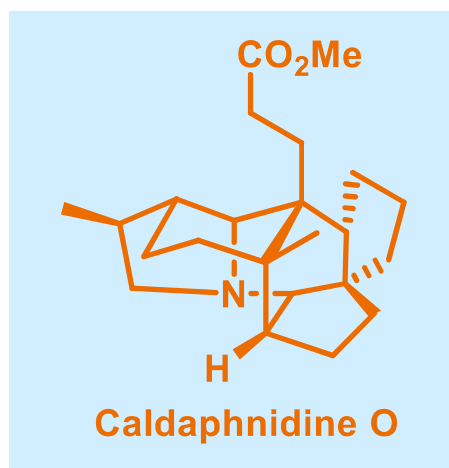


Enantioselective Total Synthesis of (–)-Caldaphnidine O via a Radical Cyclization Cascade

Lian-Dong Guo, Jingping Hu,[†] Yan Zhang,[†] Wentong Tu,[†] Yue Zhang, Fan Pu, and Jing Xu*[‡]

Department of Chemistry and Shenzhen Grubbs Institute, Southern University of Science and Technology, Shenzhen, China



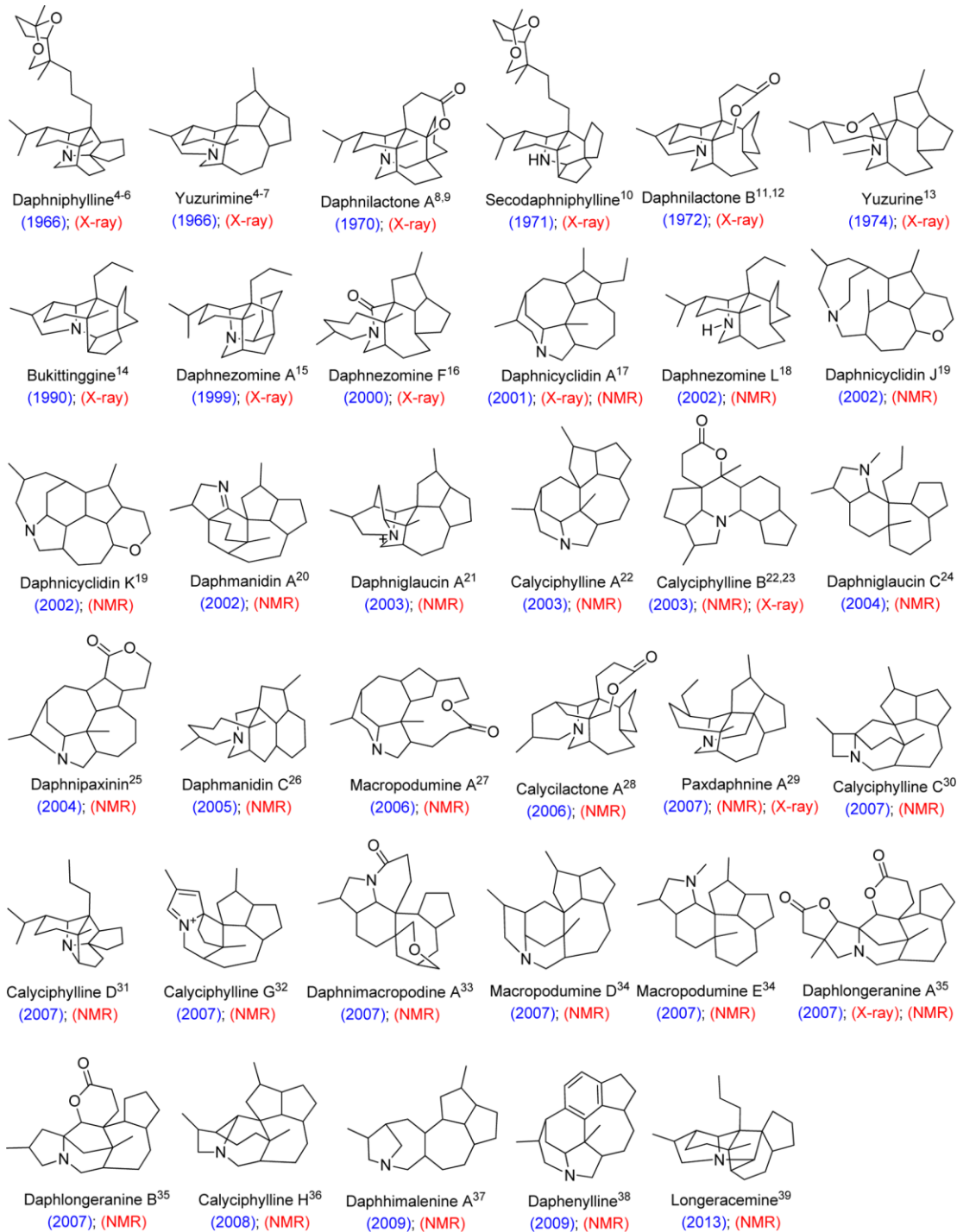
Daphniphyllum alkaloid skeletal structures



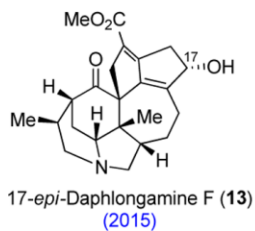
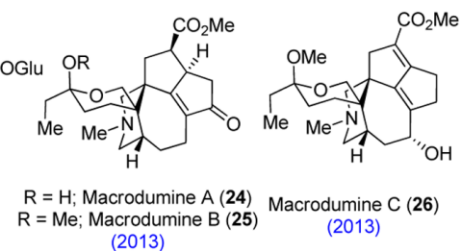
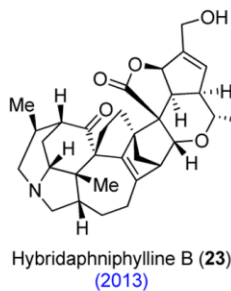
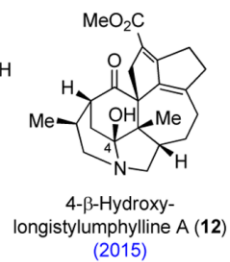
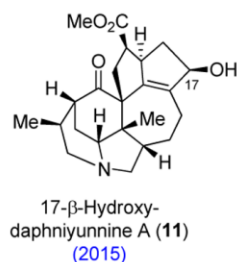
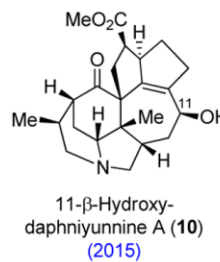
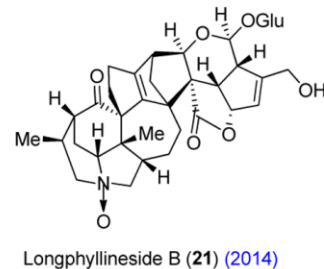
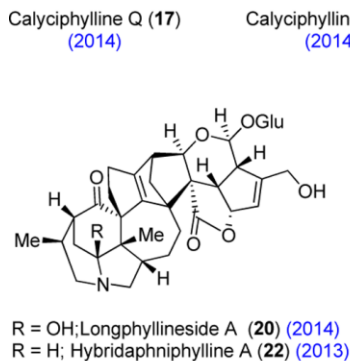
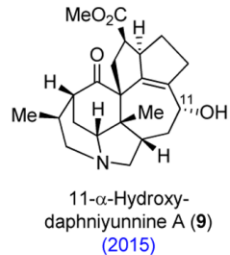
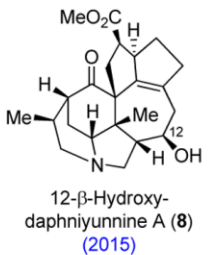
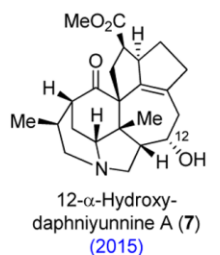
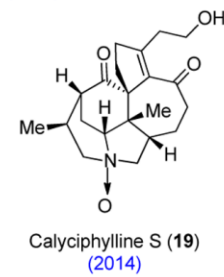
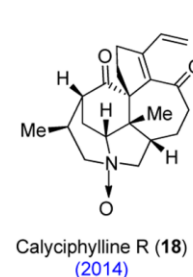
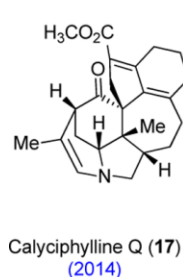
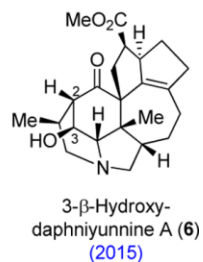
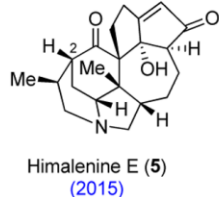
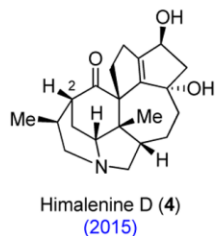
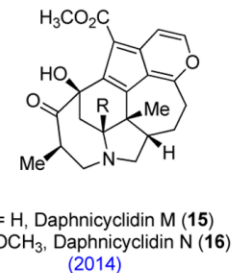
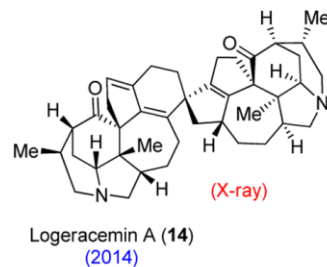
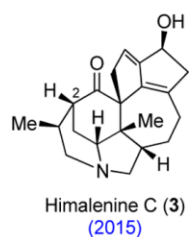
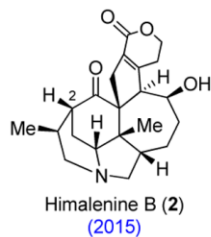
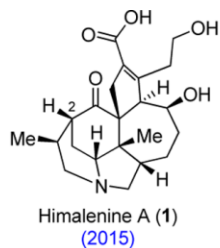
Daphniphyllum macropodum



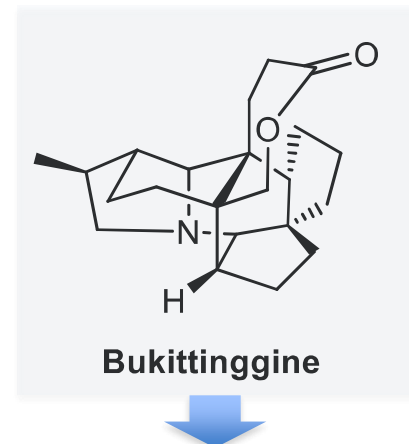
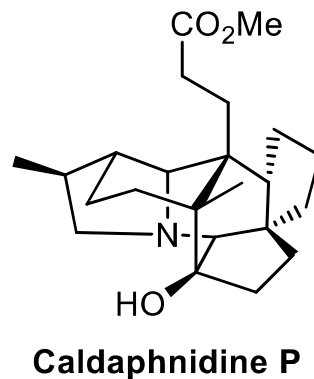
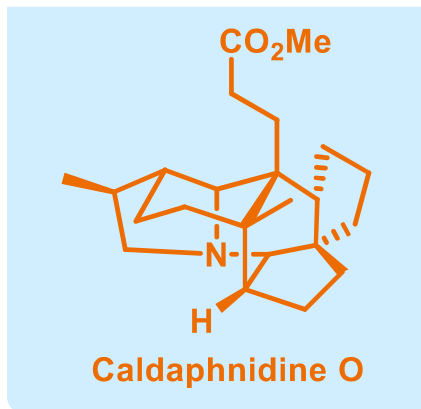
Daphniphyllum calycinum



Newly isolated Daphniphyllum alkaloids



Bukittingine-Type Alkaloids



Heathcock, Clayton H. Chief Scientist, QB3 Berkeley

收藏

University of California, Berkeley Department of Chemistry

邮箱 : heathcock@berkeley.edu

电话 : 510-666-3316

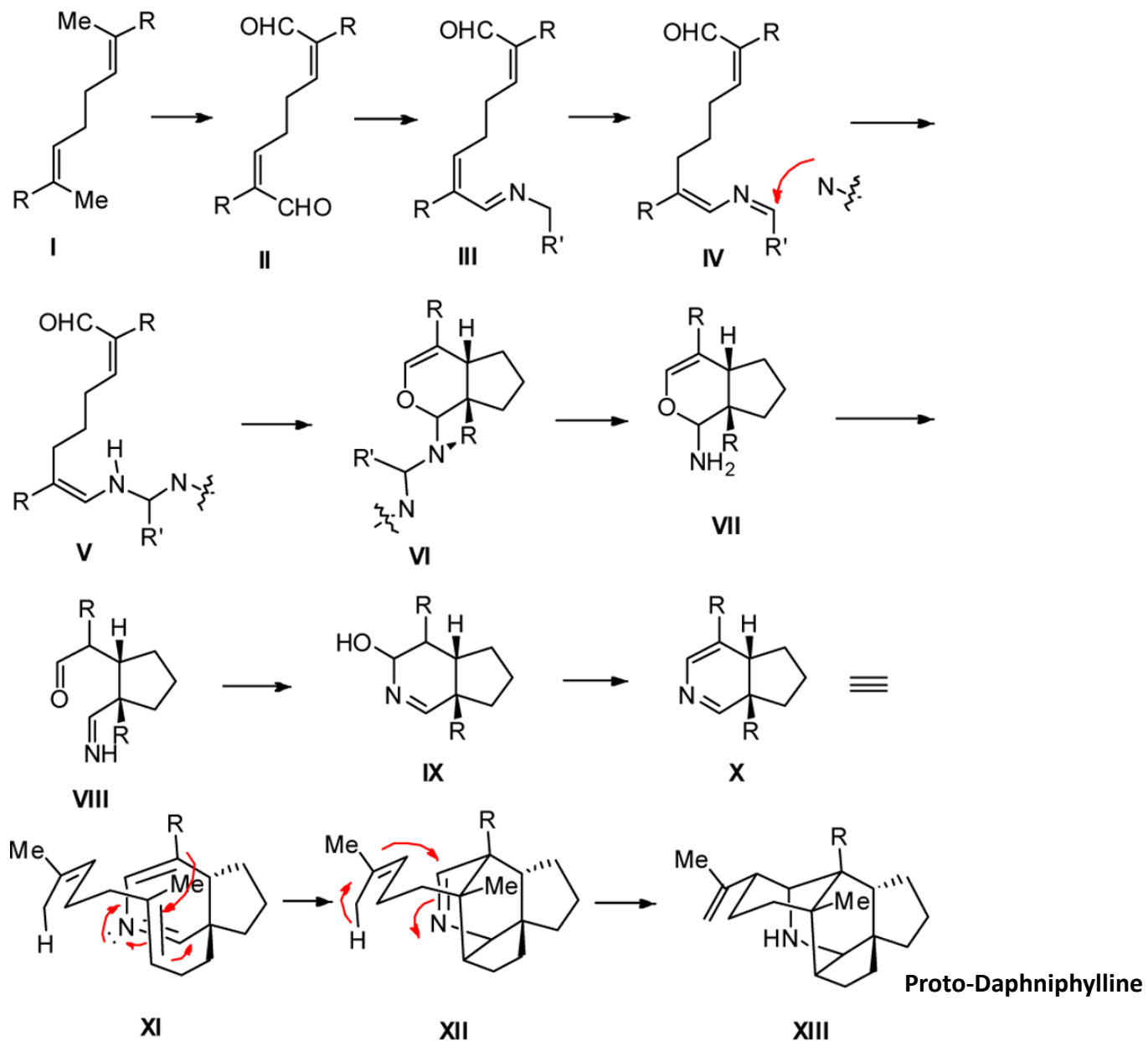
主页 : <http://heathcock.org/chhgrp/>

个人简介

Professor, born 1936; B.Sc. Abilene Christian College, Texas (1958); Ph.D. Organic Chemistry, University of Colorado (1963); Postdoctoral, Columbia University (1963-64); National Science Foundation Fellow (1961-64); Alfred P. Sloan Foundation Fellow (1967-69); Alexander von Humboldt Senior Scientist (1978); Guest Professor, ETH, Zurich (1971); University of Erlangen-Nurnberg (1978); Miller Research Professor, UCB (1983-84 and 1991-92); Chairman, Division of Organic Chemistry, American Chemical Society (1985); Chairman, National Institutes of Health Medicinal Chemistry Study Section (1981-83); Chairman, Gordon Research Conference on Stereochemistry (1986); Chair, Chemistry Division of the American Association for the Advancement of Science (1991); Editor-in Chief, Organic Syntheses (1986), Journal of Organic Chemistry (1989-99); Scientific Advisory Committee of Abbott Laboratories (1986-97); Ernest Guenther Award (ACS) (1986); ACS Award for Creative Work in Organic Synthesis (1990); A.C. Cope Scholar (1990); Prelog Medal, ETH (1991); American Academy of Arts and Sciences (1991); National Academy of Sciences (1995); Centenary Medal, Royal Society of Chemistry (1996); H. C. Brown Award (ACS) (2002); Paul Gassman Award for Distinguished Service (ACS) (2004).



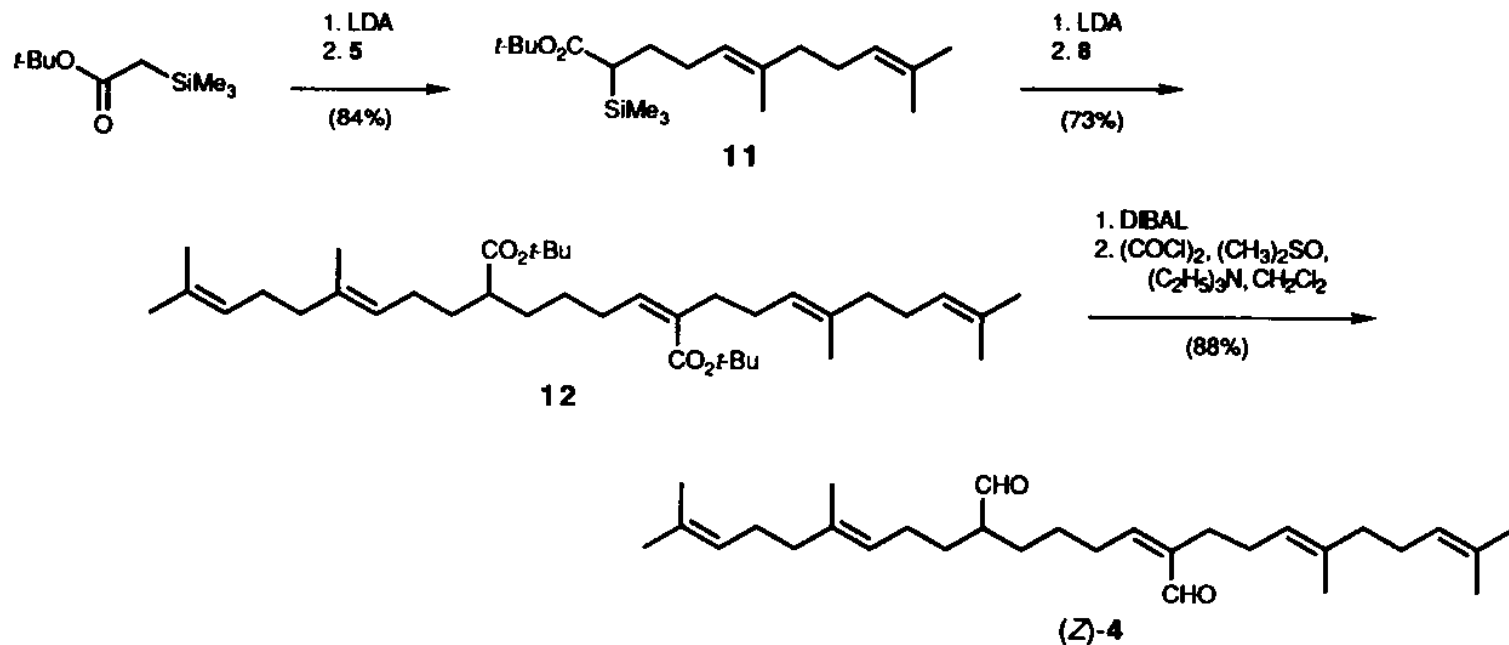
Bukittinggine-Type Alkaloids--Proposed Biosynthetic Pathway



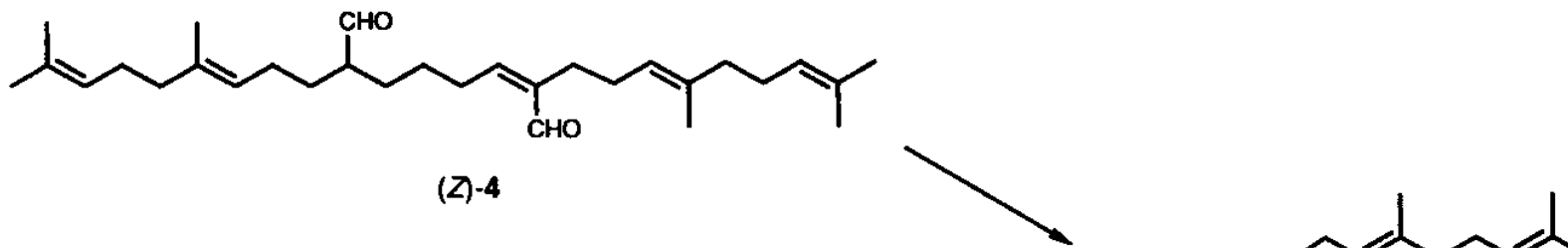
Shosuke Yamamura, *Tetrahedron Lett.* 1973, 14, 2129–2132

Heathcock, C. H. *Proc. Natl. Acad. Sci. U. S. A.* 1996, 93, 14323–14327

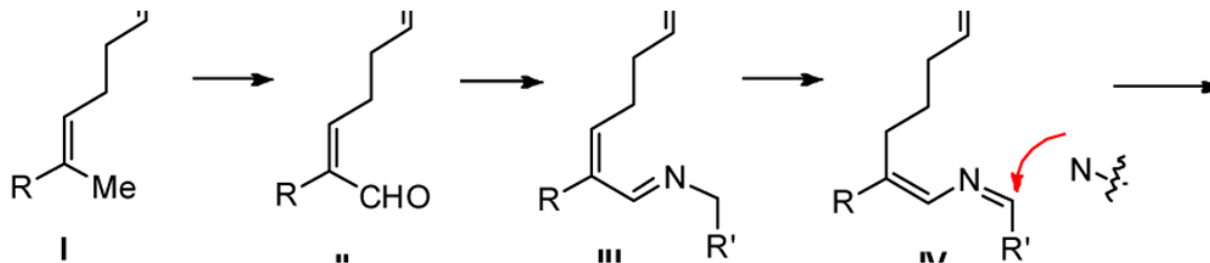
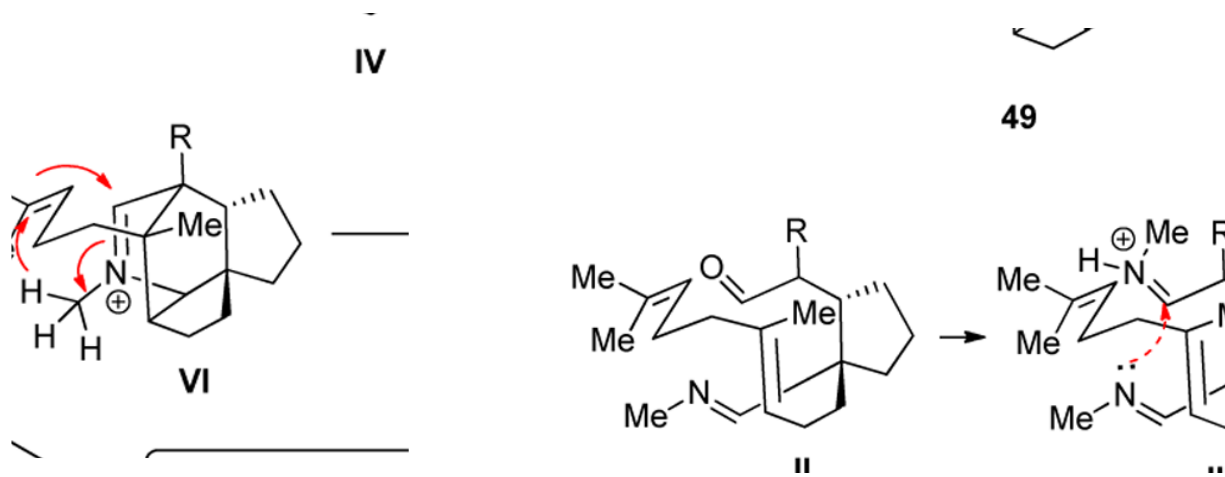
Bukittingine-Type Alkaloids—Total synthesis



Scheme 2. Synthesis of acyclic dialdehyde (Z)-4.

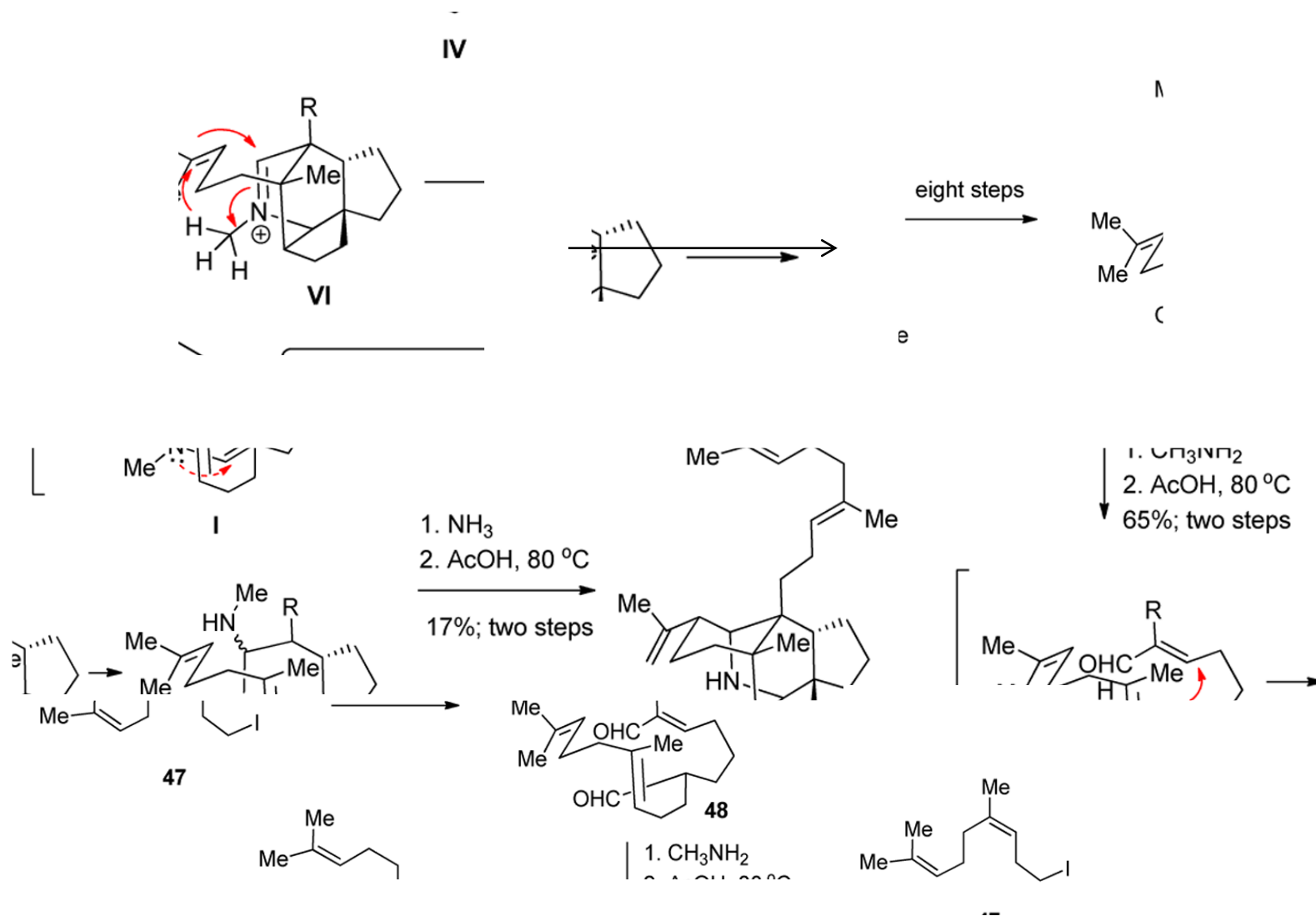


Bukittinggine-Type Alkaloids—Total synthesis

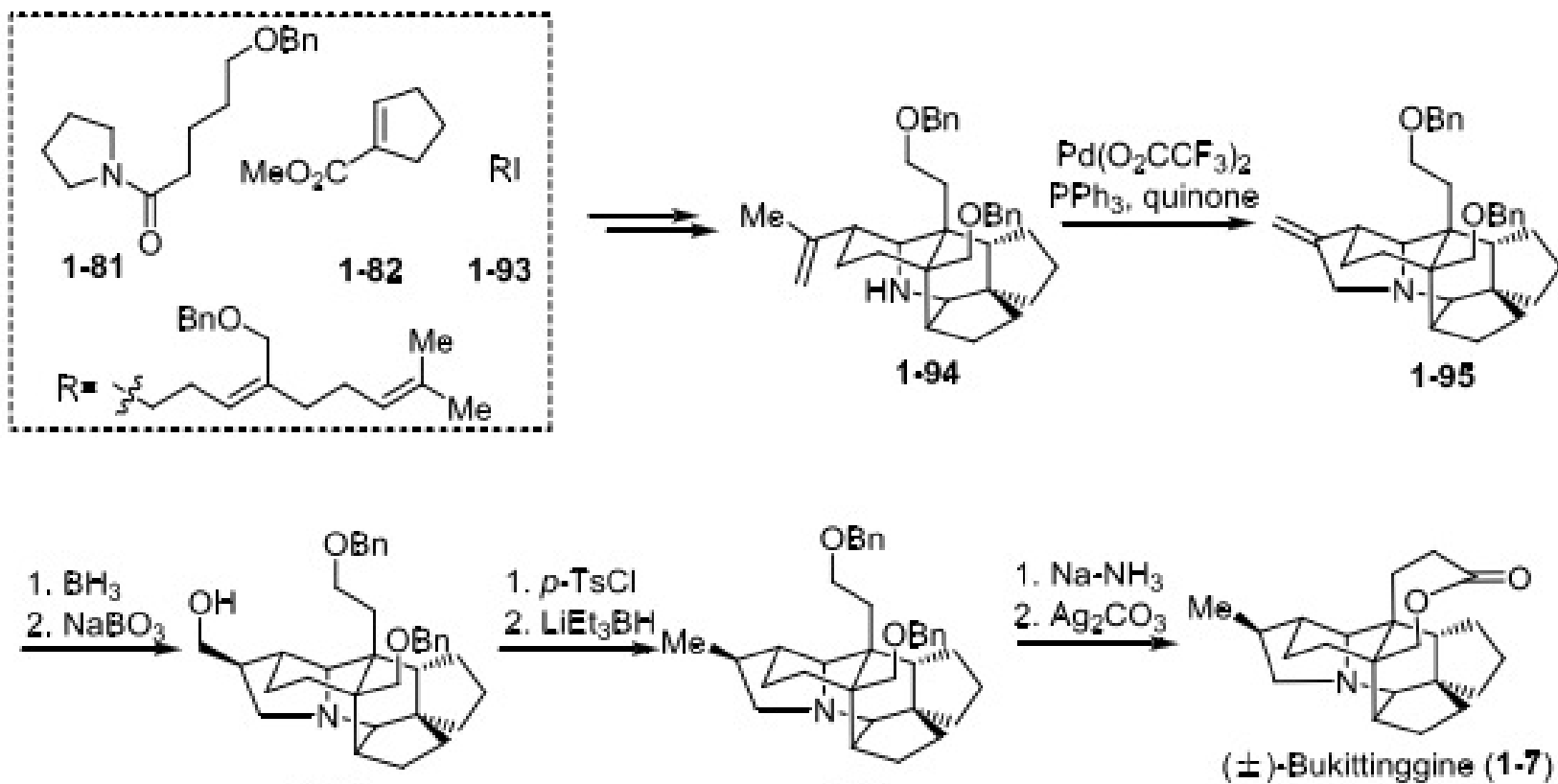


Heathcock, C. H. Science 1990, 248,
1532–1534

Bukittinggine-Type Alkaloids—Total synthesis

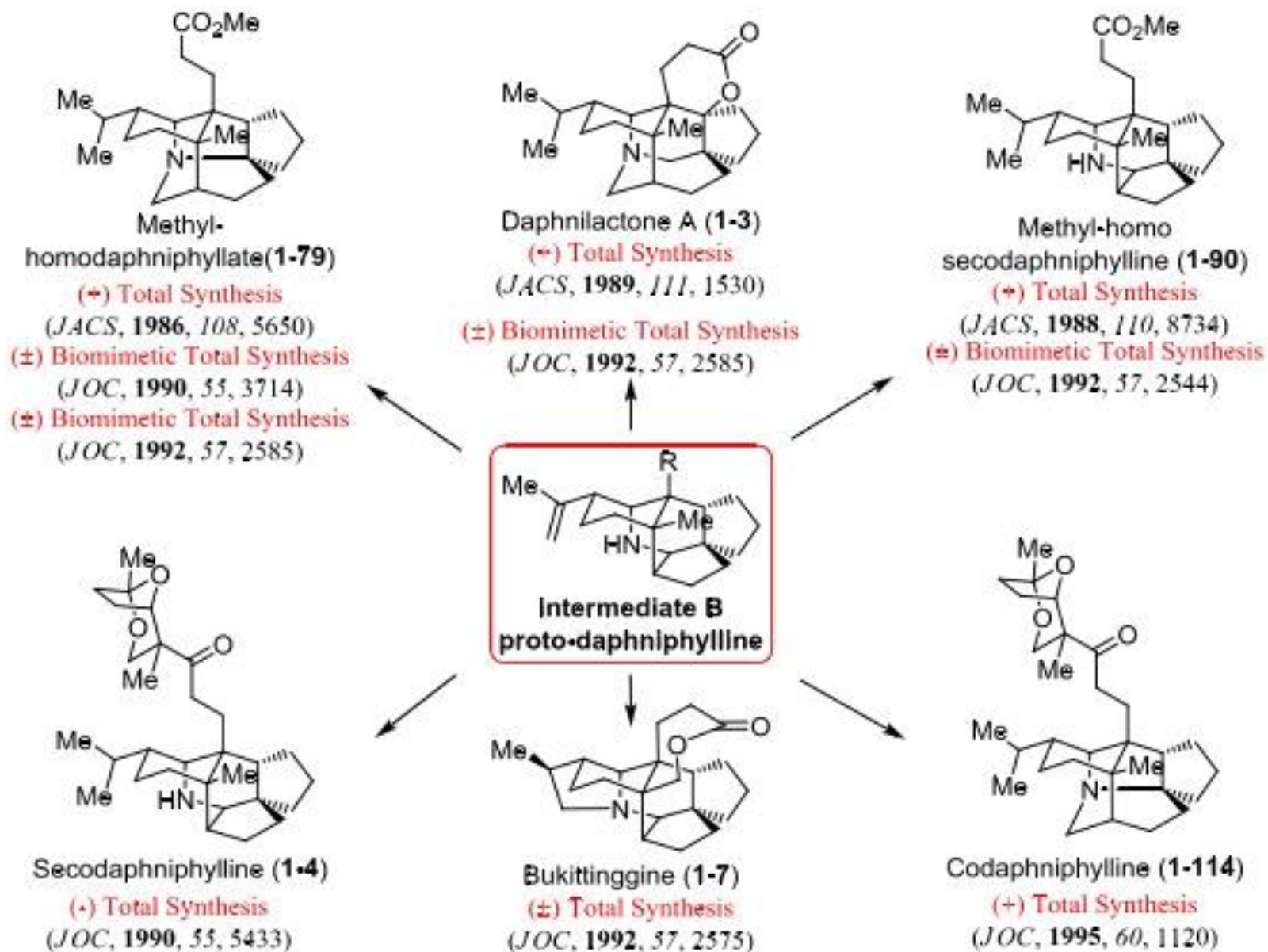


Bukittinggine-Type Alkaloids—Total synthesis

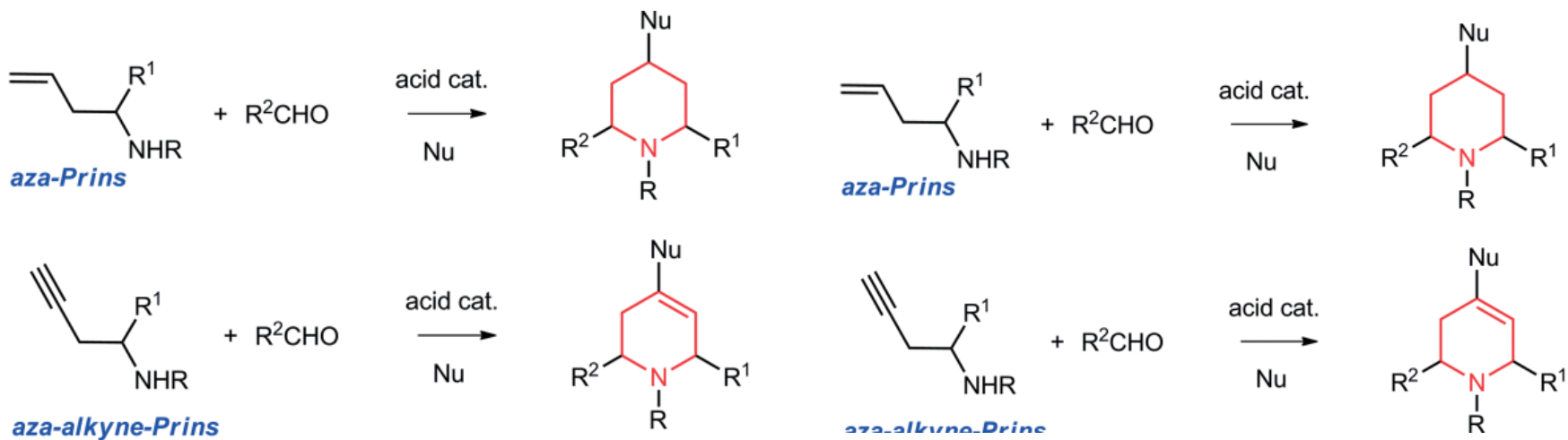
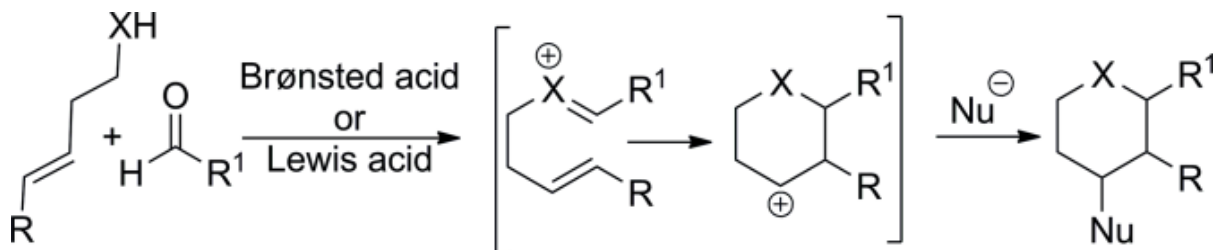


Heathcock, C. H. J. Org. Chem. 1992, 57, 2575–2585.

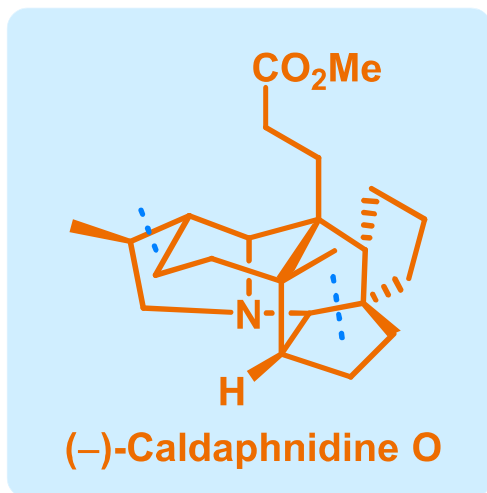
Heathcock's works



Prins cyclization and the related aza-Prins reaction

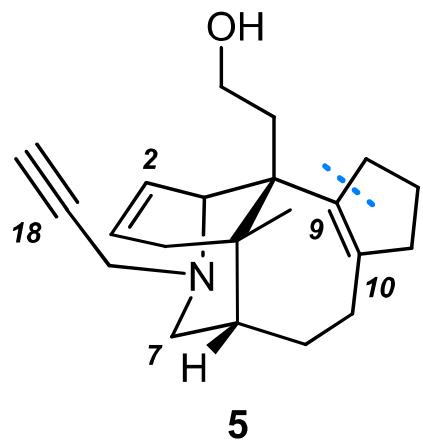


Retrosynthetic analysis of the bukittinggine-type alkaloid (-)-caldaphnidine O



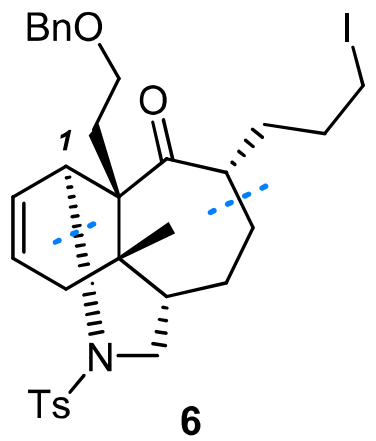
Radical cyclization cascade

⇒



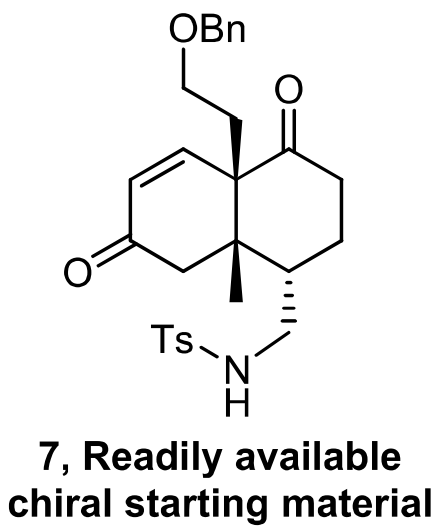
Sm(II)/Fe(III)-mediated Kagan-Molander coupling

⇓



IMAM & Ring expansion

⇐



Key inspiration:

An unexpected detosylation triggered by a Barton-McCombie deoxygenation

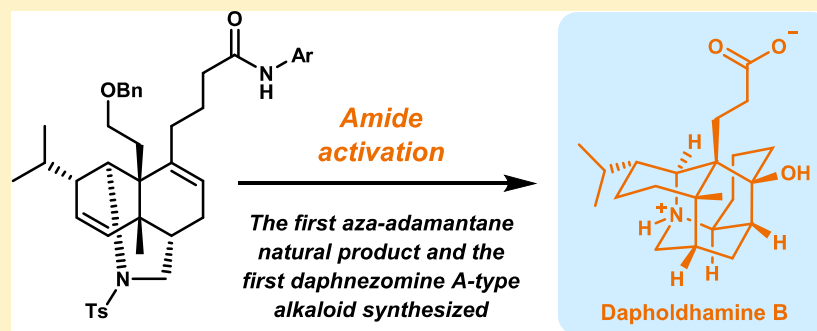
Total Synthesis of Dapholdhamine B and Dapholdhamine B Lactone

Lian-Dong Guo, Jieping Hou,[†] Wentong Tu,[†] Yan Zhang,[†] Yue Zhang, Louxi Chen, and Jing Xu*[Ⓜ]

Department of Chemistry and Shenzhen Grubbs Institute, Southern University of Science and Technology, Shenzhen, China

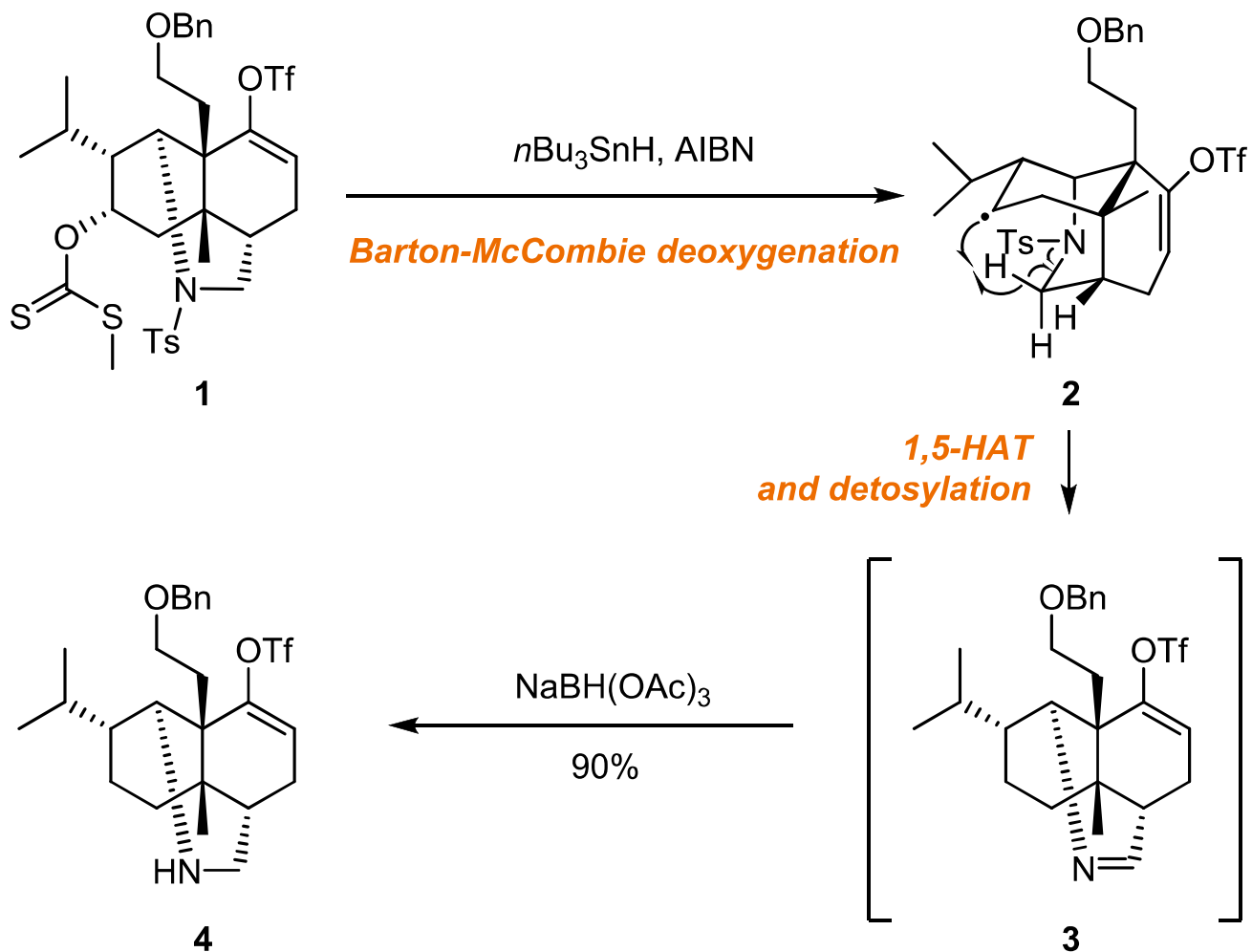
S Supporting Information

ABSTRACT: The intriguing structural complexity and bioactivities of the *Daphniphyllum* alkaloids have long attracted much attention. Herein, we report the first and enantioselective total synthesis of *Daphniphyllum* alkaloid dapholdhamine B and its lactone derivative. The chemical structure of dapholdhamine B contains a unique aza-adamantane core skeleton and eight contiguous stereocenters, including three contiguous fully substituted stereocenters, which present a formidable synthetic challenge. This concise approach used to achieve the first synthesis of an aza-adamantane natural product features a vinylogous Mannich reaction, an optimized α -bromo- α,β -unsaturated ketone synthesis, a substrate-dependent intramolecular aza-Michael addition, a key annulation via amide activation, an S_N2' -type lactonization, and a facile Horner–Wadsworth–Emmons reaction that converts the hemiacetal moiety to the corresponding homologated carboxylic acid.



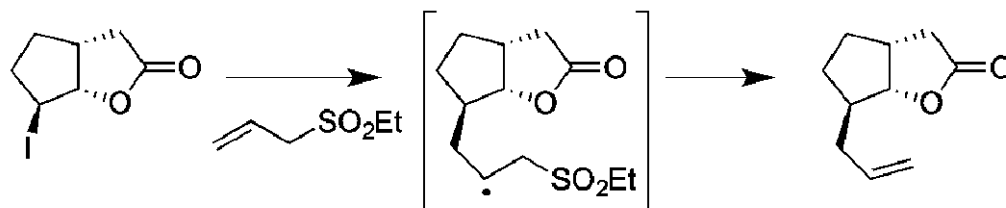
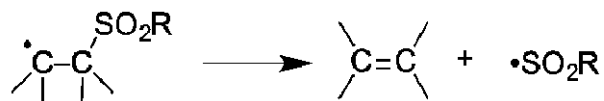
Key inspiration:

An unexpected detosylation triggered by a Barton-McCombie deoxygenation



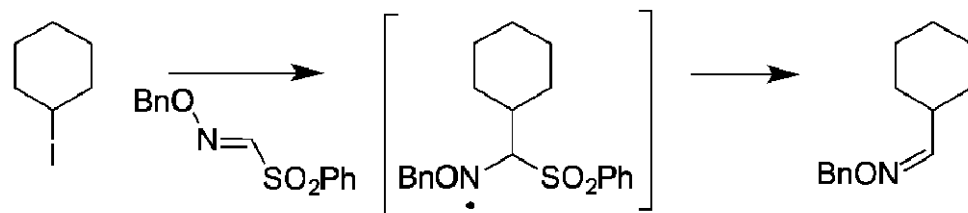
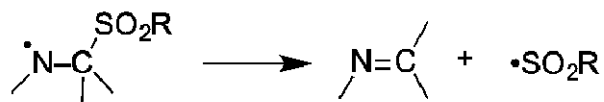
β -Elimination of sulfonyl radicals to make C=C and C=N bonds

a) β -sulfonyl alkyl radicals: base reaction and example



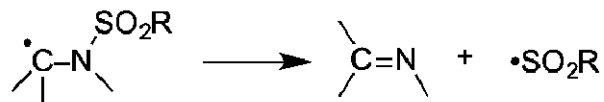
Zard, S. Z. *J. Am. Chem. Soc.* 1997, 119, 7410–7411

b) β -sulfonyl aminyl radicals: base reaction and example



Kim, S. *J. Am. Chem. Soc.* 1996, 118, 5138–5139

c) α -sulfonamidoyl radicals: base reaction



β -Elimination of a sulfonyl group from an α -sulfonamidoyl radical

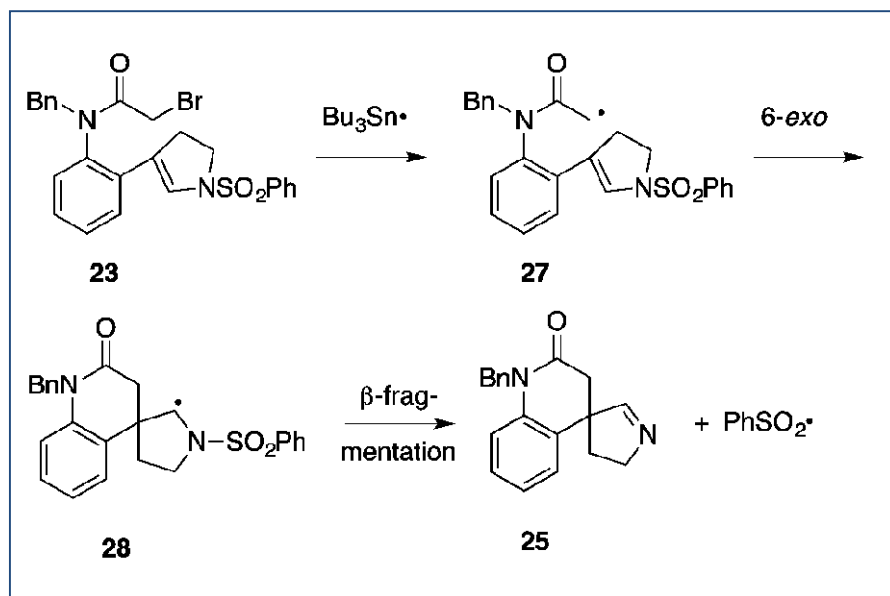


Table 1. Scope of the New Imine Forming Reaction^a

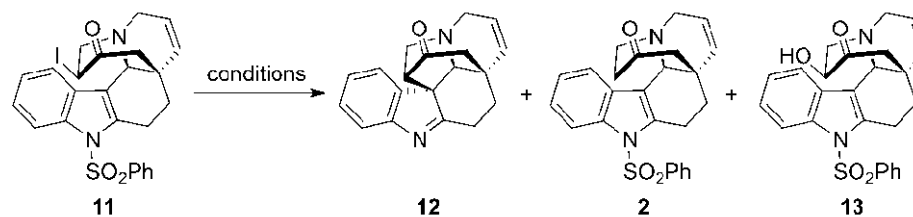
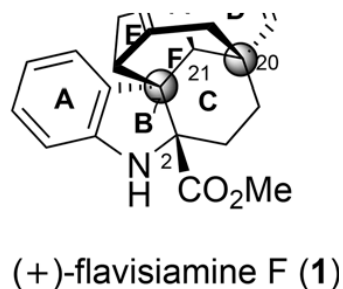
entry	precursor	product	yield
1			81%
2			73%
3			50%
4			61%
5			40%

β -Elimination of a sulfonyl group from an α -sulfonamidoyl radical

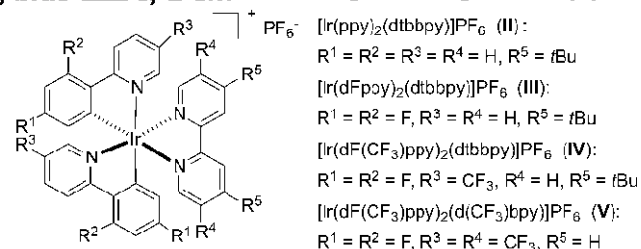
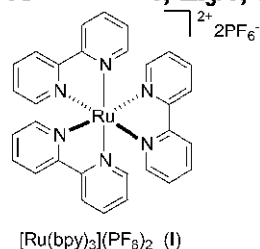
Enantioselective Total Synthesis of (+)-Flavisiamine F via Late-Stage Visible-Light-Induced Photochemical Cyclization

Xiaogang Tong, Bingfei Shi, Kangjiang Liang, Qian Liu, and Chengfeng Xia*

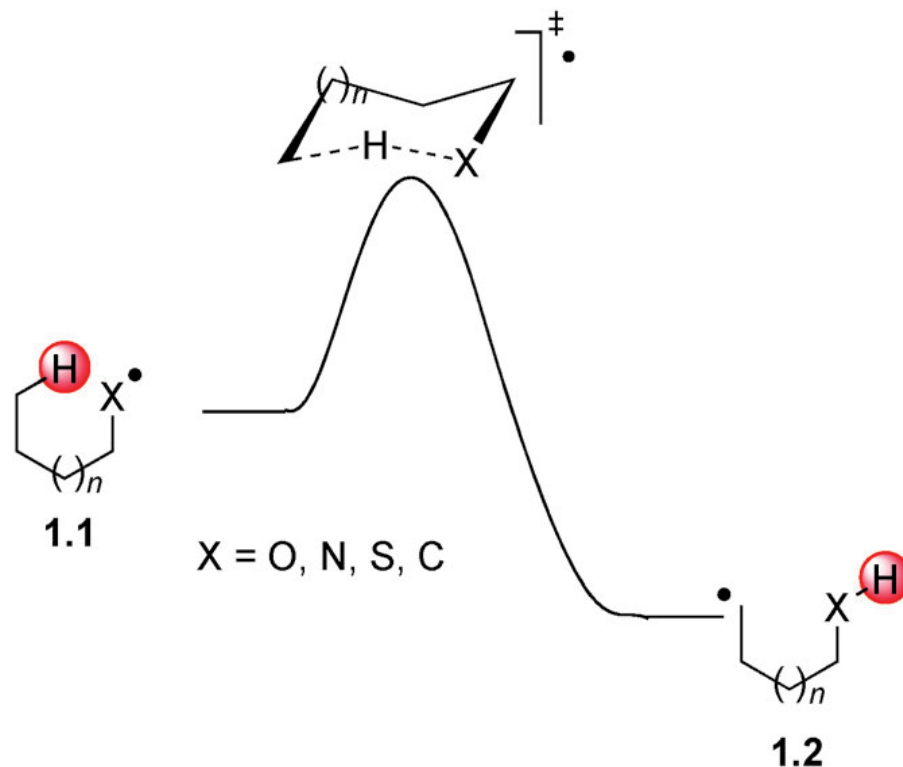
Angew. Chem. Int. Ed. 2019, 58, 1 – 5



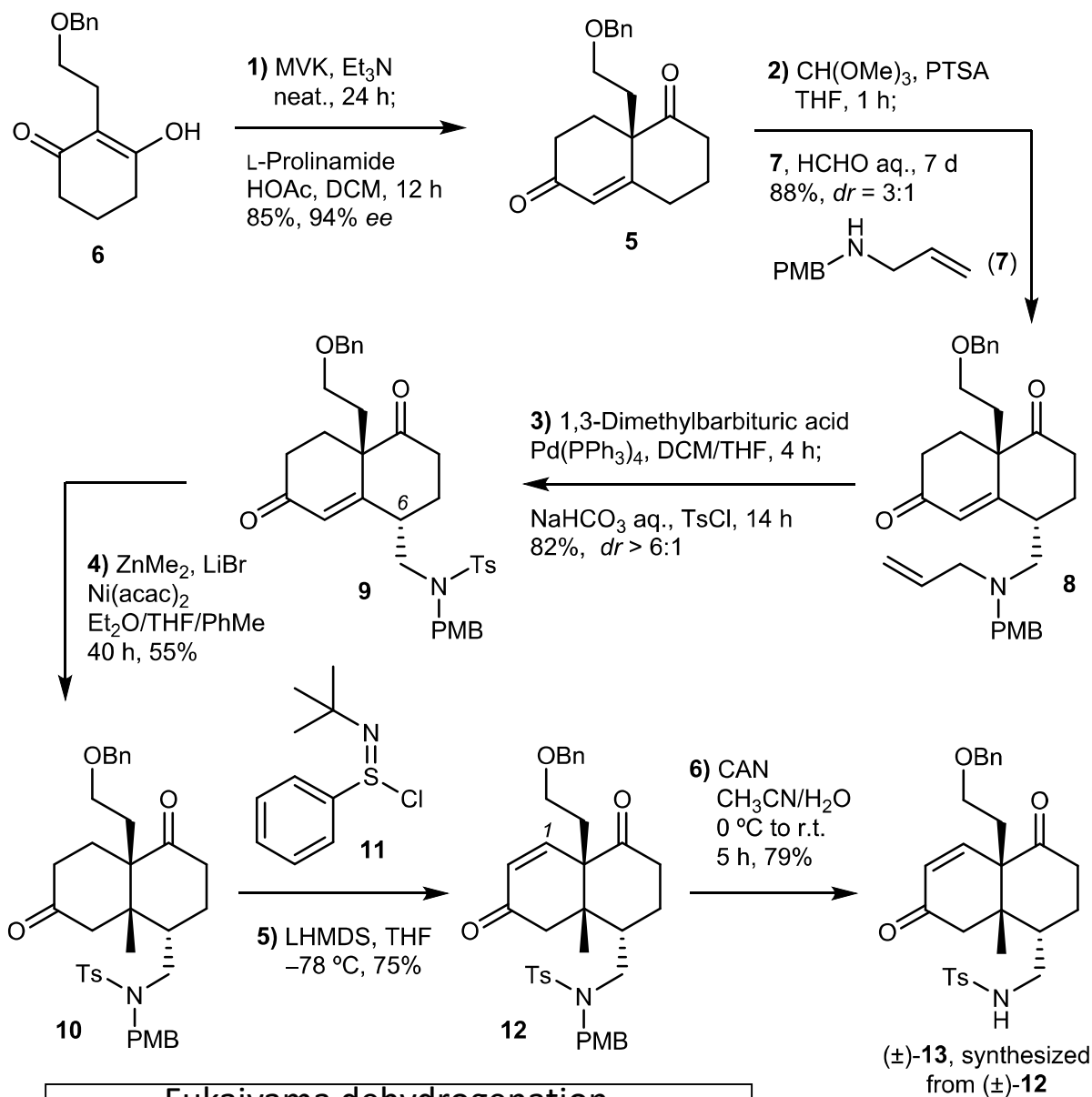
Entry	Conditions	Yields [%] ^[a]		
		12	2	13
1 ^[b]	Bu ₃ SnH, AIBN, benzene	0	93	0
2 ^[b]	(TMS) ₃ SiH, AIBN, benzene	0	89	0
3 ^[c]	I, Et ₃ N, air, blue LEDs, MeCN	0	0	81
4 ^[c]	II, Et ₃ N, air, blue LEDs, MeCN	0	0	77
5 ^[c]	III, Et ₃ N, air, blue LEDs, MeCN	0	0	83
6 ^[c]	IV, Et ₃ N, air, blue LEDs, MeCN	0	0	79
7 ^[c]	V, Et ₃ N, air, blue LEDs, MeCN	26	0	39
8 ^[c]	V, Et ₃ N, air, blue LEDs, DMF	77	0	6
9 ^[c]	V, DIPEA, air, blue LEDs, DMF	0	0	69
10 ^[c]	V, Et ₃ N, air, blue LEDs, DCM	0	0	74



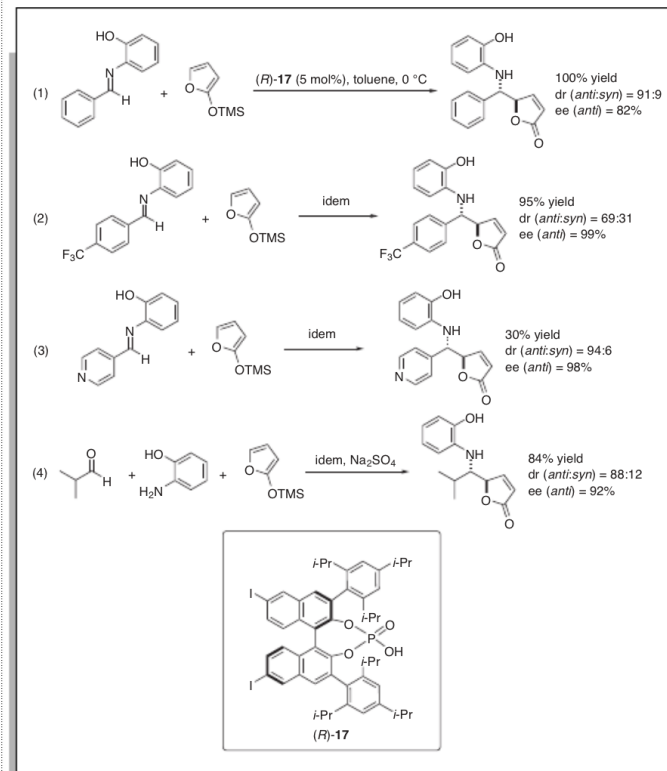
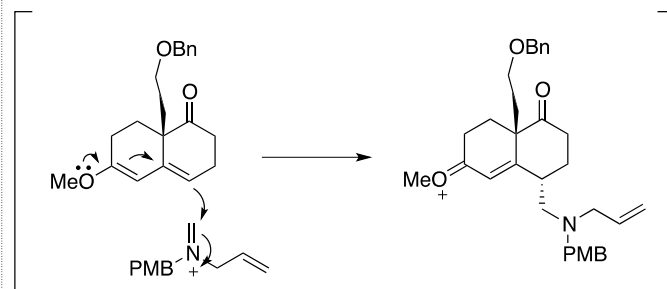
General reaction profile of 1,n-HAT.



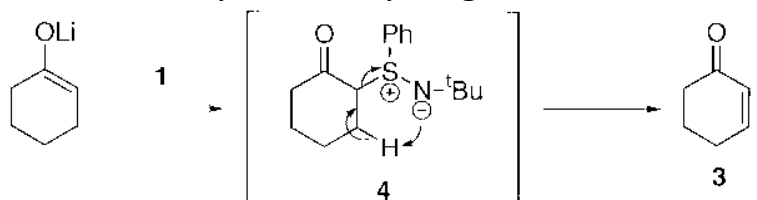
- Small distortion from linearity (X-H-C angle between 145–180°) was shown to have little energetic cost.
- The distance between the radical center and the hydrogen atom to be abstracted should be ≤ 3 Å.
- 1,5-HAT are the most favored processes because the six-membered transition structure can readily accommodate a C-H-X angle close to 180°.

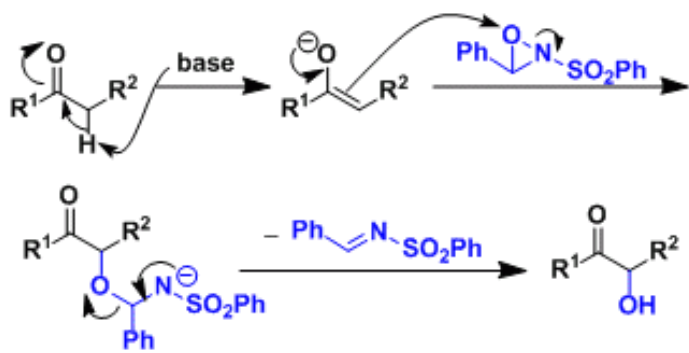
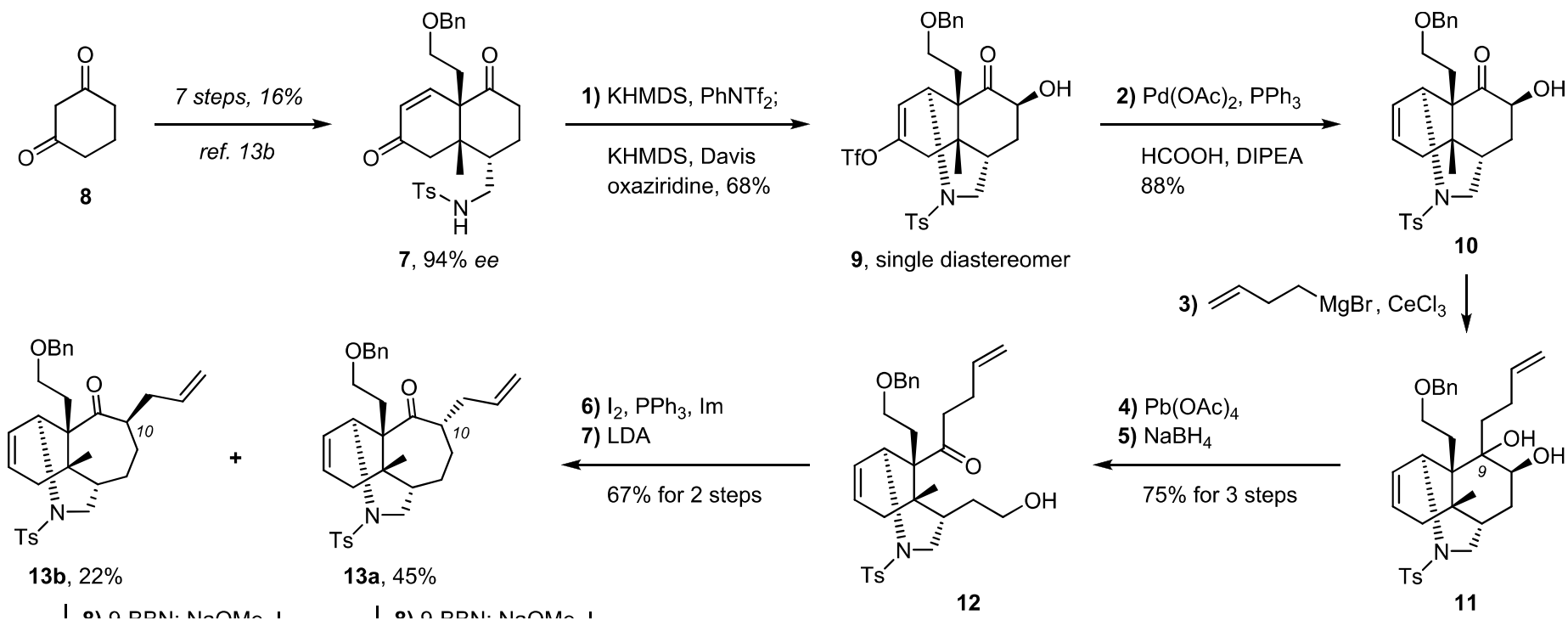


Vinylogous Mannich Reaction

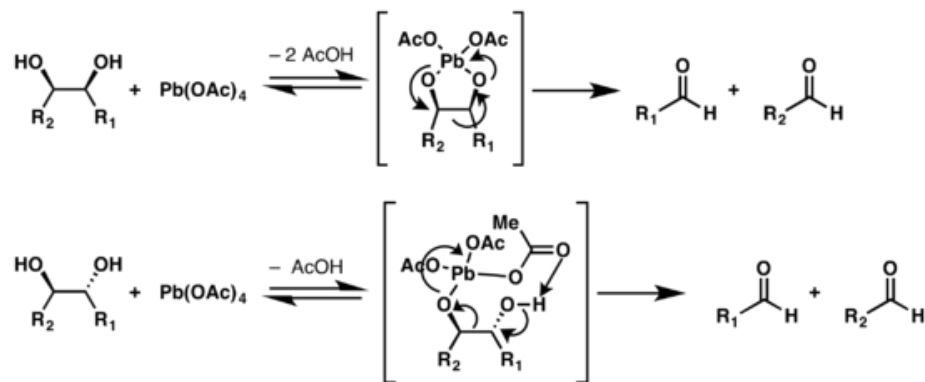


Fukaiyama dehydrogenation

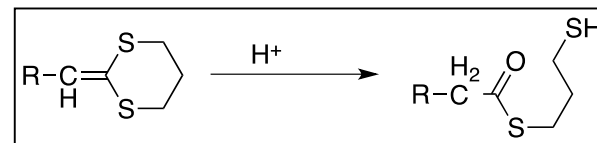
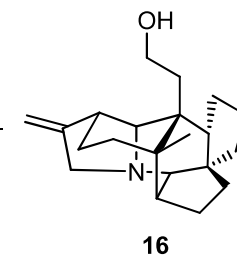
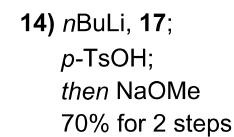
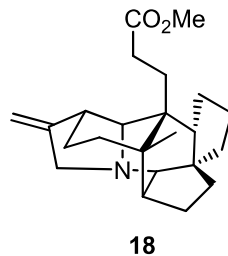
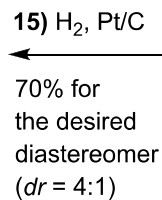
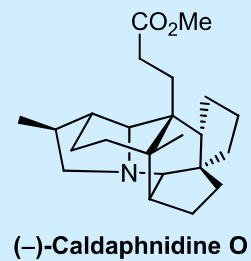
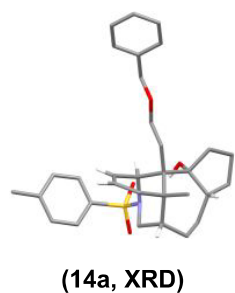
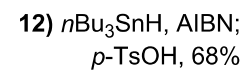
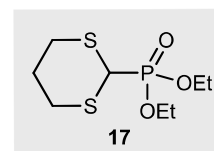
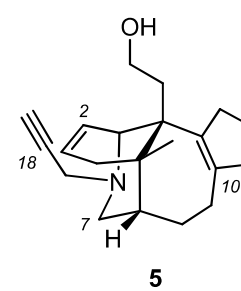
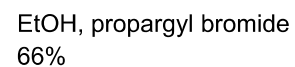
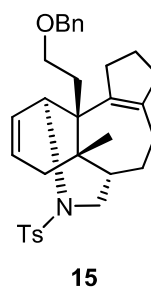
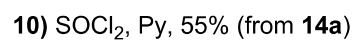
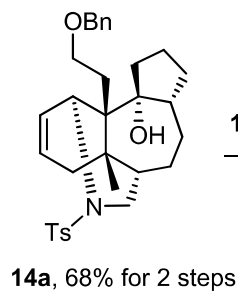
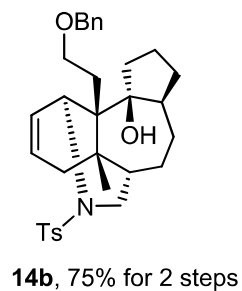
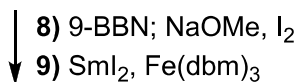
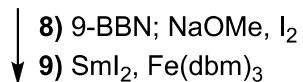
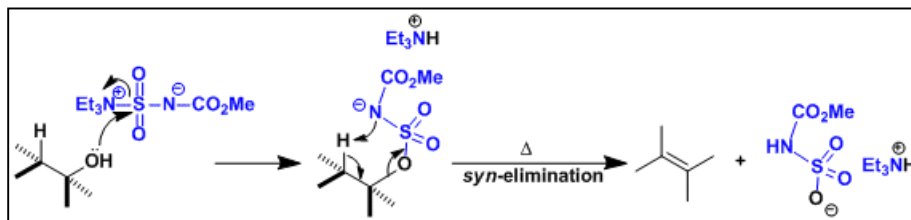
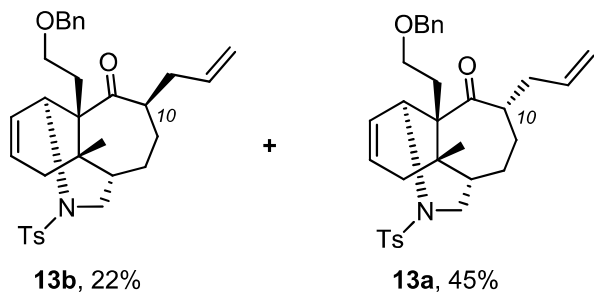




Davis oxidation



Criegee oxidation



Thank You