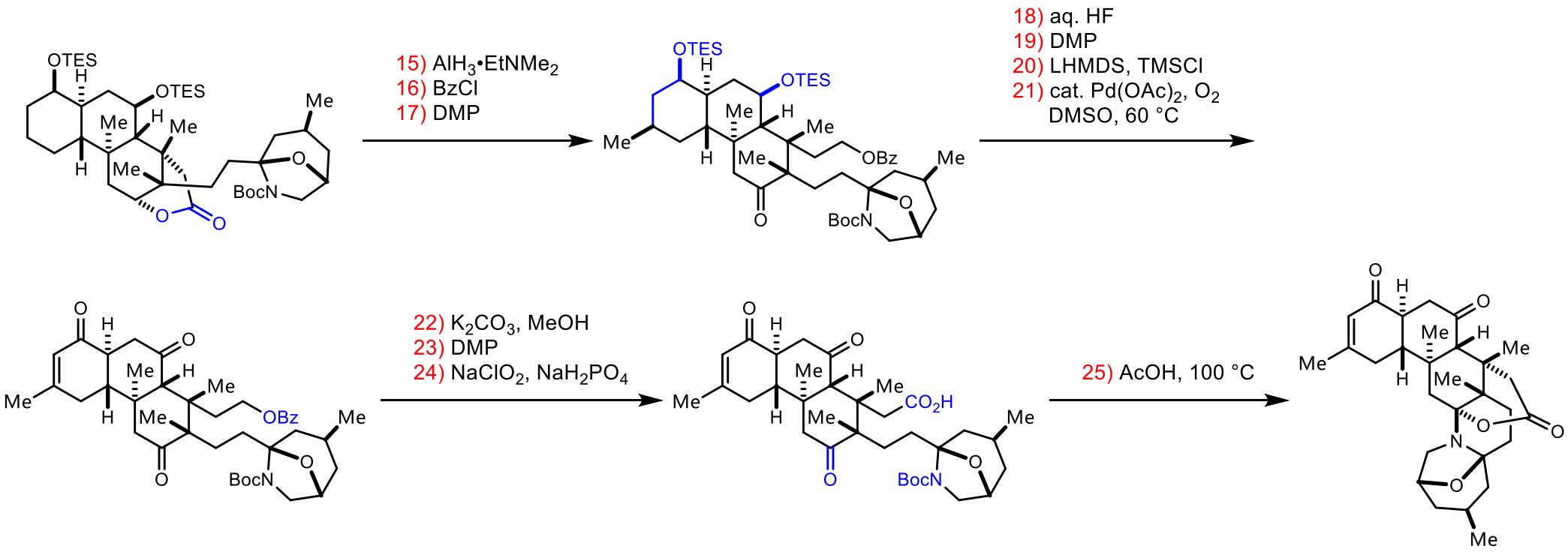
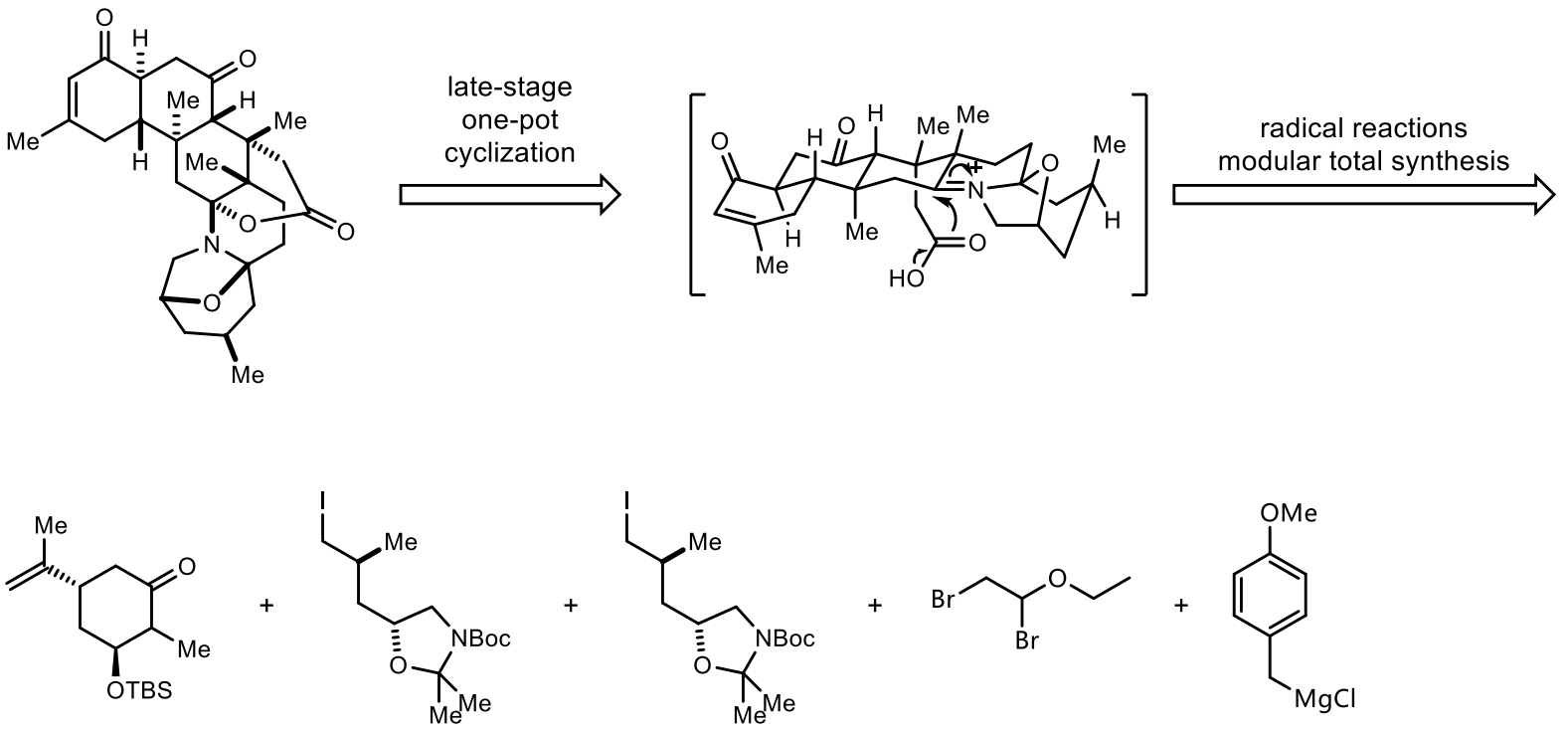
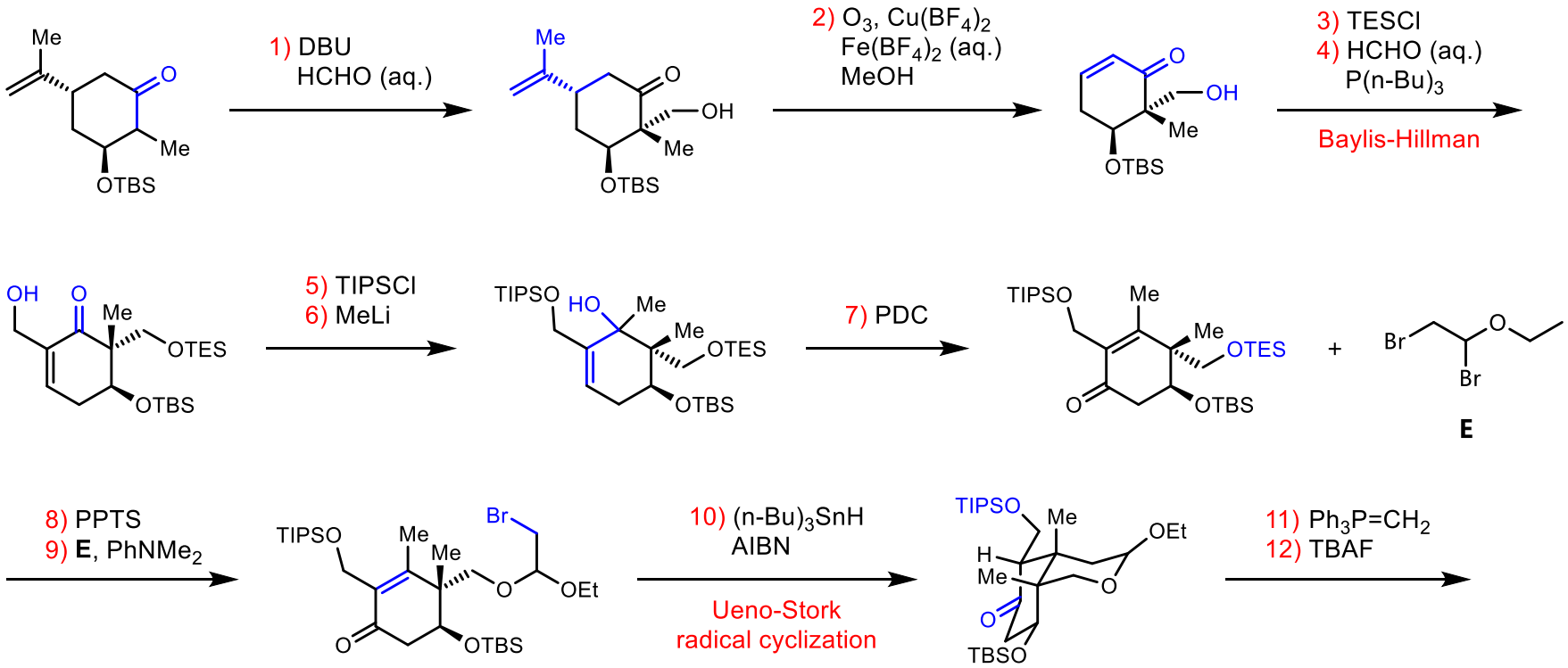


♦**Gao Shuanhu课题组的工作**（*Angew. Chem. Int. Ed.*, **2021**, *60*, 12807–12812.)
♦**Asymmetric Total Synthesis of Norzoanthamine**



♦**Gao Shuanhu课题组的工作**（*Angew. Chem. Int. Ed.*, **2021**, *60*, 12807–12812.)

♦**Asymmetric Total Synthesis of Norzoanthamine**



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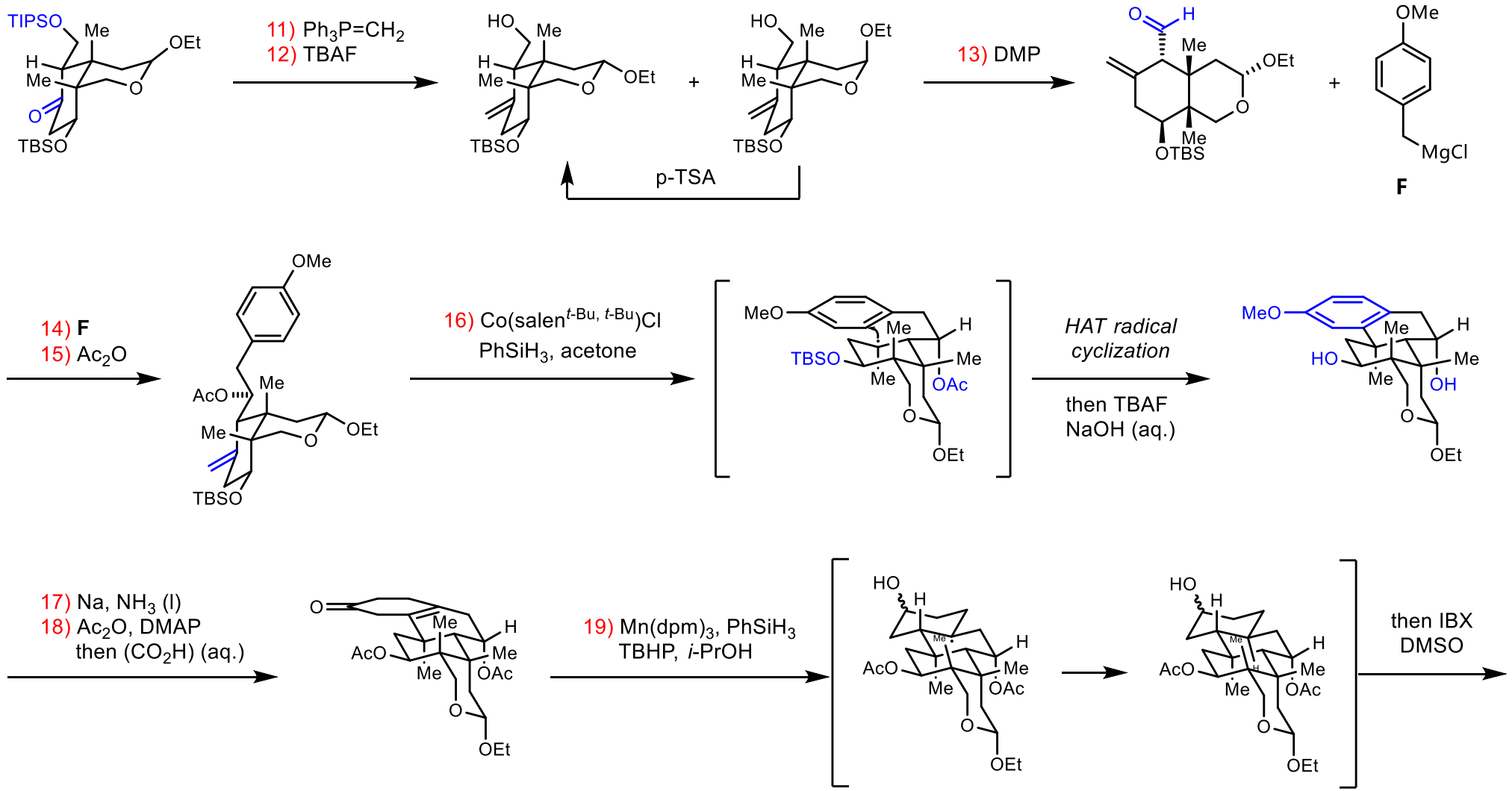

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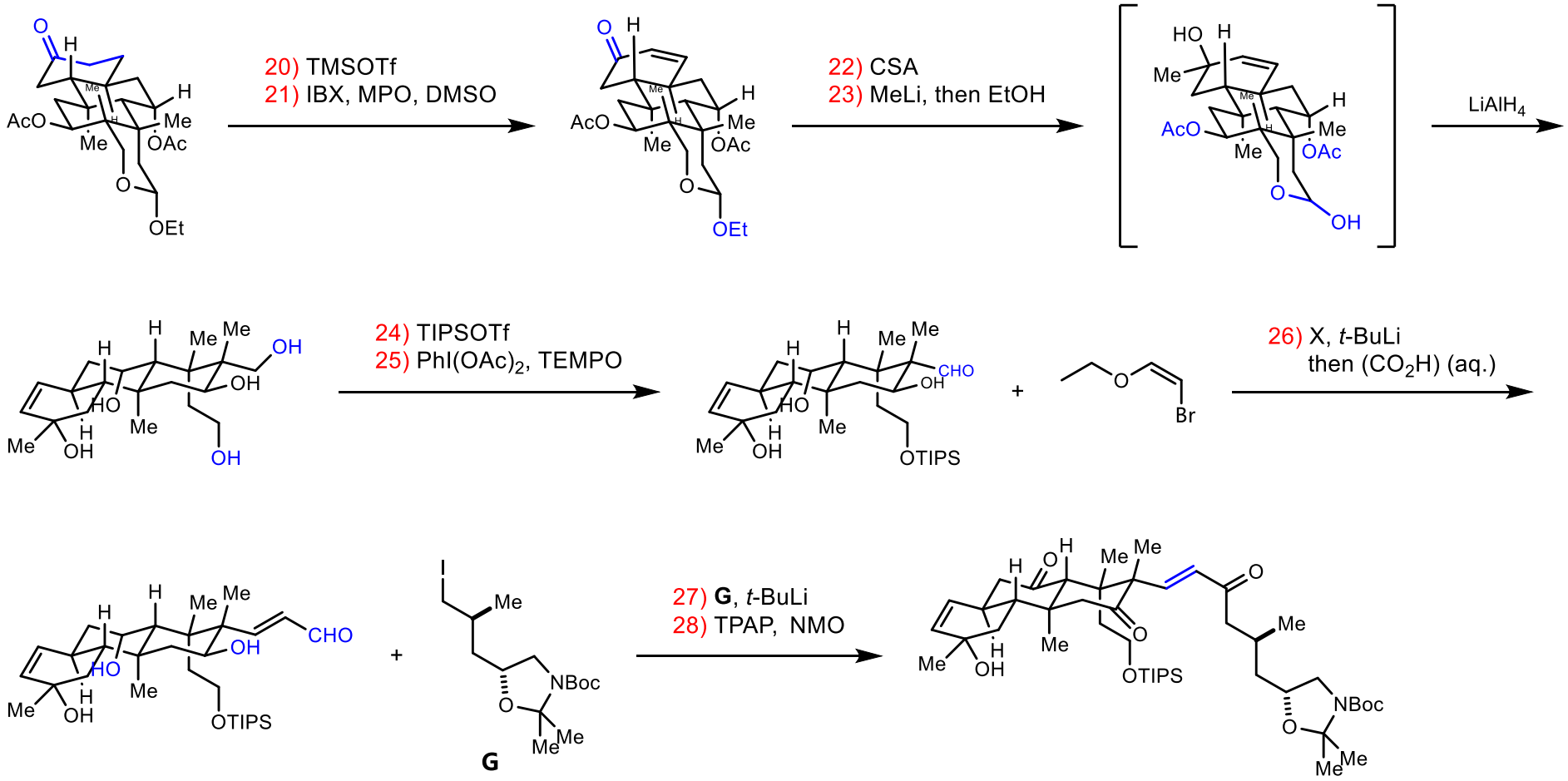
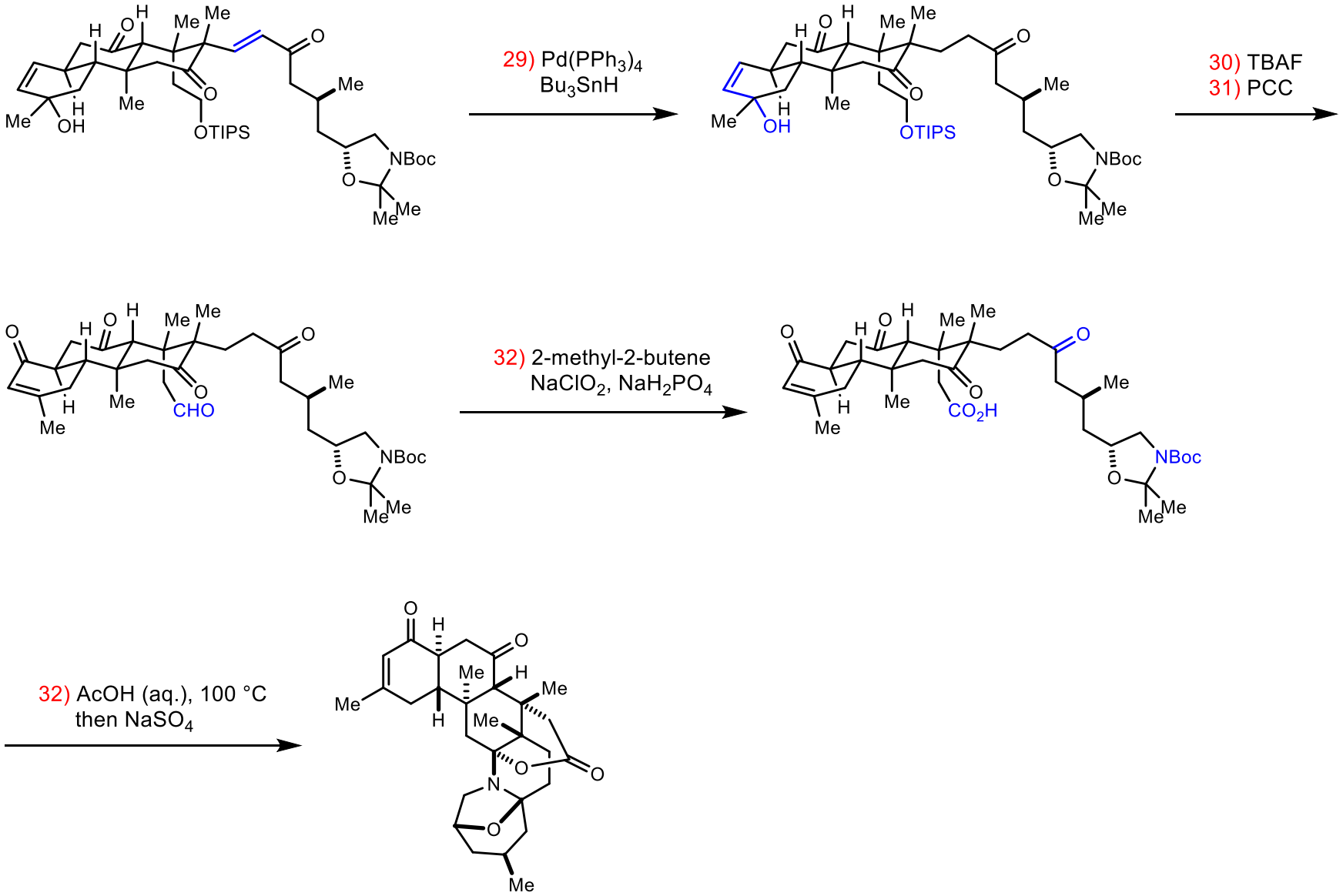


♦**Gao Shuanhu课题组的工作**（*Angew. Chem. Int. Ed.*, **2021**, *60*, 12807–12812.)

♦**Asymmetric Total Synthesis of Norzoanthamine**



Author	Year	LLS	TS	Yield	A–B–C ring
Miyashita	2004		41	3.5%	IMDA(B-C)
Miyashita	2009		5	63%	
Miyashita	2009		7	27%	
Kobayashi	2009		47		IMDA(A-B)
Gao Shuanhu	2021	36			radical cyclization

感谢聆听

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COMMUNICATION | November 11, 2024

Concise Synthesis of Norzoanthamine Enabled by a Set of Photochemical Transformations

Yuchen Sun, Xiao Zhang, Fuyin Jiang, Mengling Zhang, Wanru Wu, and Yu Sun*

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Abstract

Norzoanthamine is a structurally complex polycyclic natural product that expresses a broad range of biological activities, rendering facile access to it and its analogs of considerable importance in drug discovery and development. However, strategies for efficient access to this class of marine alkaloids remain lacking. Here, we report a strategy, characterized by three key photochemical reactions, that we used to synthesize norzoanthamine in 16 steps. A photoinduced dearomative-6π-desymmetrization was developed for facile access to the ABC-tricyclic core of the alkaloid. This was supplemented by a [2 + 2]-photocycloaddition, a visible-light-induced decarboxylative borylation, and a retro-aldol process, constituting an effective solution to the challenging problem of establishing the C9−C22 vicinal all-