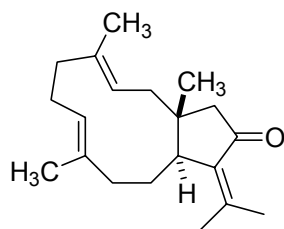


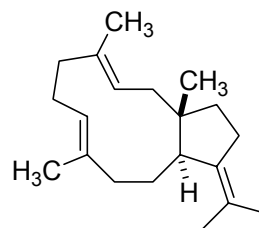
Rising Stars Of Synthesis: The Post-doctoral work of Scott A. Snyder

J. Am. Chem. Soc. **2006**, *128*, 740

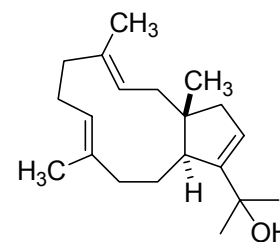
Tetrahedron Lett. **2006**, *47*, 2083



dolabellatrienone



β -araneosene



palominol

Scott A. Snyder

-B. S. Williams College, Summa Cum Laude

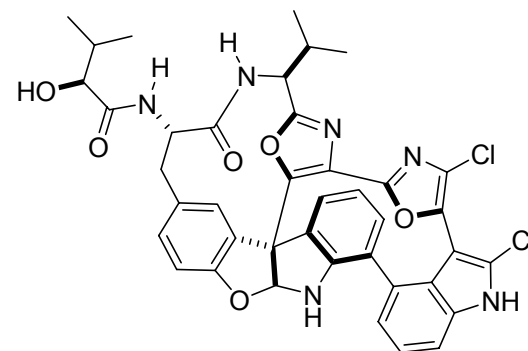
-Ph. D. The Scripps Research Institute, under K. C. Nicolaou

-Postdoc- Harvard University, under E. J. Corey

-Author on more than 30 papers, patents and books, including Classics II.

-As a Ph. D. describes more than six new bond constructions developed, along with two syntheses of Diazonamide A.

-Junior faculty at Columbia in Fall, 2006.



Diazonamide A

The Dolabellane diterpenoids

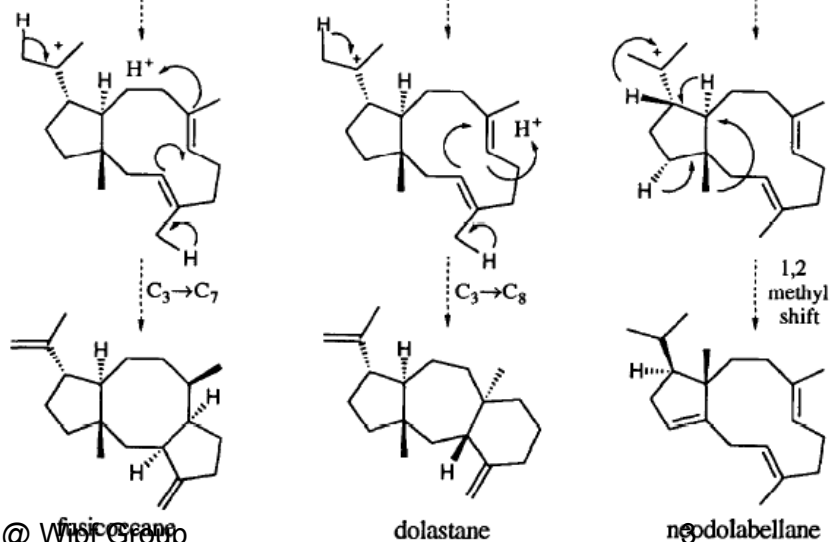
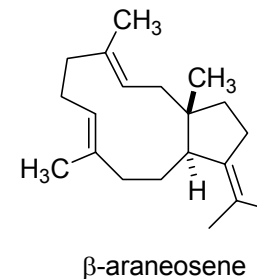
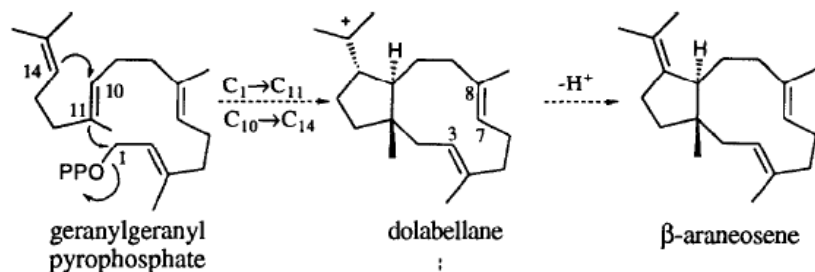
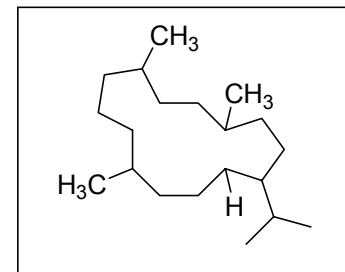
-Dolabellanes are produced principally by mollusks, coelenterates and brown algae.

- The biological activity of the dolabellanes includes cytotoxicity, antibacterial, antifungal, antiviral, antimalarial, molluscicidal, ichthyotoxic, and phytotoxicity.

-The first dolabellane isolated was β -araneosene (1975).

-Now, more than 140 compounds have been isolated with this structure.

-They are characterized by the [9.3.0] nucleus, which is on the biosynthetic pathway to the fusicocanes, dolastanes, and neodolabellanes.



Tetrahedron 1998, 54, 11683

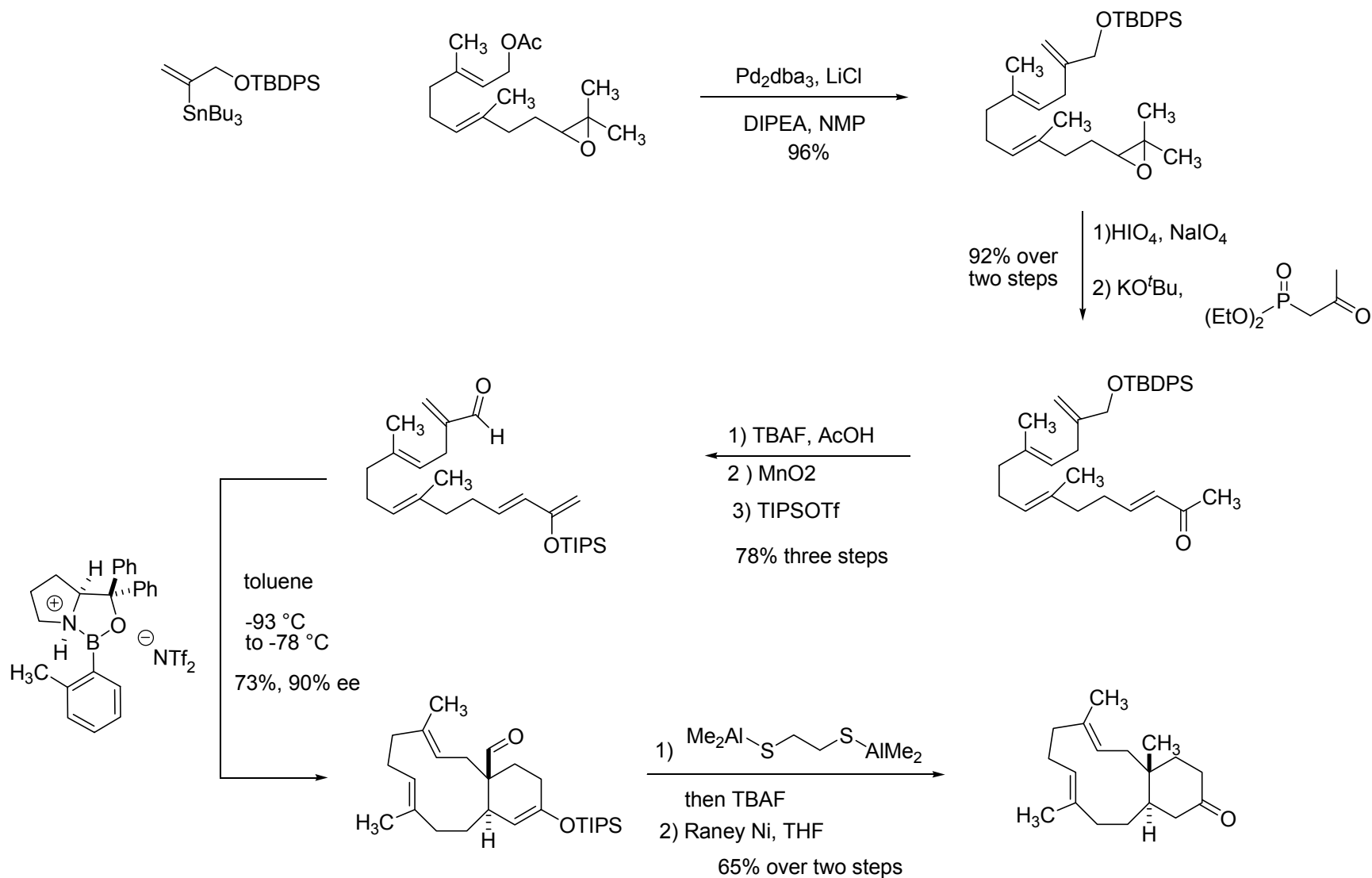
Biological Activity of the Dolabellanes

Table 1. Biological Properties of Naturally Occurring Dolabellane Diterpenes.

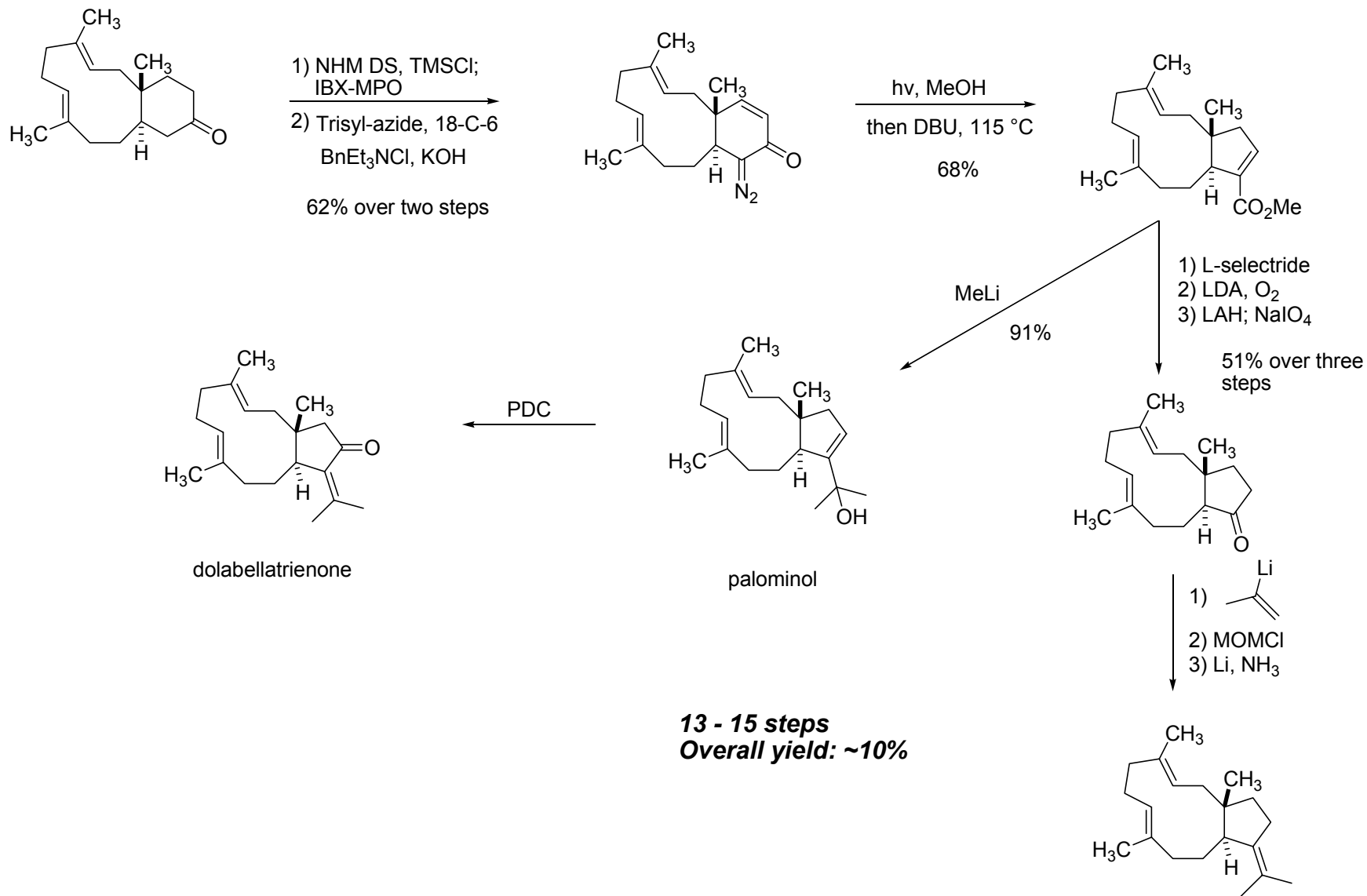
Struct. No.	Source	Collection Site	Biological Activity	Reference
15,16	<i>Aplysia dactylomela</i>	Canary Islands	antimicrobial activity (Gram-positive and Gram-negative bacteria)*	6,7
22,23	<i>Clavularia viridis</i>	Japan	cytotoxic (P388 leukemia cells) and ichthyotoxic activity	16-18
24	<i>Clavularia viridis</i>	Japan	inhibits cell division in fertilized sea urchin eggs	18
25	<i>Clavularia viridis</i>	Xisha Islands, China	inhibits K ⁺ induced contractions of blood aortic strips	20
27-29	<i>Clavularia viridis</i>	Xisha Islands, China	Ca ²⁺ channel blocker in isolated smooth rabbit muscles	21
28	<i>Clavularia viridis</i>	Xisha Islands, China	50% negative inotropic activity and 43.7% bradycardia activity, decreases blood pressure of rats	21
27-29,33	<i>Clavularia viridis</i>	Xisha Islands, China	cytotoxic (Ehrlich ascites carcinoma cells)	21
36,37,42	<i>Eunicea laciniata</i>	Puerto Rico	weakly cytotoxic (HCT 116 cells)	28-30
37	<i>Eunicea laciniata</i>	Puerto Rico	antimicrobial activity (Gram-negative bacteria)	28-30
43-46	<i>Eunicea laciniata</i>	Puerto Rico	weakly cytotoxic (HeLa cells)	28-30
52	<i>Dictyota dichotoma</i>	Sicily, Italy	cytotoxic and <i>in vivo</i> antiviral activity (influenza and adenoviruses)	35
52-55	<i>Dictyota dichotoma</i>	Sicily, Italy	antimicrobial activity (Gram-positive and Gram-negative bacteria)	35
57	<i>Dictyota dichotoma</i>	Sicily, Italy	cytotoxic (KB cells)	36
58,62,63	<i>Dictyota</i> sp.	Sicily, Italy	antimicrobial activity	38
83-86	<i>Dictyota dichotoma</i>	Cádiz, Spain	cytotoxic (P-388 mouse lymphoma, A-549 human lung carcinoma, HT-29 human colon carcinoma, MEL-28 human melanoma cells)	45
88	<i>Dictyota pardalis</i>	Australia	weak but specific antimalarial activity	49
106-108	<i>Dilophus fasciola</i>	Yugoslavia	ichthyotoxic, phytotoxic	55
112-114	<i>Odontoschisma denudatum</i>	Japan	growth-inhibitory activity on a series of plant pathogenic fungi	60
123-140	<i>Chrozophora obliqua</i>	Egypt	hypoglycemic activity*	64,65

* The biological activity described is actually that of the crude extract and not of the purified isolates.

Preparation of dolabellanes



Preparation of dolabellanes (cont.)



Generality of Dithiolane Formation

- Reagent introduced in 1973 by Corey for protection of lactones and lactams.
- Relatively general reaction for ketones and aldehydes.
- Non-tethered sulfides undergo transesterification to generate thioesters from esters.

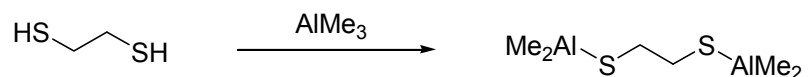
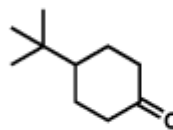
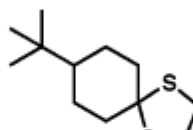
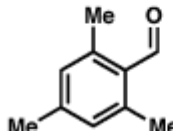
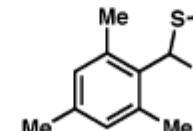
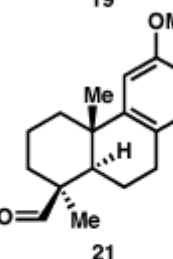
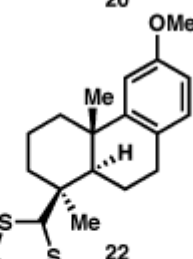
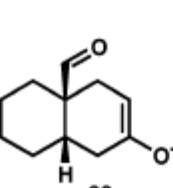
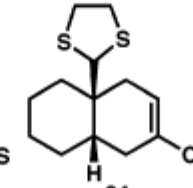
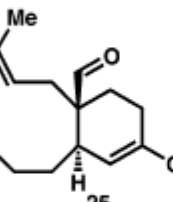
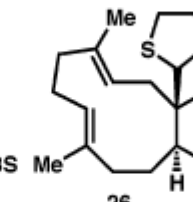
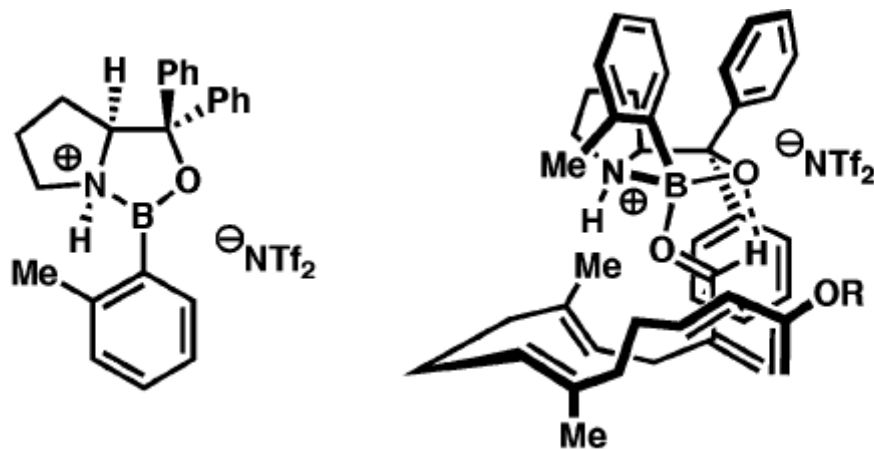
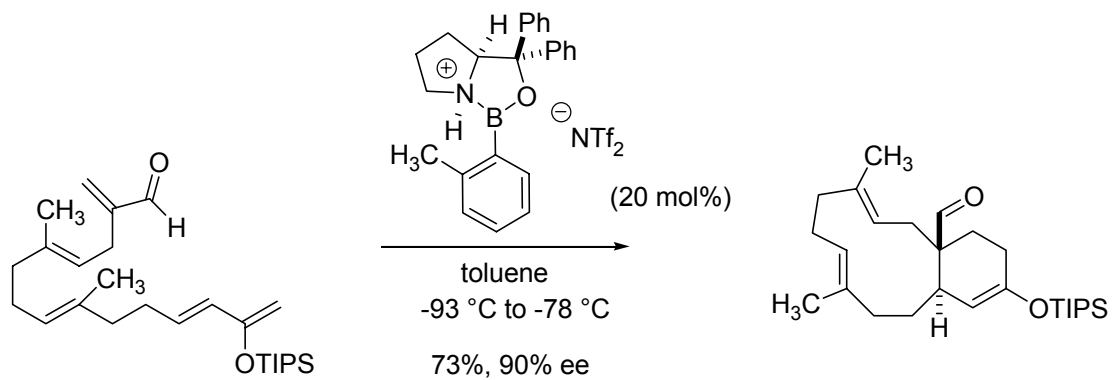


Table 1. Me₂AlSCH₂CH₂SAIMe₂-Induced Dithiane Formation^a

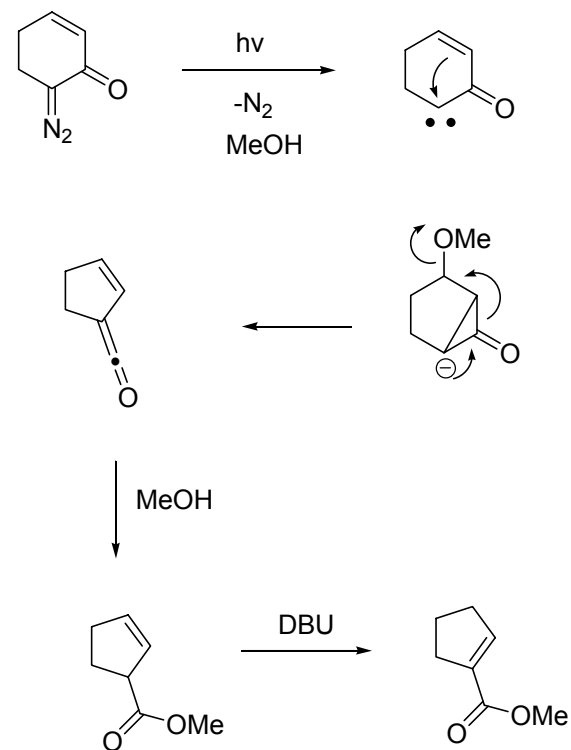
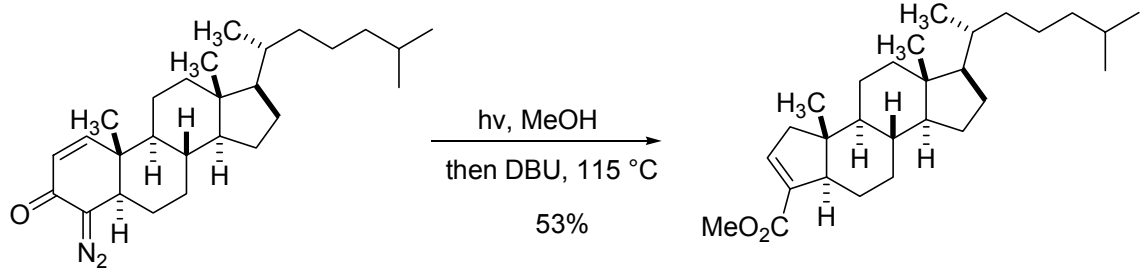
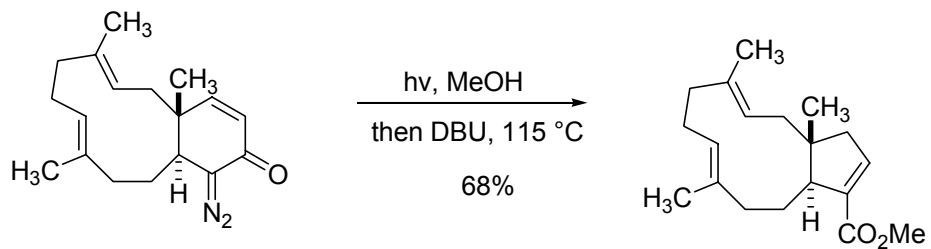
Entry	Starting material	Product	Yield (%)
1			83
2			87
3			79
4			72
5			68

^a With 3 equiv of sulfide reagent at 60 °C in 1,2-dichloroethane for 2–12 h.

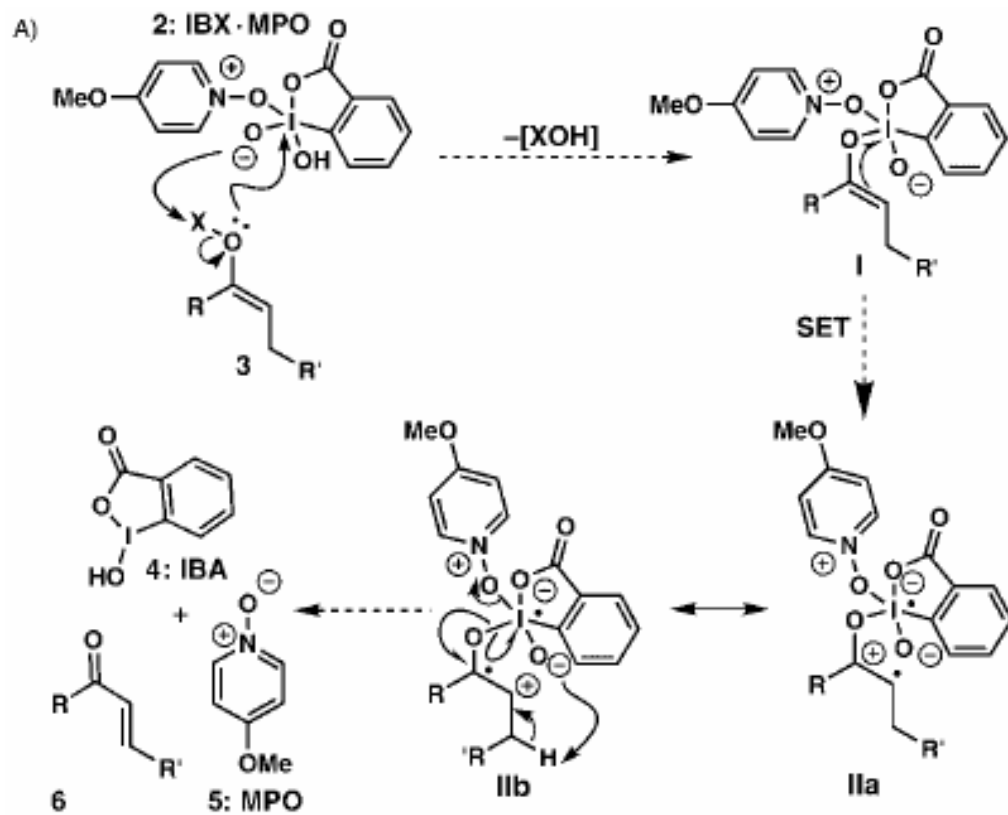
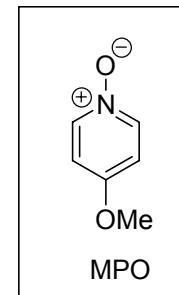
Diels-Alder Cycloaddition Under Oxazaborolidinium Catalysis



Ring Contraction via Wolff Rearrangement

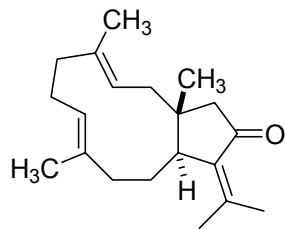


IBX-Mediated Dehydrogenation of Silyl Enol Ethers

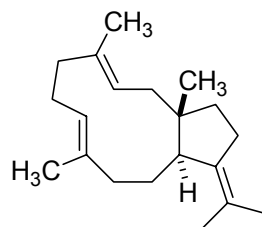


In Summary...

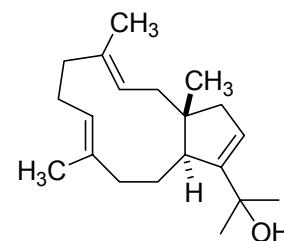
- The preparation of some interesting diterpenoids.***
- Development of some new methodology including a Wolff-based ring contraction.***
- A little of an interesting career sure to be with us during ours.***



dolabellatrienone



β -araneosene



palominol