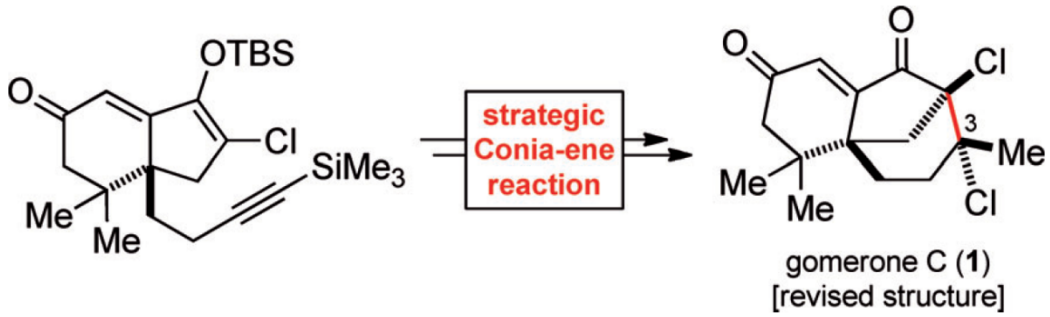
Total Synthesis and Stereochemical Revision of the Chlorinated Sesquiterpene (±)-Gomerone C

Huwyler, N.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2012**, *58*, Early View



gomerone C (**1**)
[revised structure]

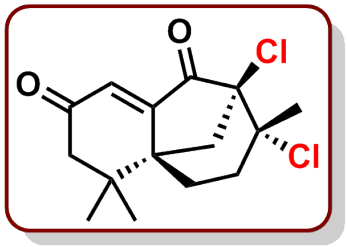
Current Literature

Jie Xu

12.01.12

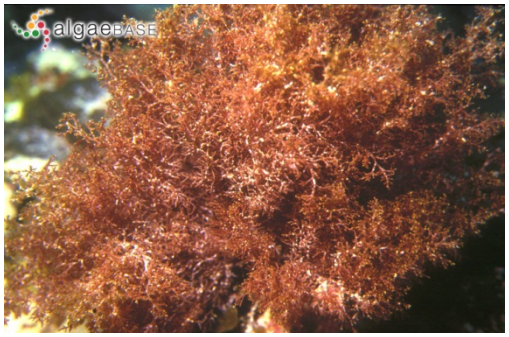
Isolation and Structure

- *Isolation from samples of Laurencia majuscula collected at the southern coast of La Gomera, Canary Islands.*
- *Unexplored biological activity*
- *Structure assigned by MS, IR and NMR (^{1}H, ^{13}C, DEPT, NOSEY, COSY).*



Gomerone C

- *Angular, tricyclic carbon skeleton*
- *Two chloride substituted tertiary carbon centers*



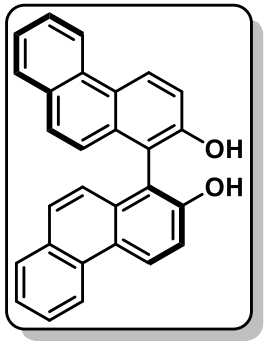
Laurencia Majuscula

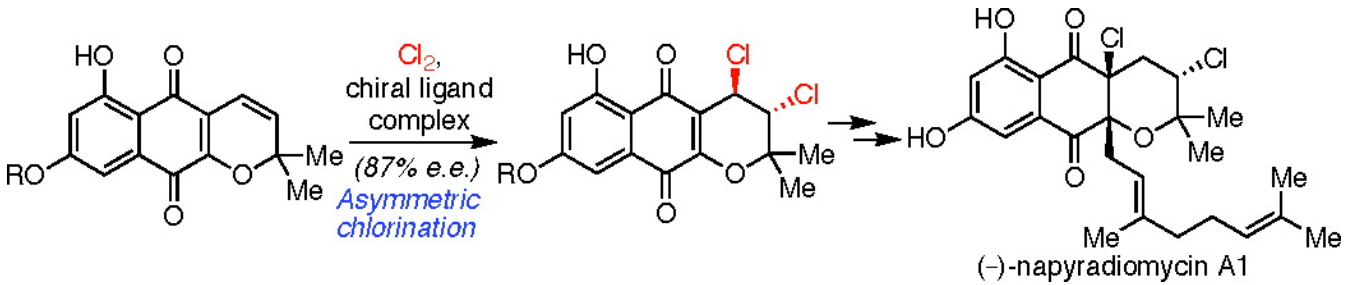
La Gomera

http://www.algaebase.org/_mediafiles/algaebase/3EE735B10772e02CC0ulS30C5A76/WF29bYakX2YC.jpg

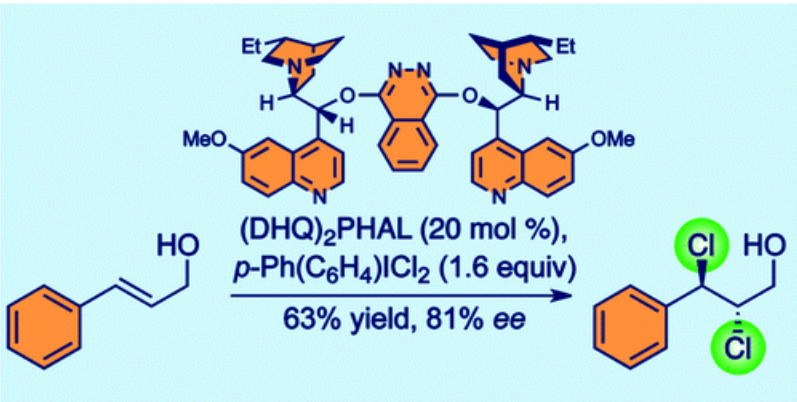
Diaz-Marrero, A. R.; Brito, I.; de La Rosa, J. M.; Darias, J.; Cueto, M. *Tetrahedron* **2008**, *64*, 10821 – 10824

Chlorinated Natural Products

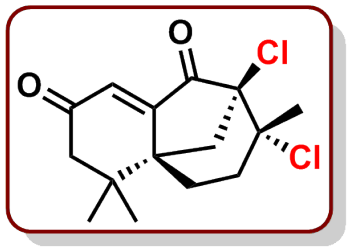




Snyder; S. A.; Tang, Z.; Gupta, R. *J. Am. Chem. Soc.* **2009,** 131, 5744 - 5745.



Nicolaou, K. C.; Simmons, N. L.; Ying, Y.; Heretsch, P. M.; Chen, J. S. *J. Am. Chem. Soc.*, **2011**, *133*, 8134 – 8137



Gomerone C

- ***Usually from chlorination of olefin under asymmetric catalyst***

Biogenetic Pathway

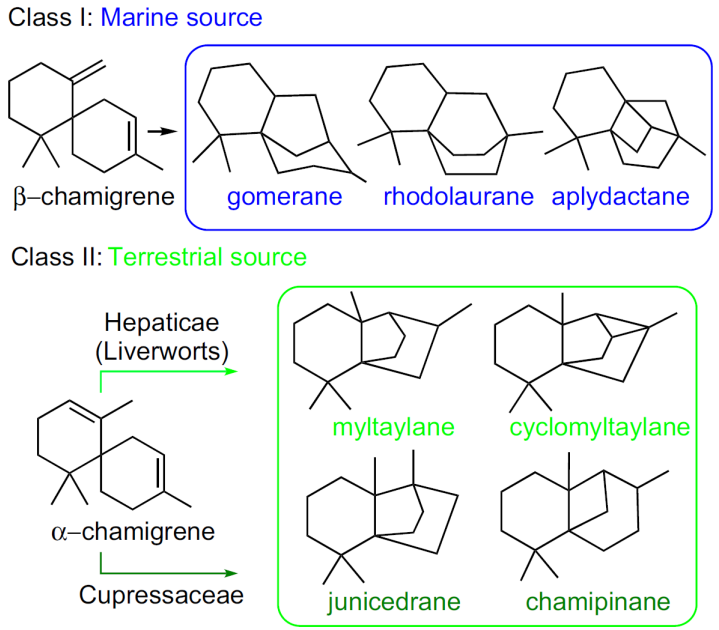
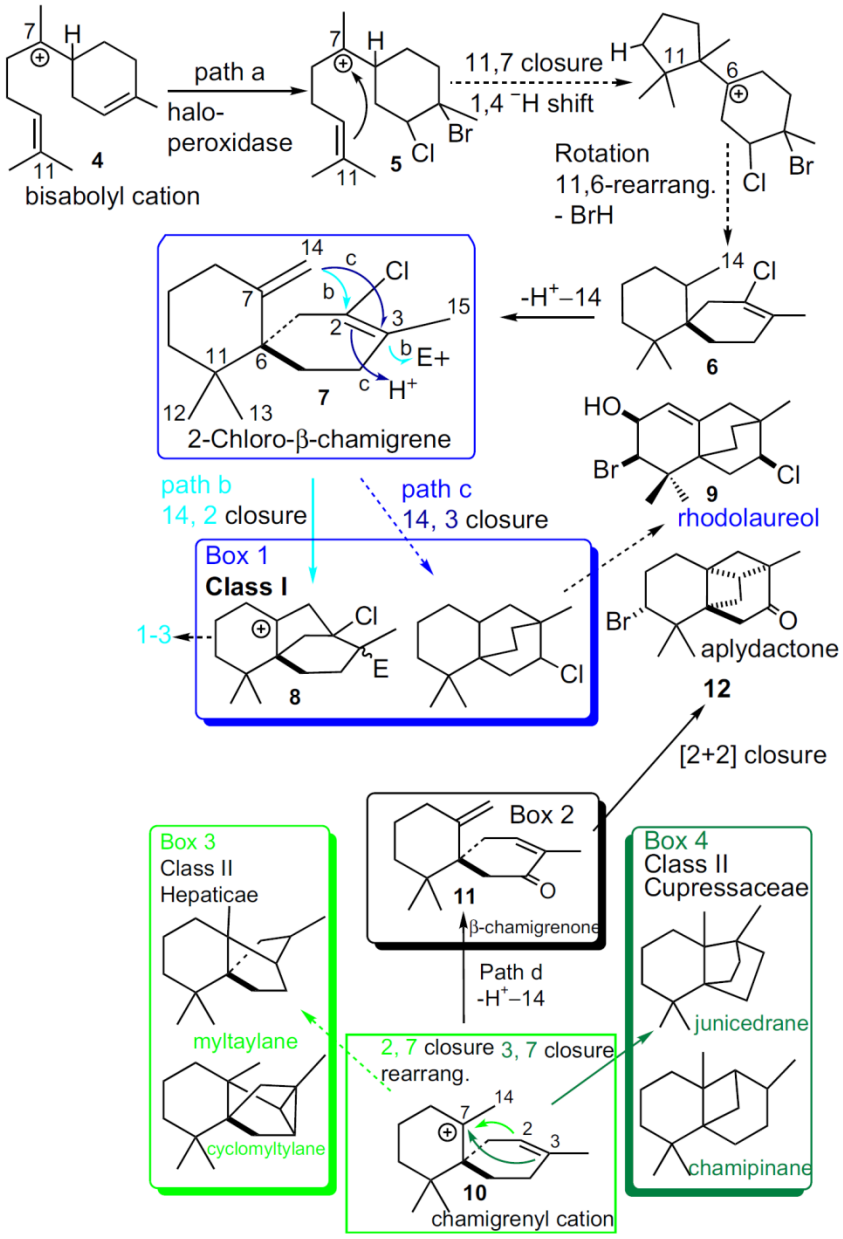


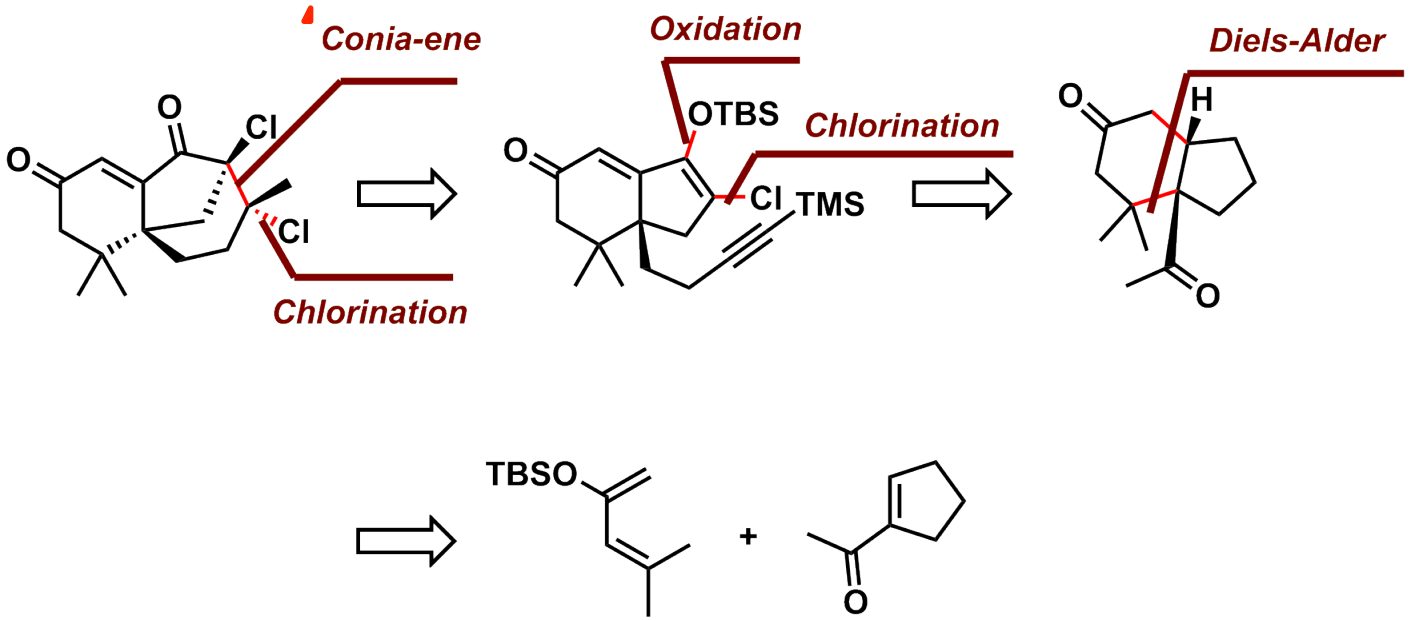
Figure 1. Class I and Class II of marine and terrestrial skeletons.



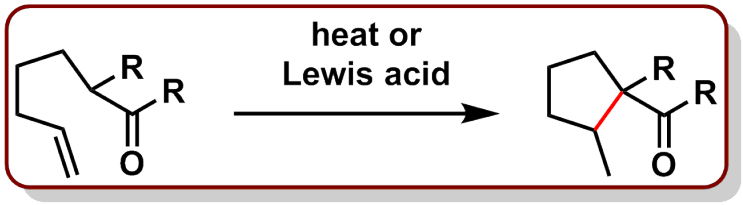
Scheme 1. Biogenesis of marine skeletons (Class I) and terrestrial skeletons (Class II).

Diaz-Marrero, A. R.; Brito, I.; de La Rosa, J. M.; Darias, J.; Cueto, M. *Tetrahedron* **2008**, *64*, 10821 – 10824

Retrosynthetic Analysis

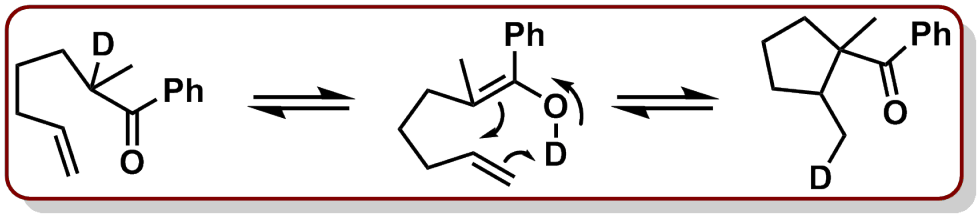


Unsaturated carbonyl compounds-> Cyclised products



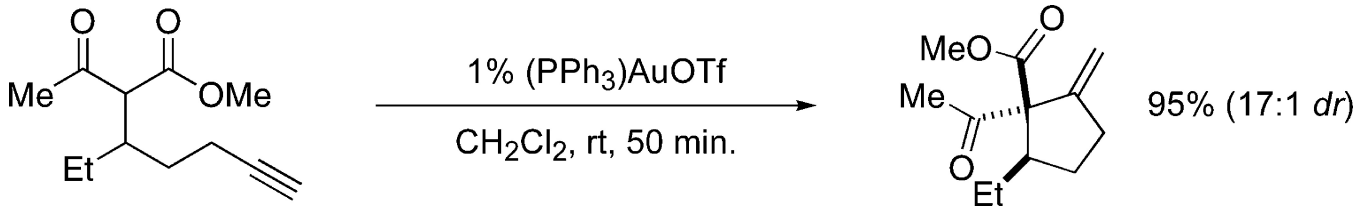
Conia, J. M.; Le Perchec, P. *Synthesis* **1975**, 1 – 19
Drouin, J.; Boaventura, M. A.; Conia, J. M. *J. Am. Chem. Soc.* **1985**, *107*, 1726 – 1729

Conia-ene Reaction

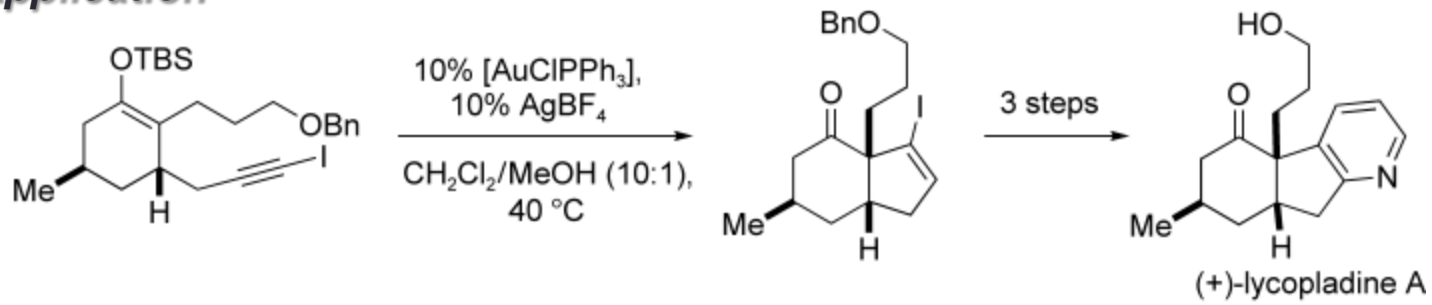


Enolisation is followed by a concerted 1,5-hydrogen shift

Lower temeperature



Application

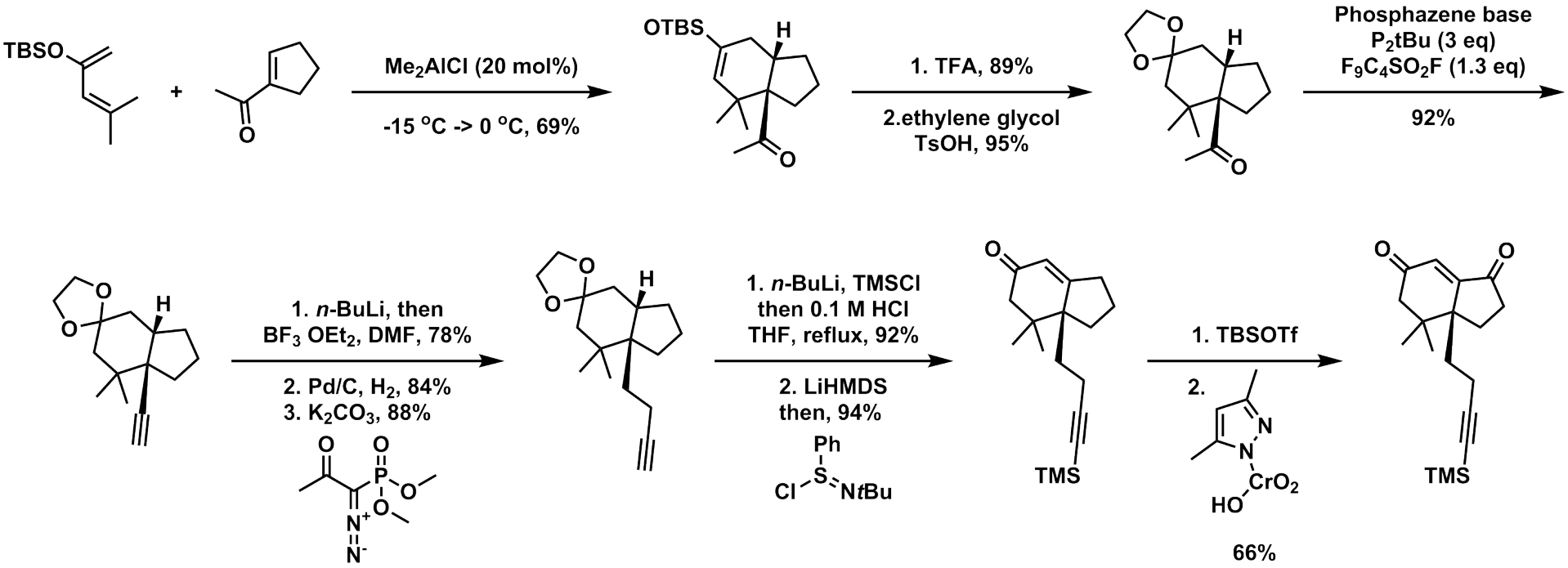


Conia, J. M.; Le Perchec, P. *Synthesis* **1975**, 1 – 19

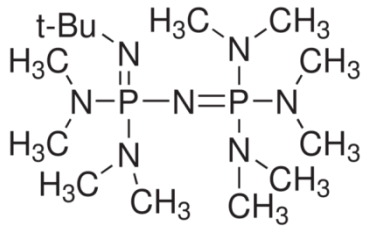
Kennedy-Smith, J. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.*, **2004**, *126*, 4526 – 4527

Staben, S. T.; Kennedy-Smith, J. J.; Huang, D.; Corkey, B. K.; LaLonde, R. L.; Toste, F. D. *Angew. Chem. Int. Ed.* **2006**, *45*, 5991 – 5994.

Synthesis

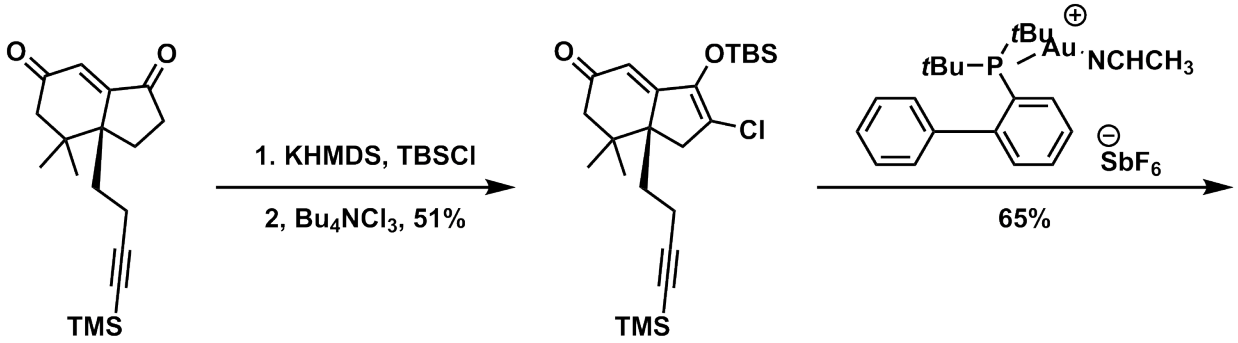


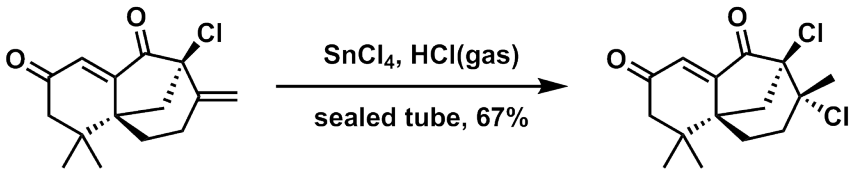
- ***Convert ketone to alkyne by strong base***
- ***Mukaiyama dehydrogenation***

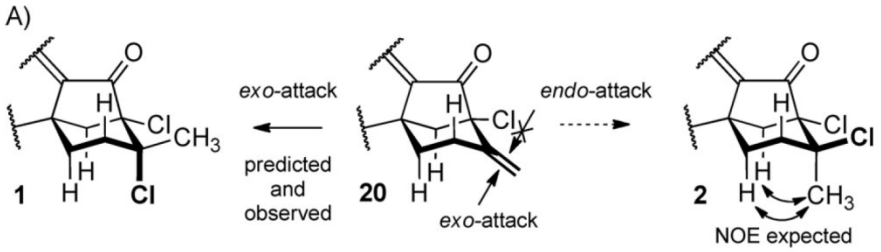


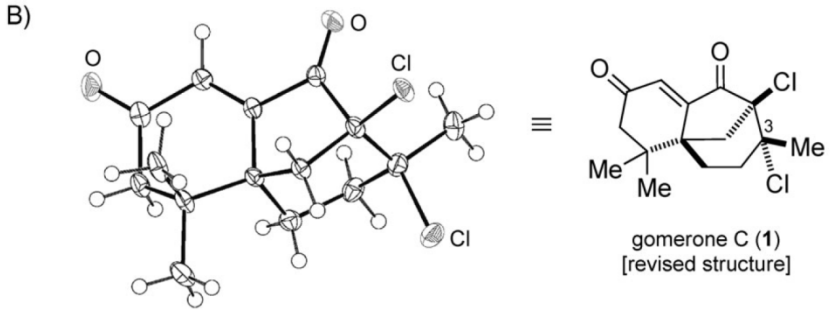
Phosphazene base P2-t-Bu

Structure Revision









Original Assignment
CH3: δ 1.90 (Compound 1),
δ 1.70(Compound 2)

Summary

- *The first synthesis of* (±)-Gomerone C *and their family members (15 steps 4% from known diene and cyclopentene)*
- *Diels–Alder Reaction*
- *Schwesinger's base/NfF (convert ketone to alkyne)*
- *Structure reassignment*