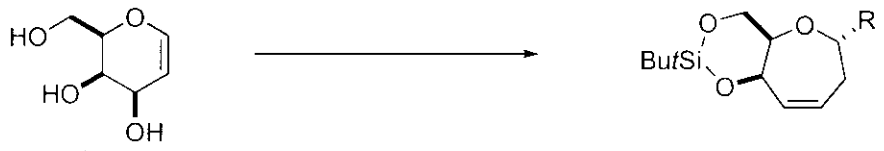
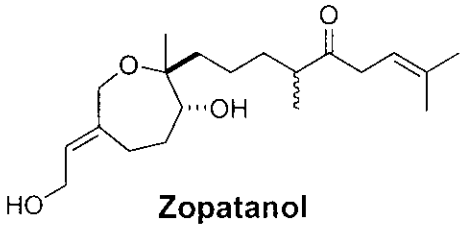
Diastereoselective formation of seven-membered oxacycles by ring-expansion of cyclopropanated galactal

Hoberg, J. O.; Batchelor, R. Tetrahedron Lett. **2003**, *44*, 9043.

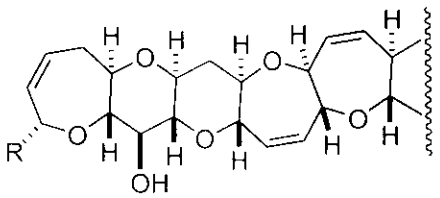


Some Natural Products Containing the Oxapane Core



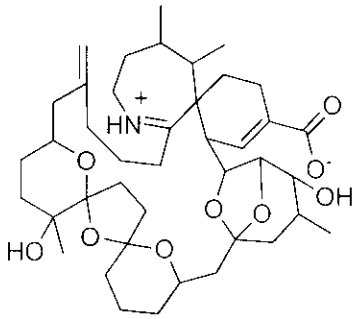
Zopatanol

Mexican folk medicine for antifertility



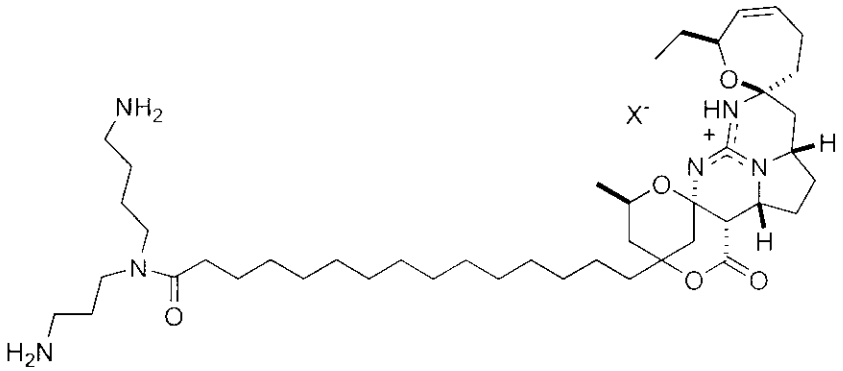
Ciguatoxin/Gambiertoxin

Polyether toxins



Pinnatoxin A

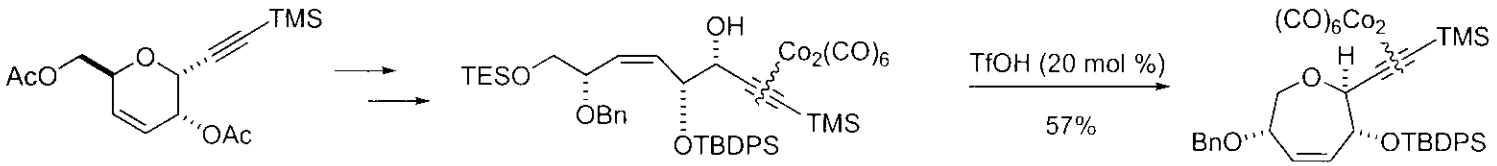
Ca^{2+} channel blocker



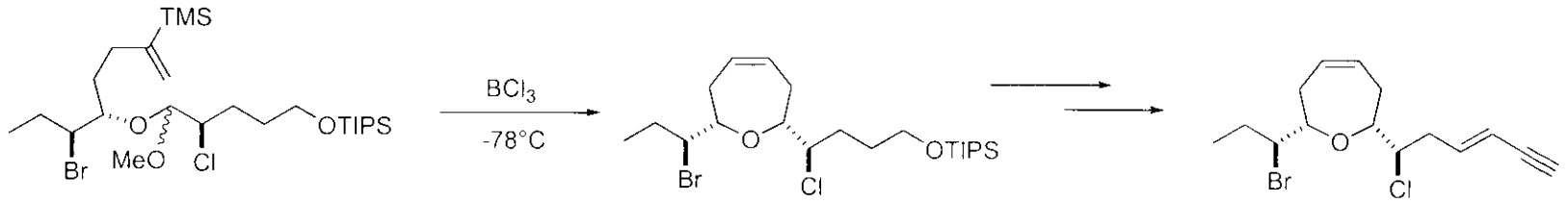
Ptilomycalin A

Antitumor, antiviral, antifungal, Ca^{2+} channel blocker

Some Methods to Prepare the Oxapane Core



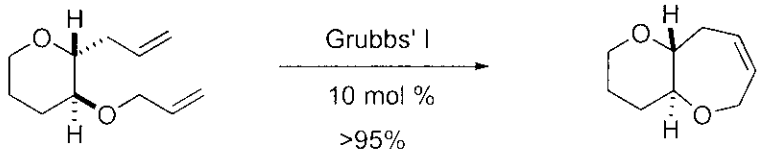
Isobe, M.; Shigeyoshi, T. *Tetrahedron Lett.* ***1994***, *35*, 7801



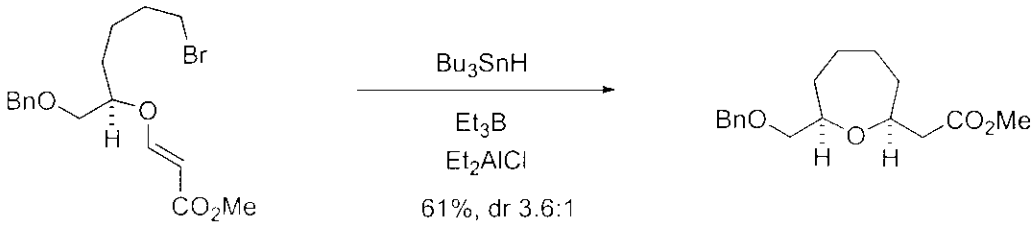
(+)-isolaurepinnacin

Berger, D.; Overman, L. E.; Renhowe, P. A. *J. Am. Chem. Soc.* **1993**, *115*, 9305

Some Methods to Prepare the Oxapane Core

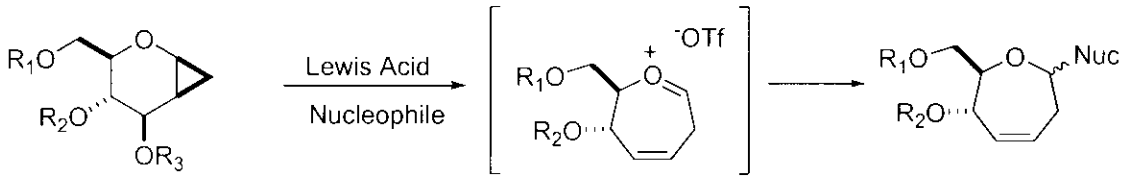


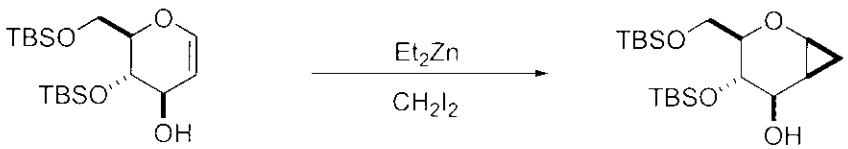
Delgado, M; Martin, J. D. *Tetrahedron Lett.* **1997**, 38, 6299

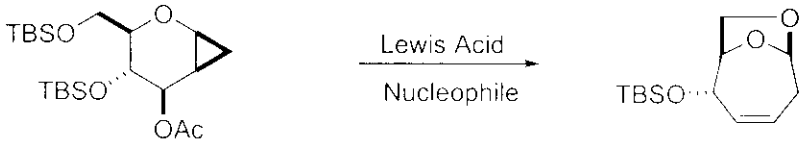


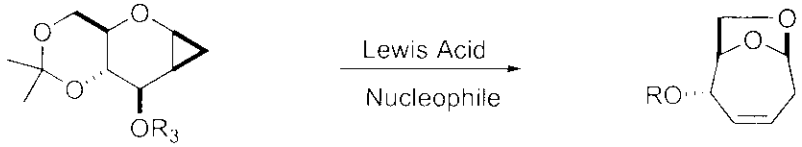
Yuasa, Y.; Sato, W.; Shibuya, S.; *Synth. Commun.* **1997**, *27*, 573

Initial Setbacks Concerning Protecting Group Lability

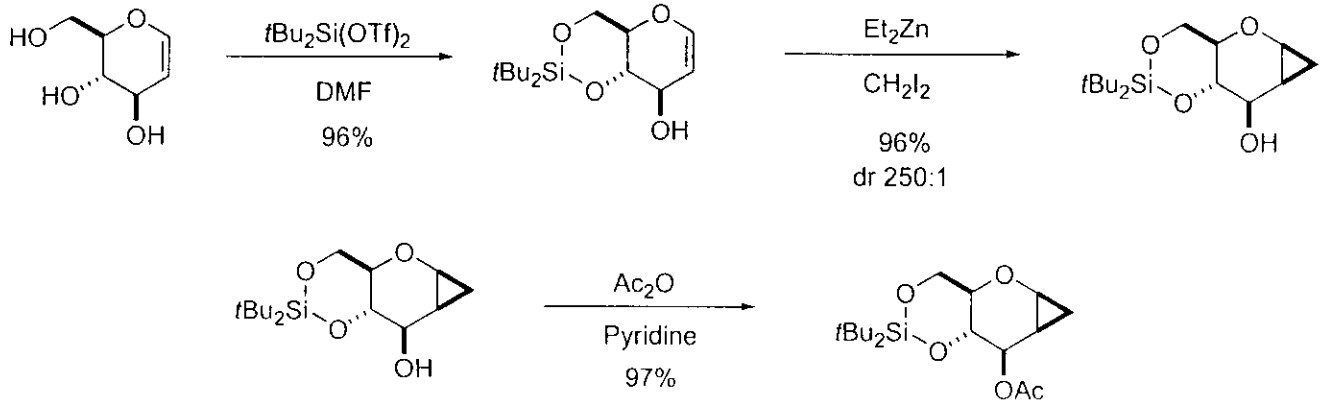


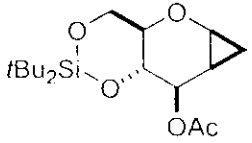




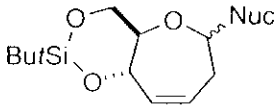


Oxapane Formation With Glucal Scaffold





R3SiNuc
TMSOTf (20 mol %)
MeCN



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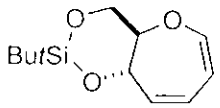

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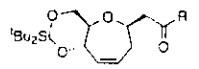
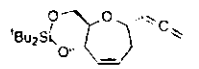
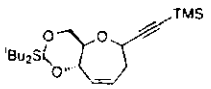
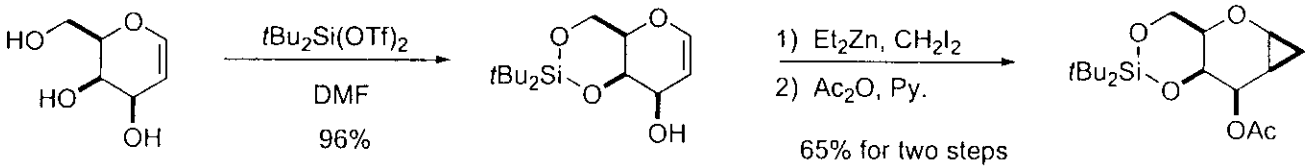
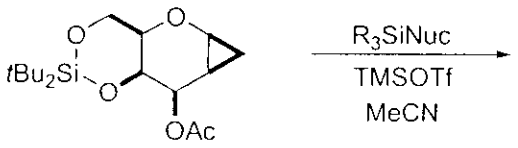
Table 1. Ring Expansion of 3

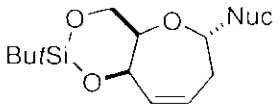
Entry	Nucleophile	Product (% yield)[a]	Diastereoselectivity[b]
1	$TMSN_3$	4a (95)	2:1
2	$TMSCH_2CH{=}CH_2$	4b (92)	1:1
3	TMSSPh	4c (93)	2:1
4	TMSCN	4d (82)	2:1
5	Et_3SiH	4e (73)	-
6			
	R = OEt	4f R = OEt (85)	2:1
	R = Ph	4g R = Ph (--)	
7			1:1
		4h (67)	
8			-
		4i (0)	
9		5 (81)	-

-Poor diastereoselectivity attributed to planar oxonium ion.

Increased Selectivity with Galactal Scaffold







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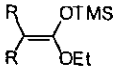
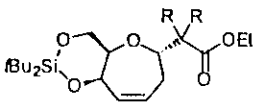
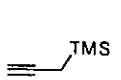
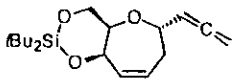
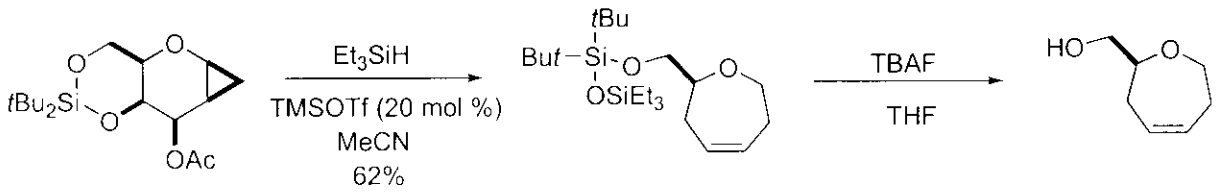
Entry	Nucleophile	Product (% yield)	Diastereoselectivity
1	TMSallyl	**5a** (91)	80:1
2	TMSSPh	**5b** (85)	6:1
3	$TMSN_3$	**5c** (69)	2.5:1
4	TMSOallyl	**5d** (00)	-
			
5	R = Me	**5e** (77)	80:1
6	R = H	**5f** (68)	3:1
7			7:1
		5g (68)	

[a] Determined on the crude reaction mixture by fused silica capillary gas chromatography.

-More facially biased oxonium intermediate provides higher diastereoselectivity

Deoxygenation at the 3-Position

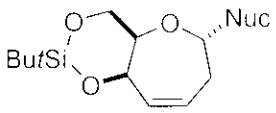


Conclusions

-Ring expansion of readily available stereodefined cyclopropanated galactals.

-Ring expansion occurs cleanly and the addition of nucleophiles occurs in good yields and with modest to excellent diastereoselectivity.

-Standard products have protected allylic oxygenation, protected primary oxygenation, a saturated allylic position as well as any functionality that comes in with nucleophile.



For a review on seven-membered oxacycles, see: Hoberg, J. O. *Tetrahedron* **1998**, *54*, 12631