

# Enantioselective Total Synthesis of ( )-Euphorikanin A

Moritz J. Classen, Markus N. A. Böcker, Remo Roth, Willi M. Amberg,  
and Erick M. Carreira\* *J. Am. Chem. Soc.* 2021, 143, 8261-8265.

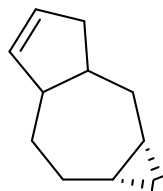
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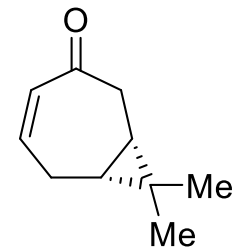
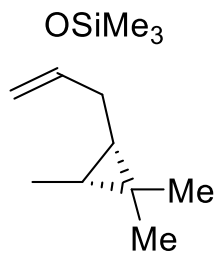
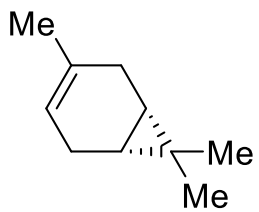
- “ First total synthesis of (+)-euphorikanin A, an ingenane-derived natural product
  - “ Isolated in 2016 and identified as a novel diterpenoid from the roots of *Euphorbia kansui*, commonly known as kansui
  - “ Extracts of the root have been widely used in traditional Chinese medicine. (+)-euphorikanin A has been shown to exhibit cytotoxicity against two human tumor cell lines (NCI-446 and HeLa)
  - “ Features an unprecedented 5/6/7/3-fused tetracyclic skeleton
  - “ Prepared in 19 steps from (+)-3-carene
  - “ Key step is an SmI<sub>2</sub>-mediated ketyl-enoate cyclization cascade
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Ricky Alvarado  
November 16th, 2021

# Retrosynthesis

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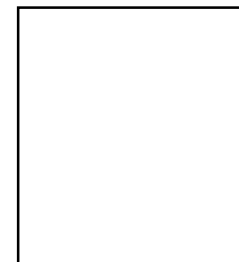
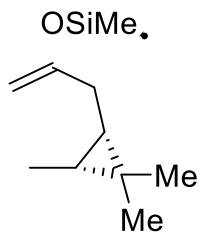




Ozonolysis and formation of silyl ketene acetal



Acid-cyclization and dehydration

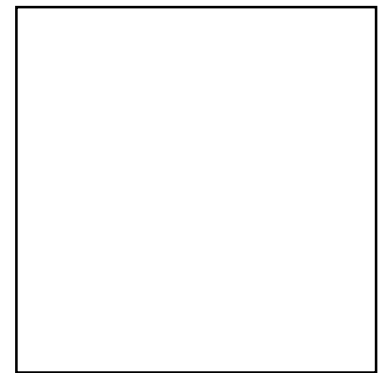
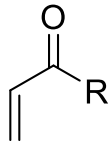


(5)  $\text{Me}_2\text{CuLi}$   
Et

Conjugate addition . Aldol addition

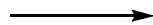
$\text{CuI} + \text{MeLi}$

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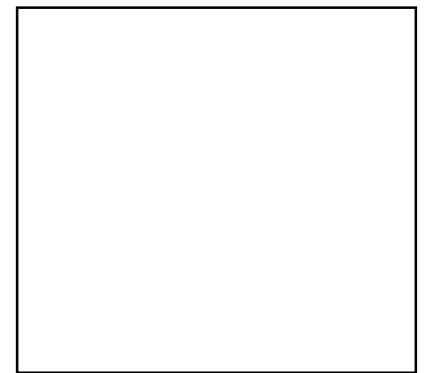


Alcohol protection with TBSOTf

Si



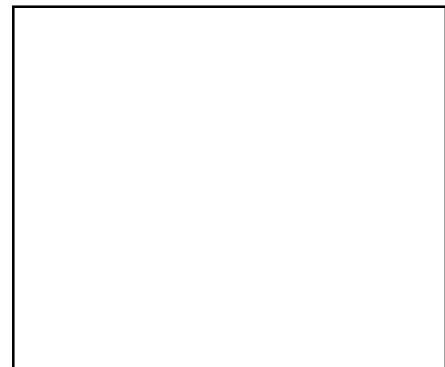
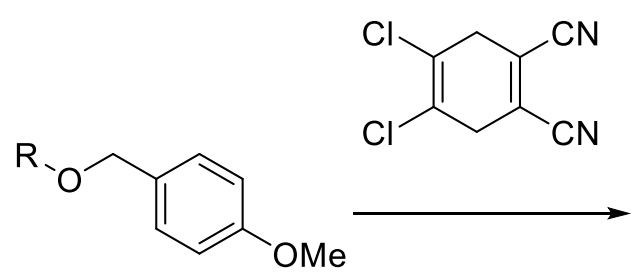
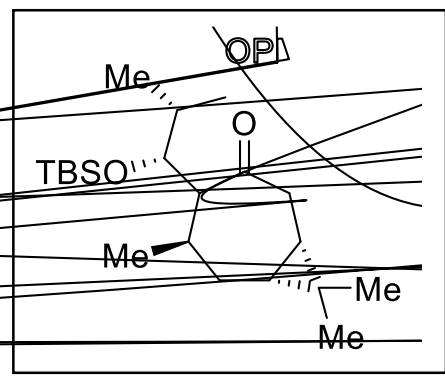
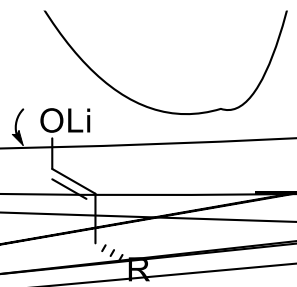
$\text{R}-\text{OTBS} \equiv$



(7) LiHMDS, 11  
THF,

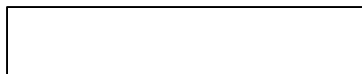
Enolate addition

*p*-OMe Benzyl Deprotection



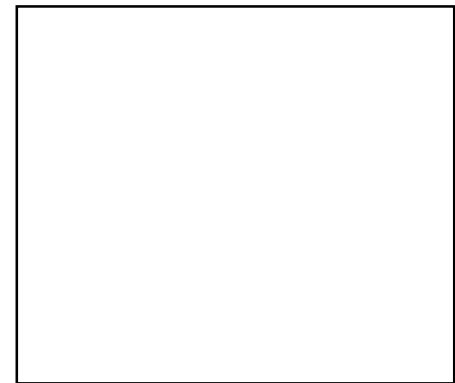
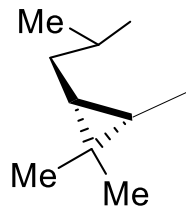
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Parikh-Doering Oxidation





Umpolung Cyclization via Reduction with SmI2 . Undesired Stereoisomer



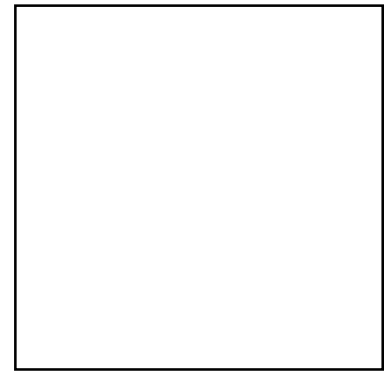




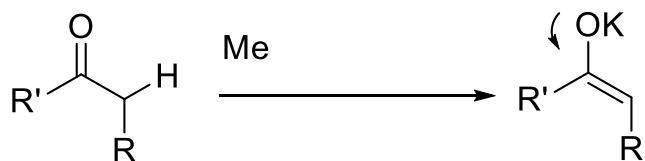


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TBS Deprotection



Davis Oxidation . DMP Oxidation



Dess-Martin Oxidation



Metallation . 1,2-addition

