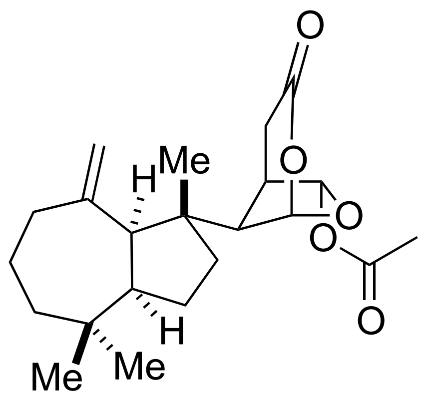
Angewandte Chemie International Edition

UNIVERSITÄT BERN

A Concise Synthesis of (–)-Aplyviolene Facilitated by a Stragetegic Tertiary Radical Conjugate Addition



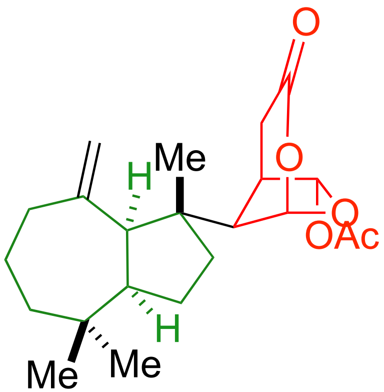
Schnermann, M. J.; Overman, L. E. *Angew. Chem. Int. Ed.* **2012**, 51, 9576.

February, 13th 2014

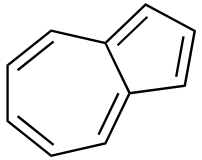
Presented by Julien

Introduction

- Isolated from sponges and nudibranchs (1986)
  (Class of rearranged spongian diterpene)
- 6-acetoxy-2,7-dioxabicyclo[3.2.1.]octan-3-one ring
- *Cis*-perhydroazulene fragment (bicyclo[5.3.0]decane)
- 7 stereogenic centers
- Second total synthesis of Aplyviolene

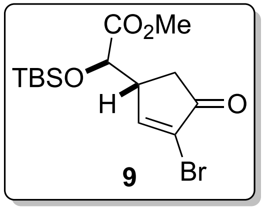


Aplyviolene
1

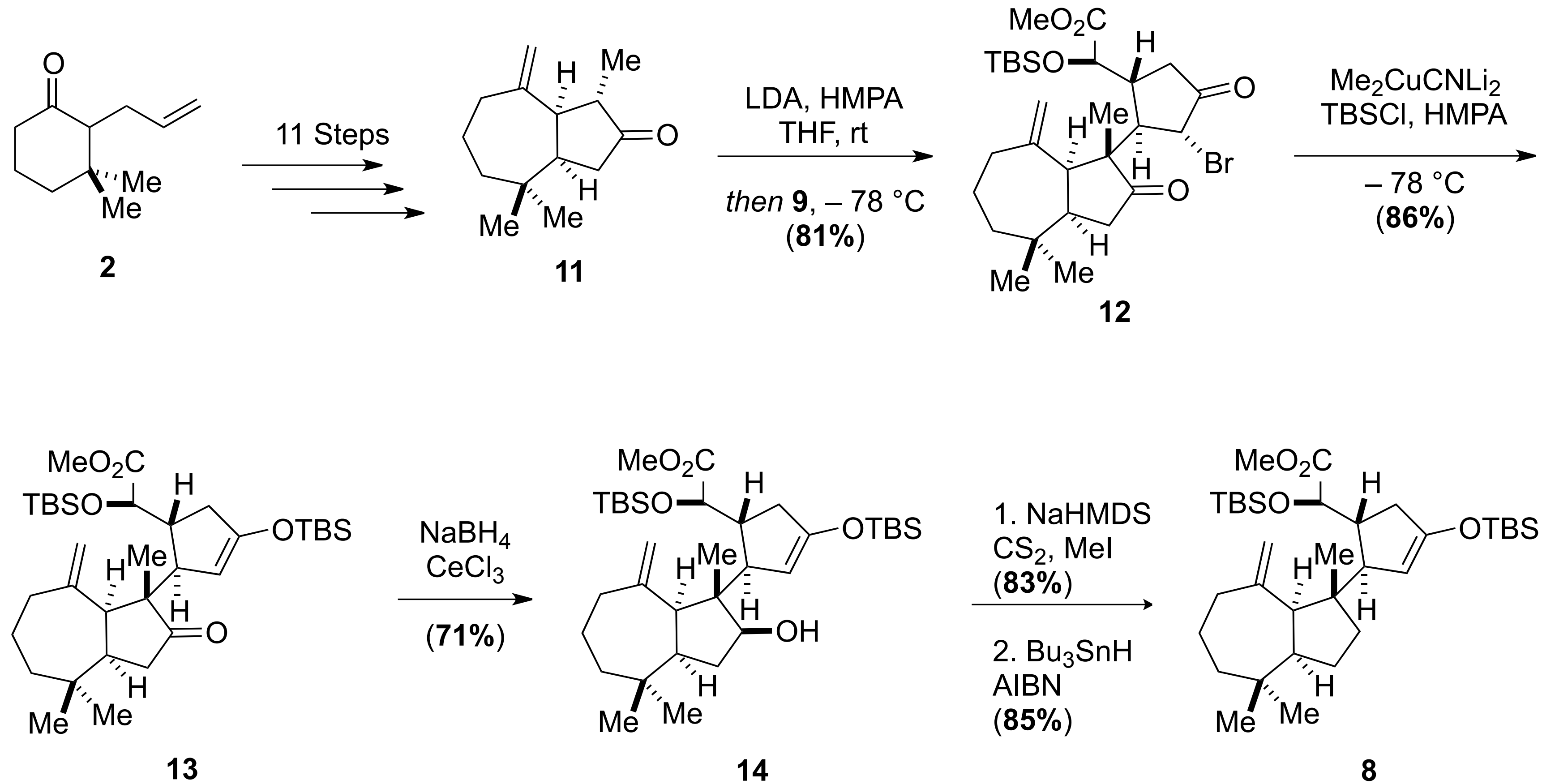


azulene

Hambley, T. W.; Poiner, A.; Taylor, W. C. *Tetrahedron Lett.* **1986**, *27*, 3281–3282.
Molinski, T. F.; Faulkner, D. J.; He, C. H.; Van Duyne, G. D.; Clardy, J. *J. Org. Chem.* **1986**, *51*, 4564–4567.

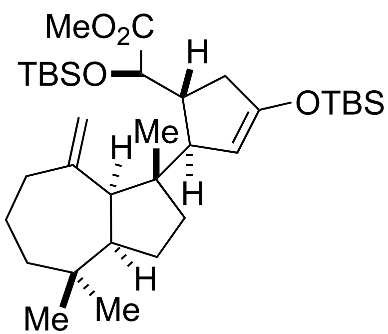


First generation Synthesis

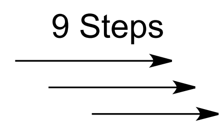


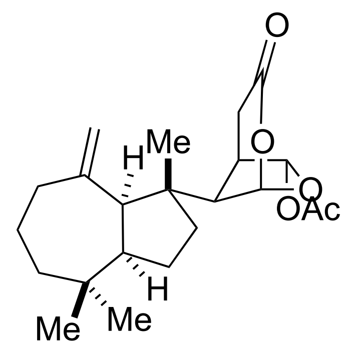
Schnermann, M. J.; Overman, L. E. *J. Am. Chem. Soc.* **2011**, *133*, 16425–16427.

First generation synthesis



8

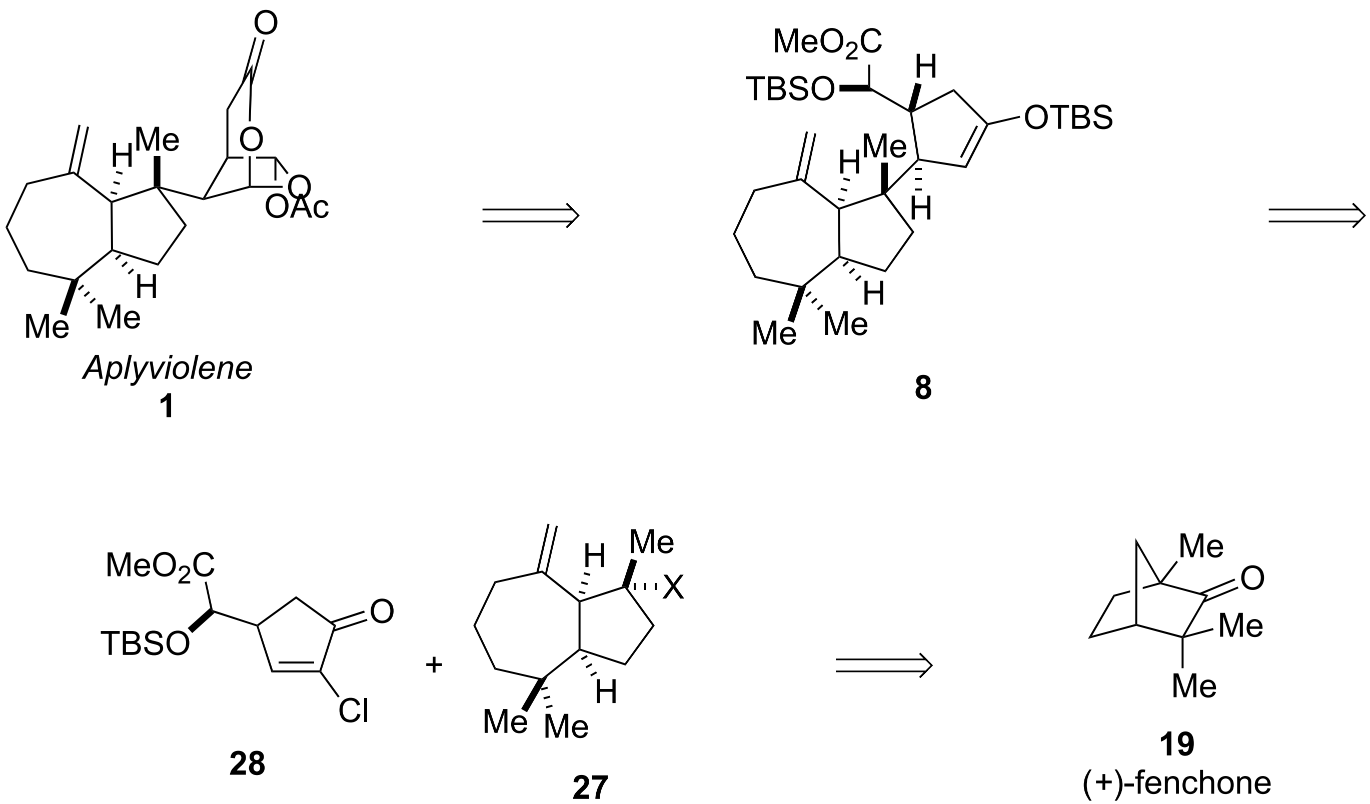




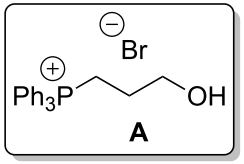
Aplyviolene
1

Schnermann, M. J.; Overman, L. E. *J. Am. Chem. Soc.* **2011**, *133*, 16425–16427.

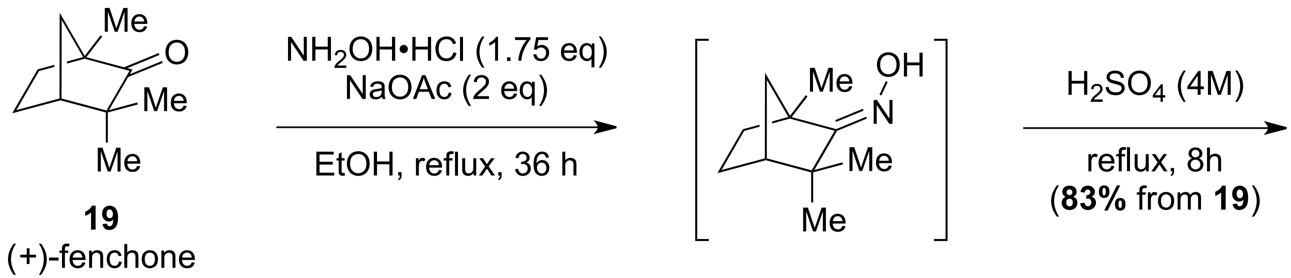
Second generation synthesis
Retrosynthesis

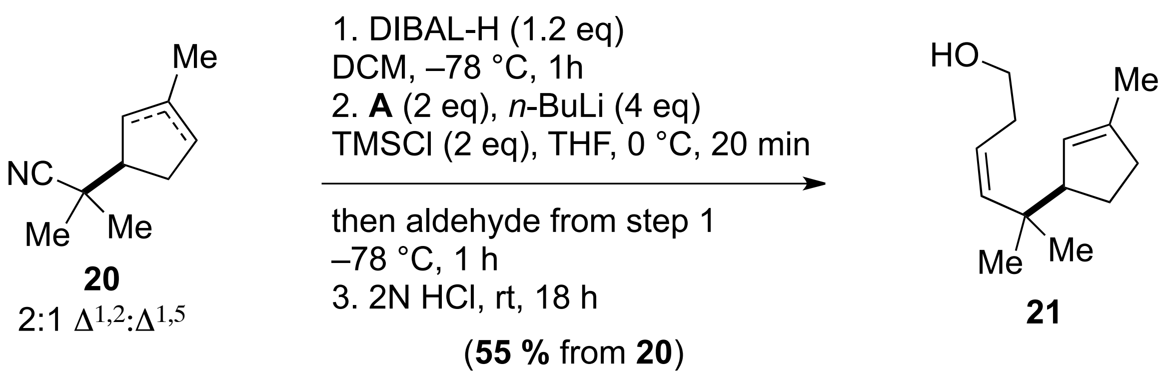


Schnermann, M. J.; Overman, L. E. *Angew. Chem. Int. Ed.* **2012**, *51*, 9576–9580.



Second generation Synthesis





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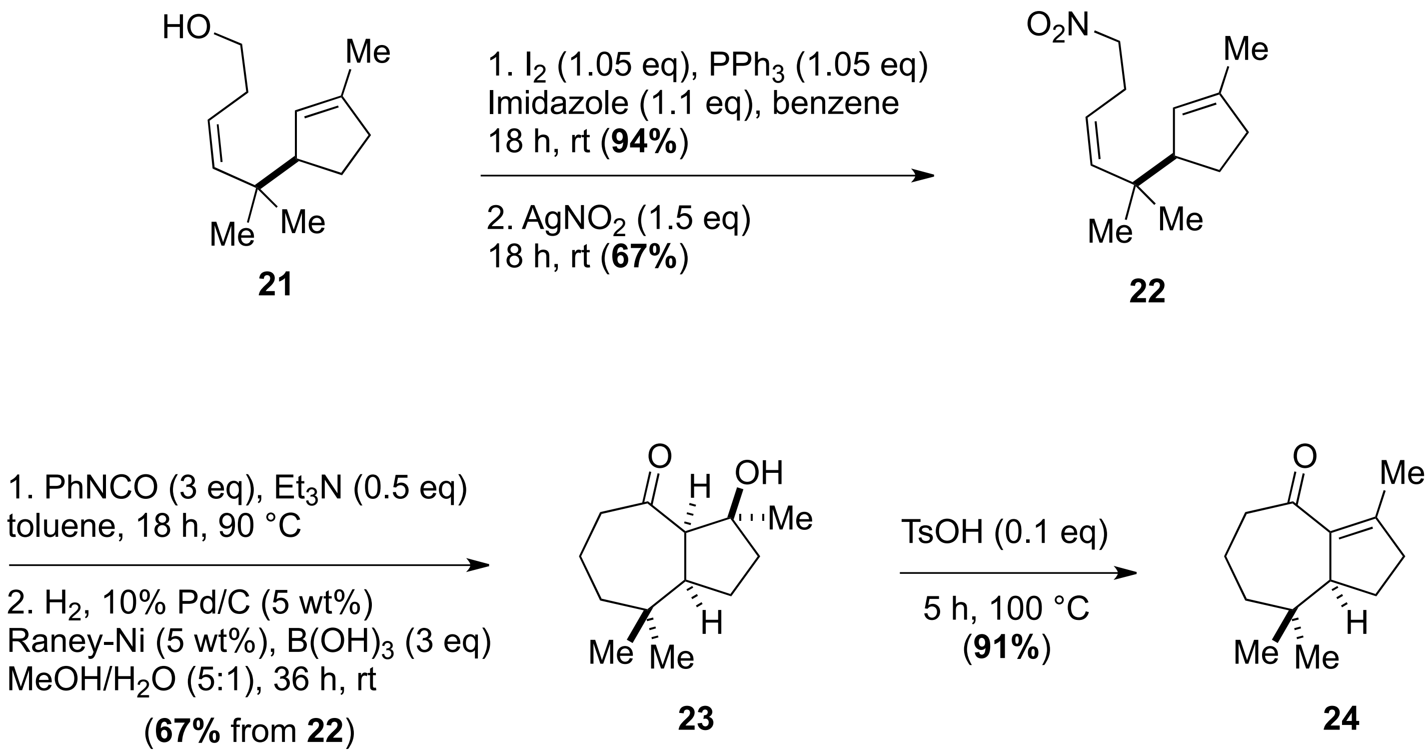
Second generation Synthesis



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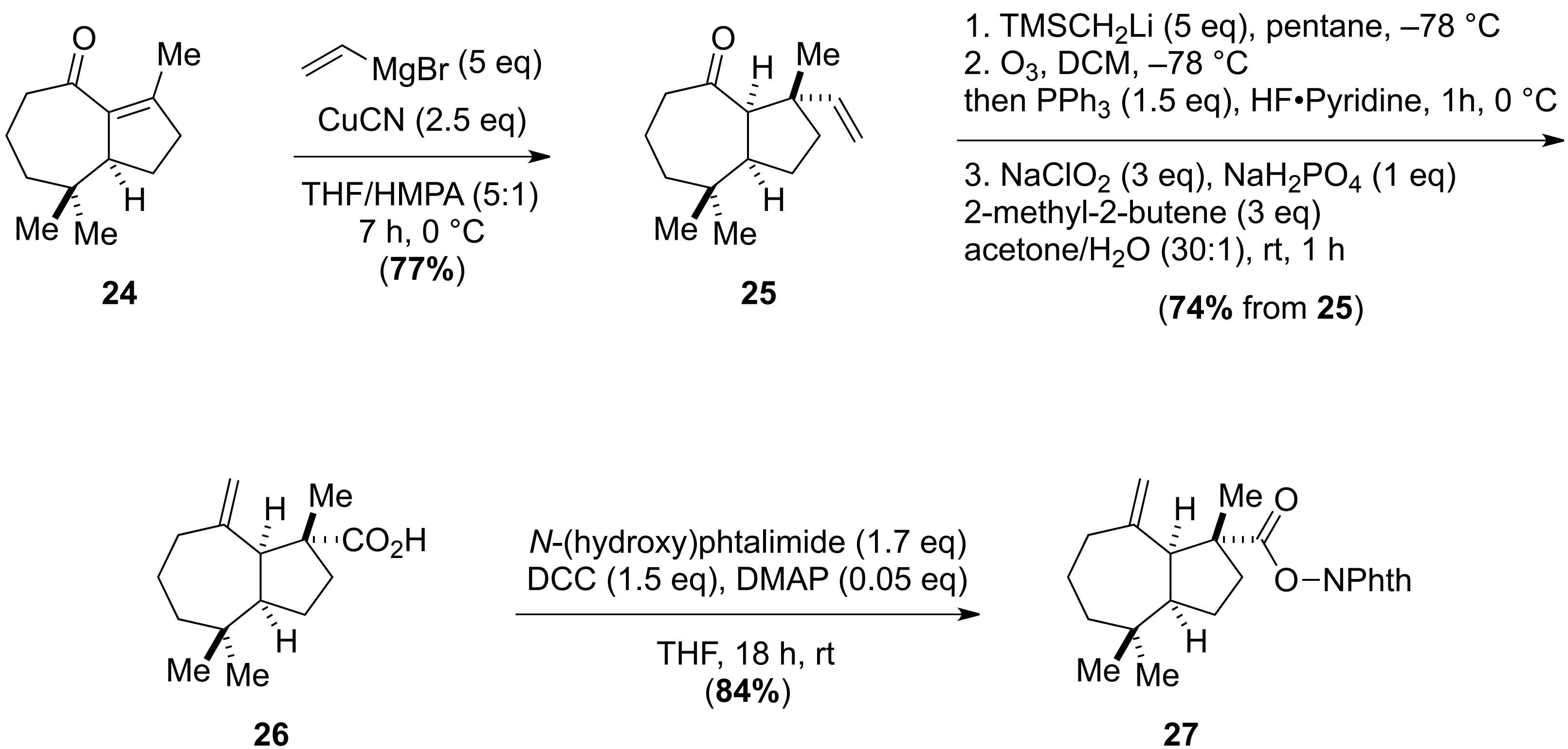
Second generation Synthesis



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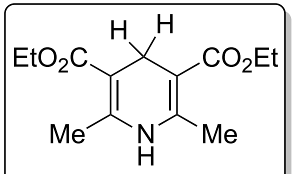
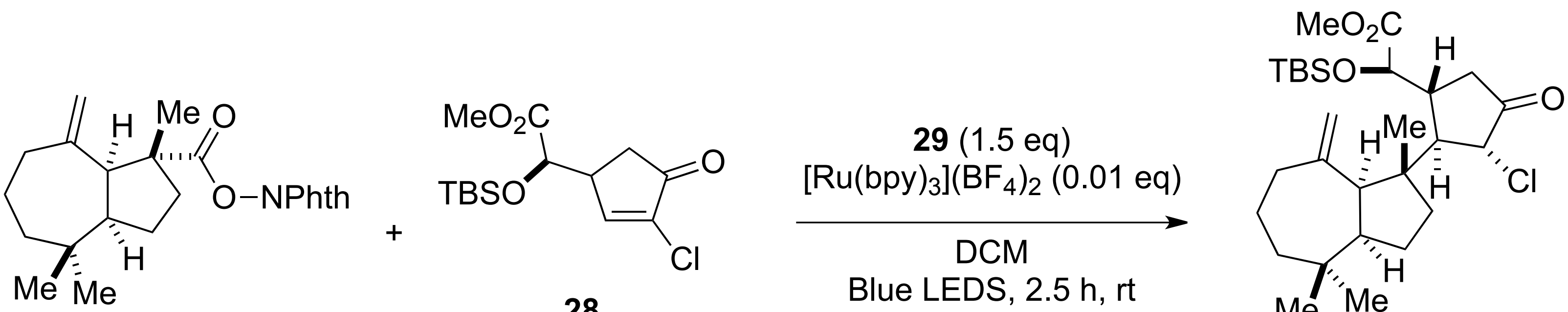


29

Second generation Synthesis



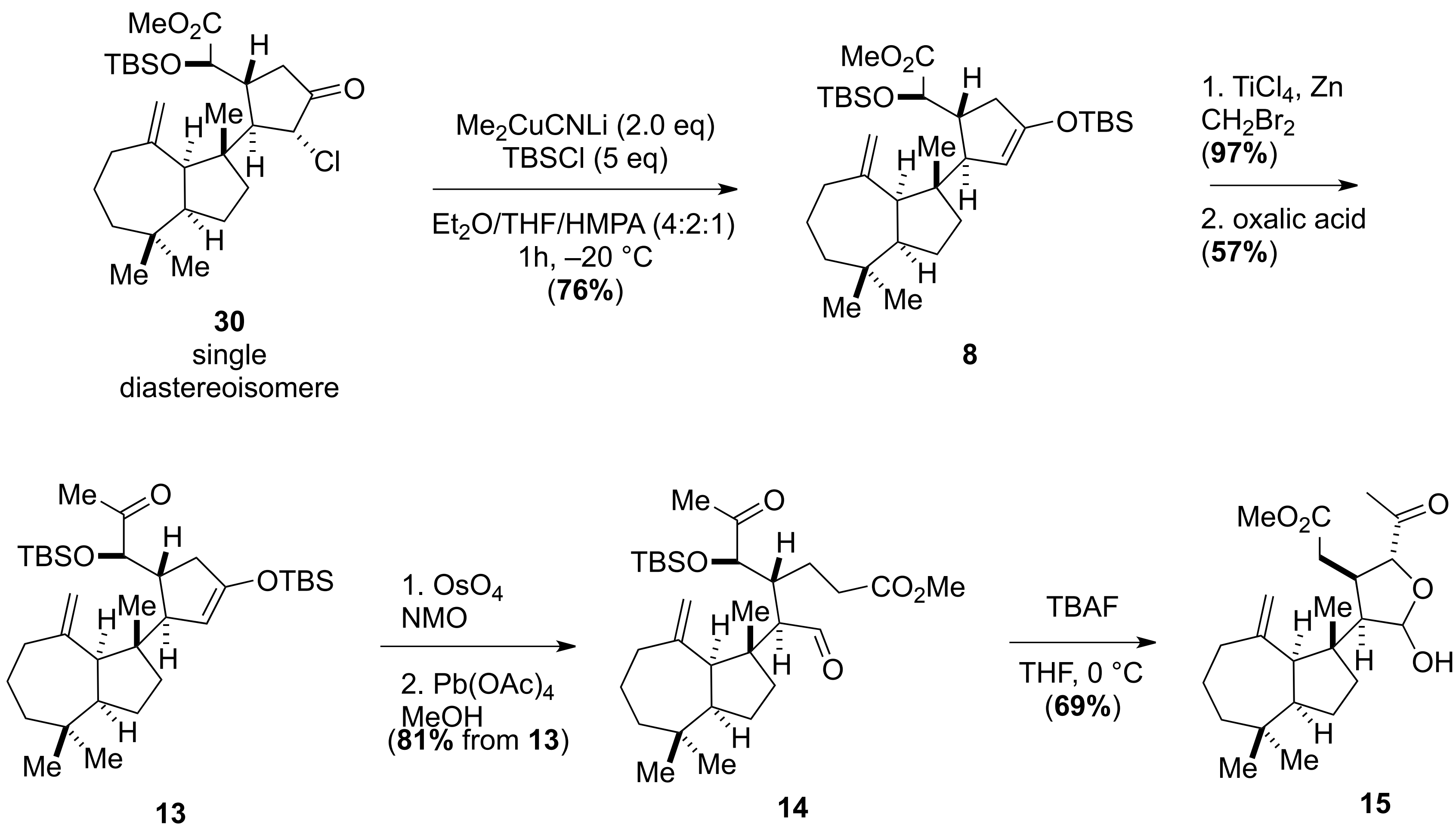
27

28
(1.5 eq)

30
single
diastereoisomere

Schnermann, M. J.; Overman, L. E. *Angew. Chem. Int. Ed.* **2012**, *51*, 9576–9580.

Second generation Synthesis



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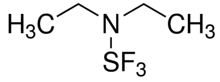
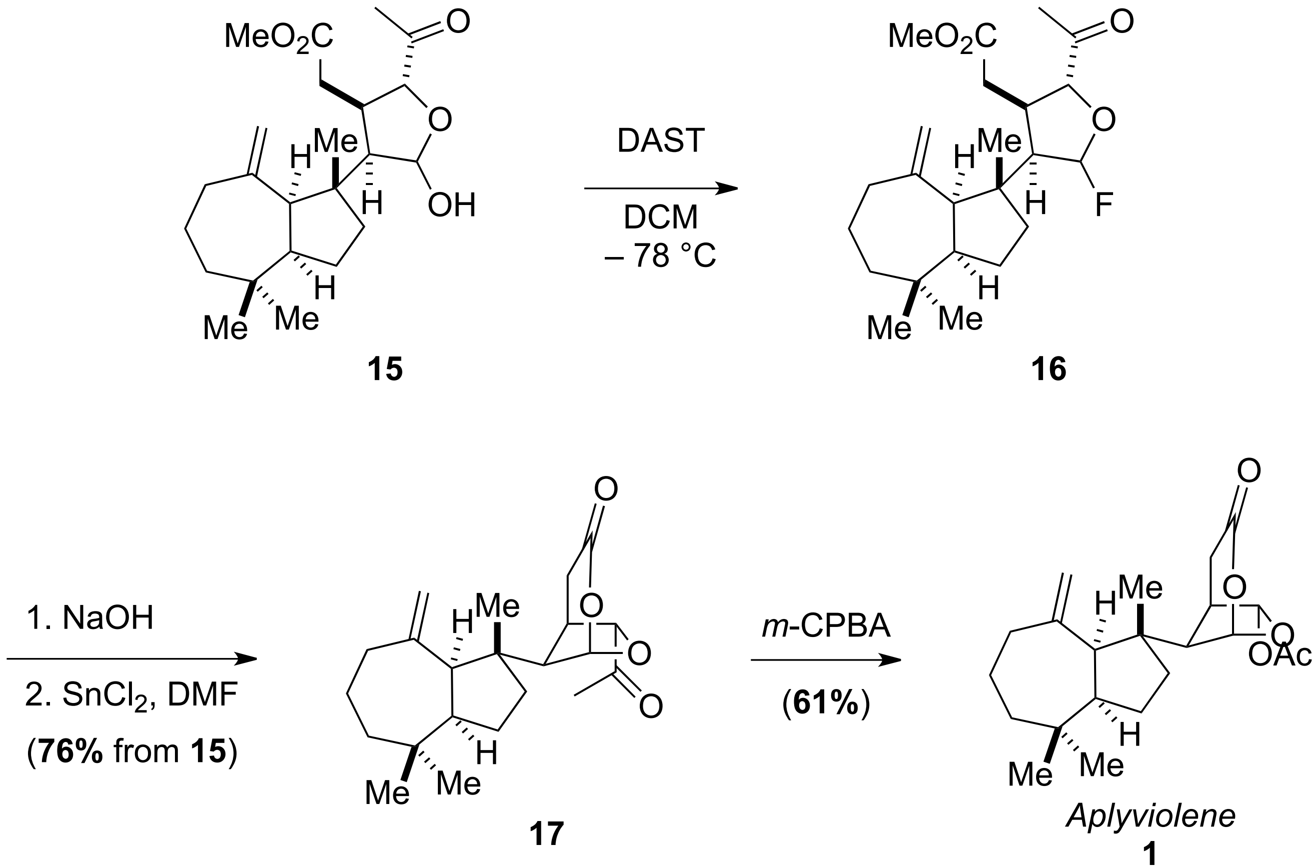


End of the Synthesis



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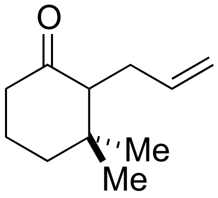
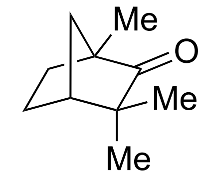


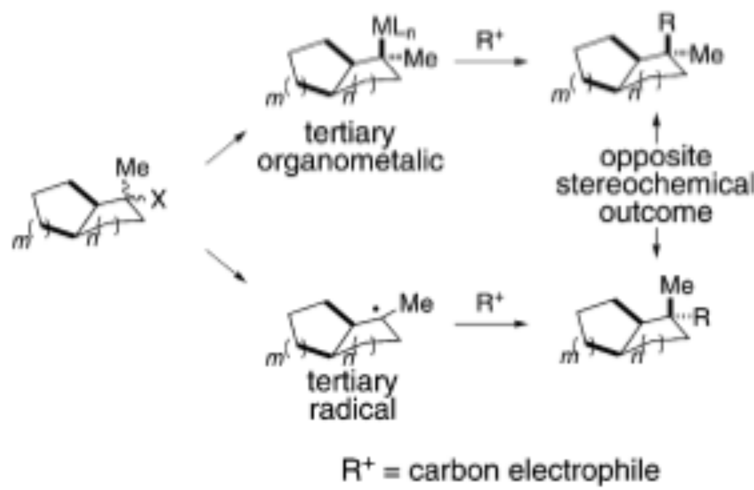
2

Conclusion



19
(+)-fenchone

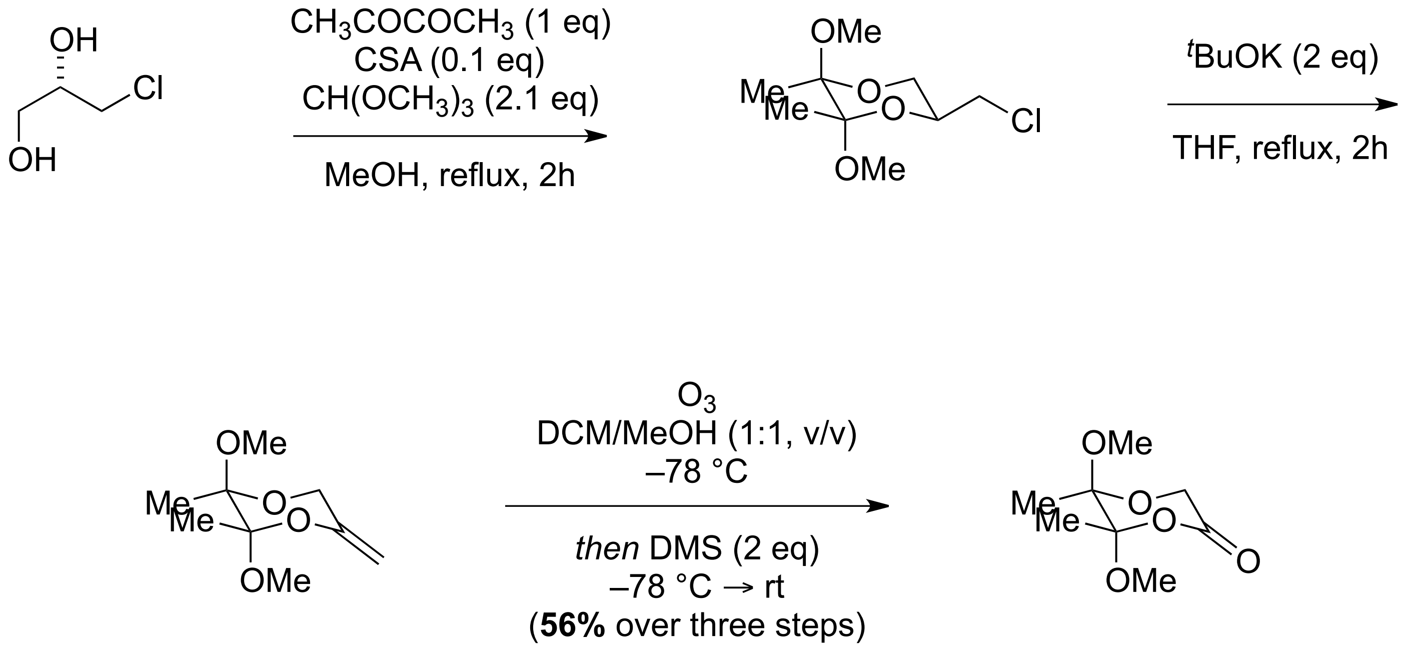
- Both synthesis by Overman (2011 and 2012)
  - 2011 : overall Yield = 0.7% (25 steps)
  - 2012: overall Yield = 0.6% (26 steps)
- 1st generation: Key step : Michael addition
- 2nd generation: Key step : Photoredox catalysis



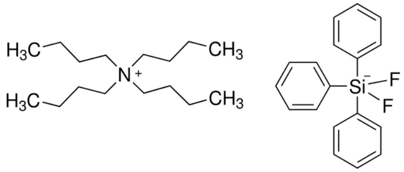
Schnermann, M. J.; Untiedt, N. L.; Jiménez-Osés, G.; Houk, K. N.; Overman, L. E. *Angew. Chem. Int. Ed.* **2012**, *51*, 9581–9586.

Thank you for your attention

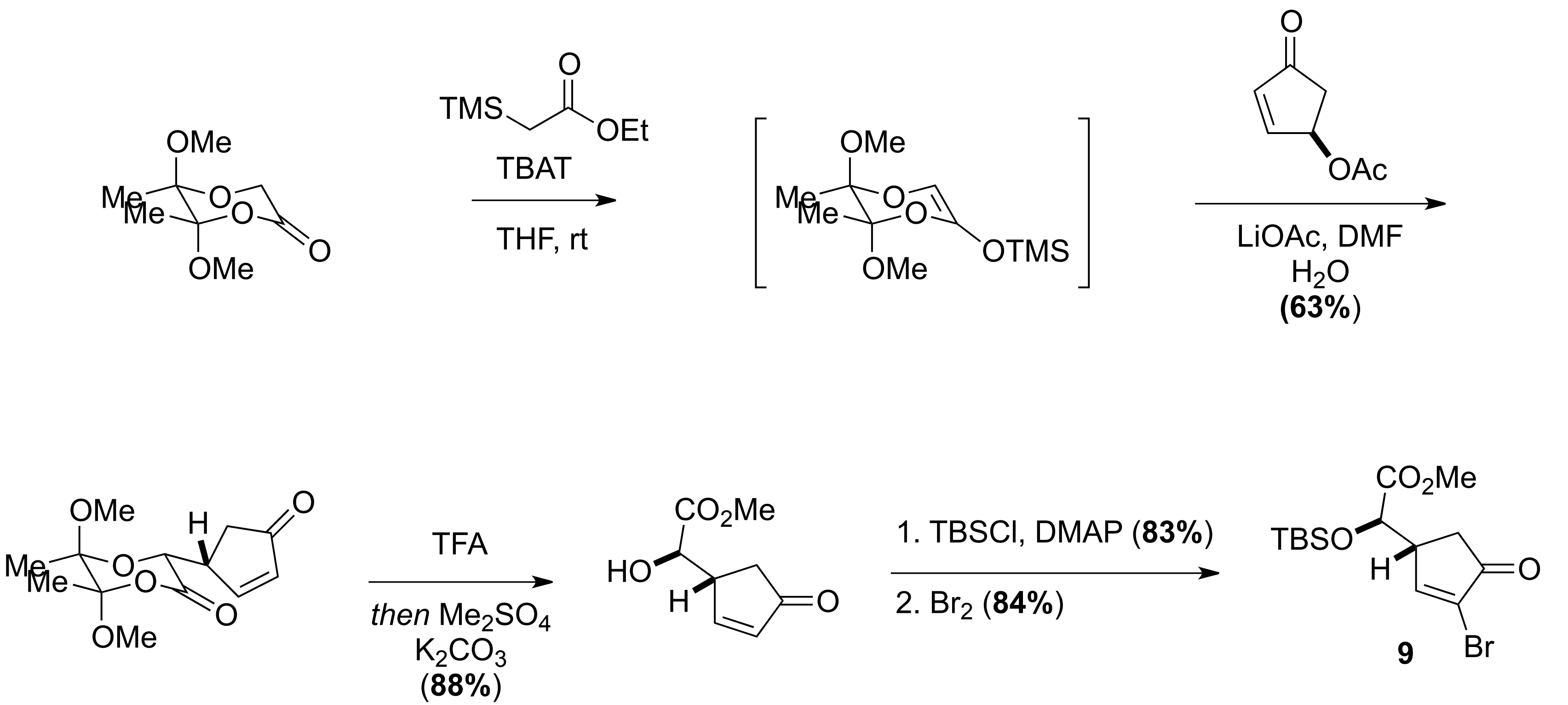
Synthesis of 9



Dixon, D. J.; Ley, S. V.; Polara, A.; Sheppard, T. *Org. Lett.* **2001**, *3*, 3749–3752.
Ley, S. V.; Baeschlin, D. K.; Dixon, D. J.; Foster, A. C.; Ince, S. J.; Priepke, H.; Reynolds, D. J. *Chem. Rev.* **2001**, *101*, 53–80.

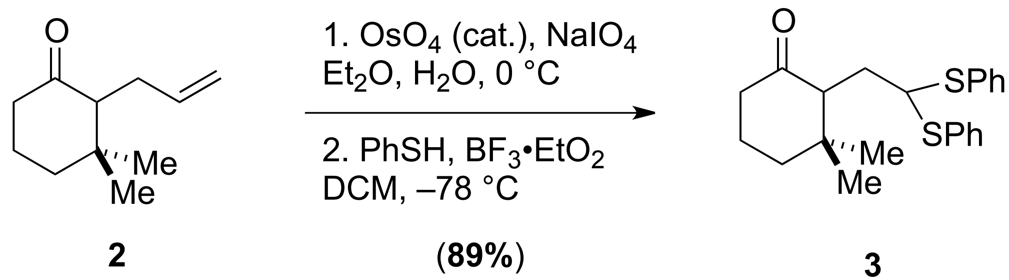


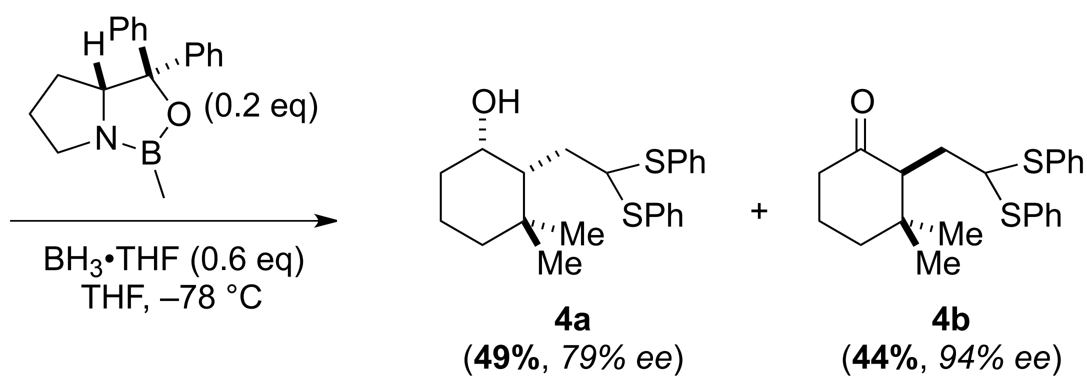
Synthesis of 9



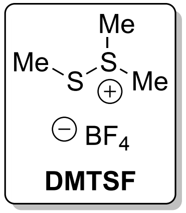
Schnermann, M. J.; Beaudry, C. M.; Genung, N. E.; Canham, S. M.; Untiedt, N. L.; Karanikolas, B. D. W.; Sütterlin, C.; Overman, L. E. *J. Am. Chem. Soc.* **2011**, *133*, 17494–17503.

Synthesis of 11

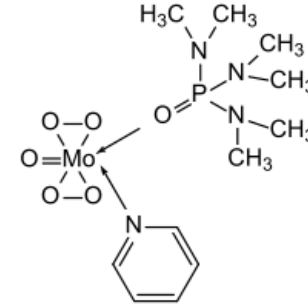


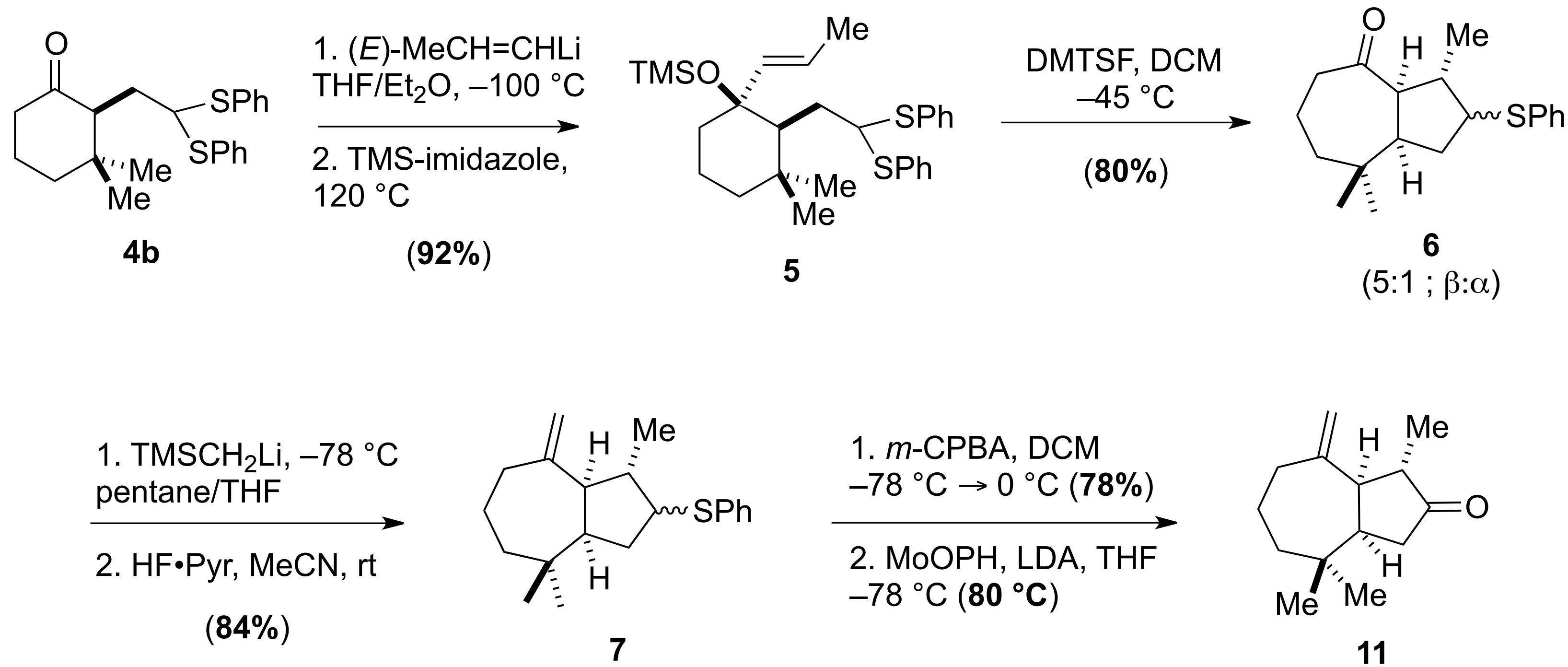


Lebsack, A. D.; Overman, L. E.; Valentekovich, R. J. *J. Am. Chem. Soc.* **2001**, *123*, 4851–4852.



Synthesis of 11





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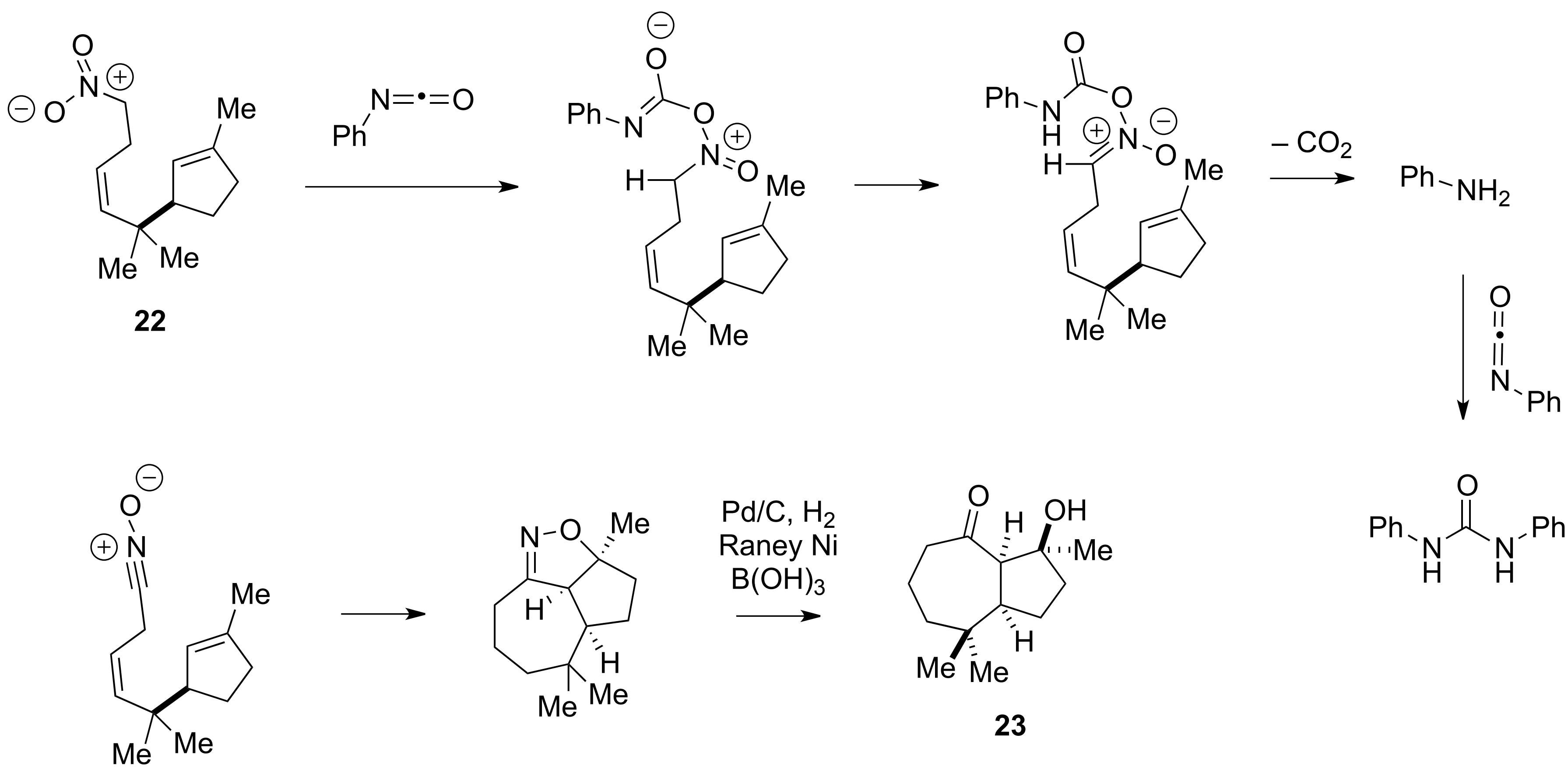
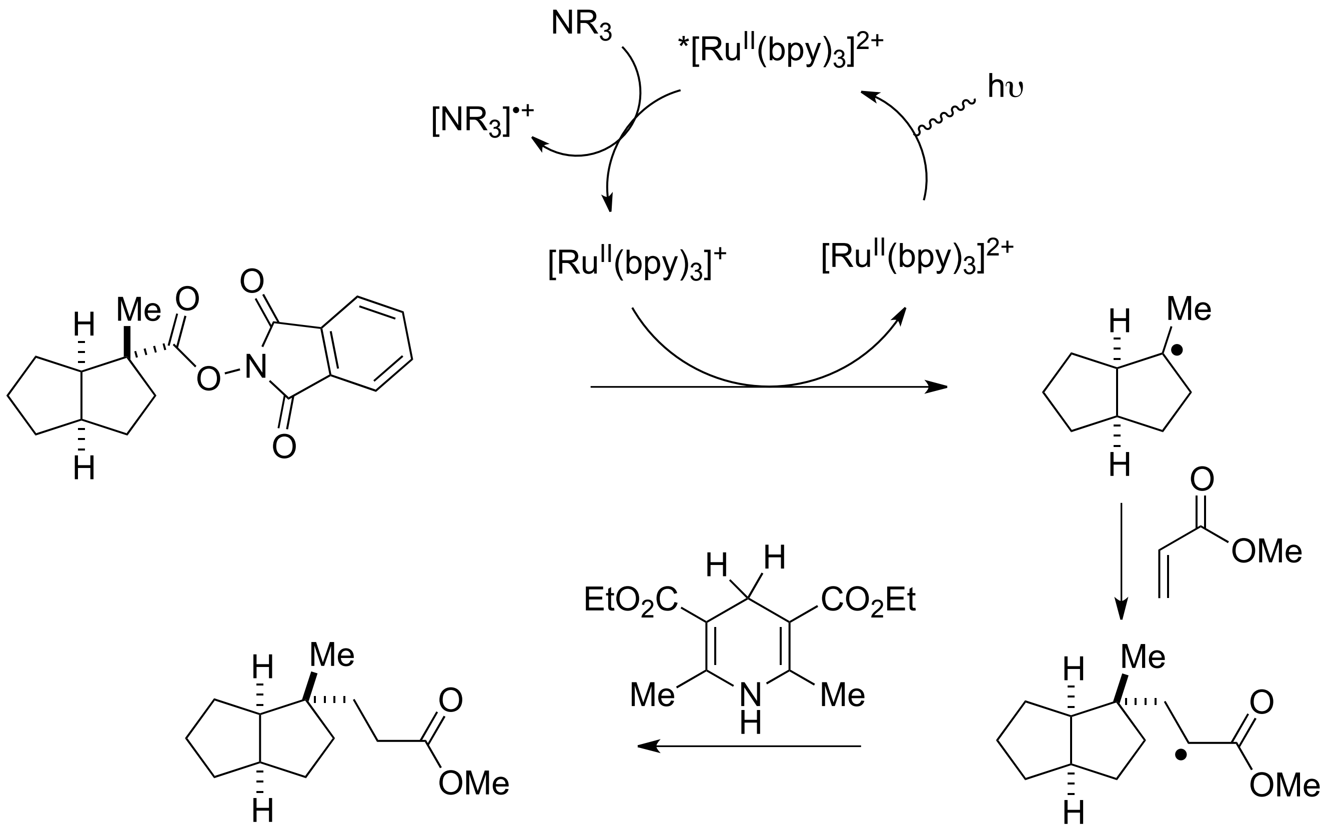
Mechanism



Mukaiyama, T.; Hoshino, T. *J. Am. Chem. Soc* **1960**, *82*, 5339–5342.
Curran, D. P. *J. Am. Chem. Soc.* **1983**, *105*, 5826–5833.

Mechanism



No reaction with : - tertiary chloride or bromide

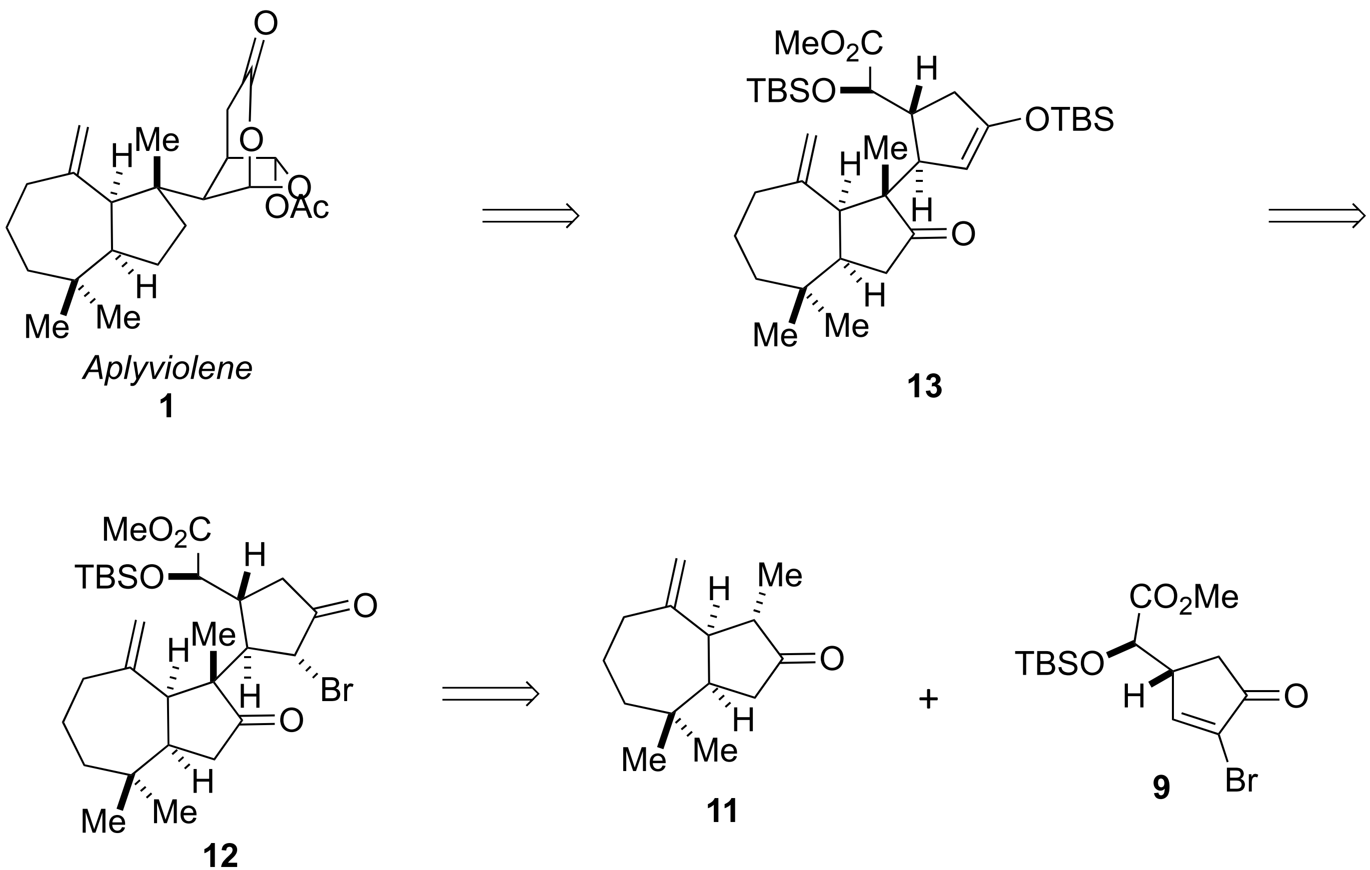
- Barton ester

Okada, K.; Okamoto, K.; Morita, N.; Okubo, K.; Oda, M. *J. Am. Chem. Soc.* **1991**, *113*, 9401–9402.

Andrews, R. S.; Becker, J. J.; Gagné, M. R. *Angew. Chem. Int. Ed.* **2010**, *49*, 7274–7276.

Andrews, R. S.; Becker, J. J.; Gagné, M. R. *Org. Lett.* **2011**, *13*, 2406–2409.

First generation synthesis
Retrosynthesis



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