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.

- 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 SmI2-mediated ketyl-enoate cyclization cascade

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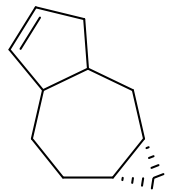
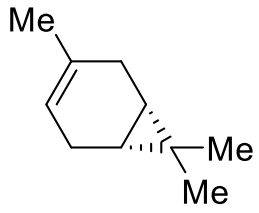
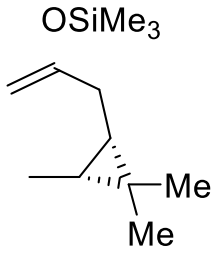
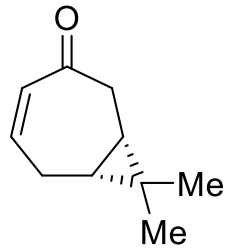
Ricky Alvarado
November 16th, 2021

Retrosynthesis

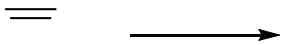


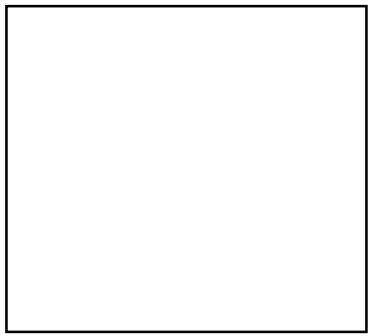




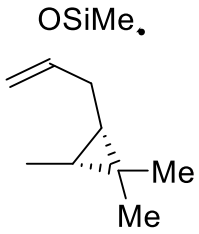


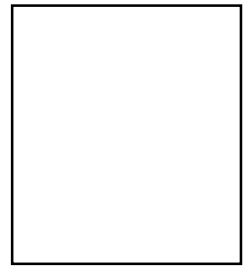
Ozonolysis and formation of silyl ketene acetal





Acid-cyclization and dehydration

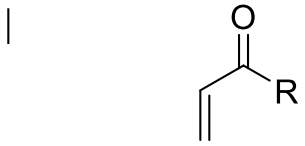


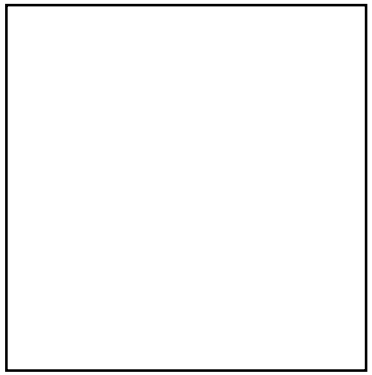


(5) Me_2CuLi
Et

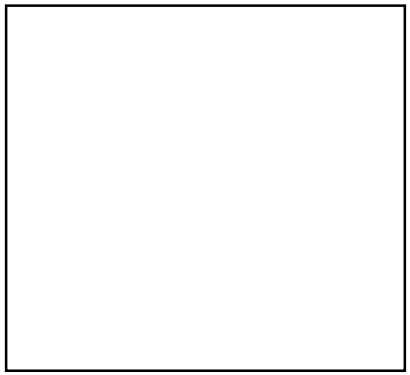
Conjugate addition ï Aldol addition

CuI + MeLi

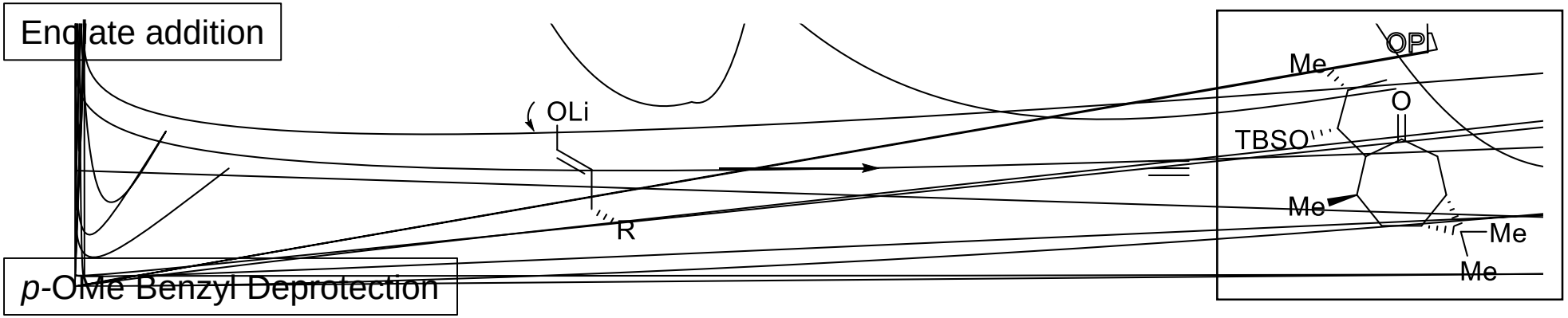




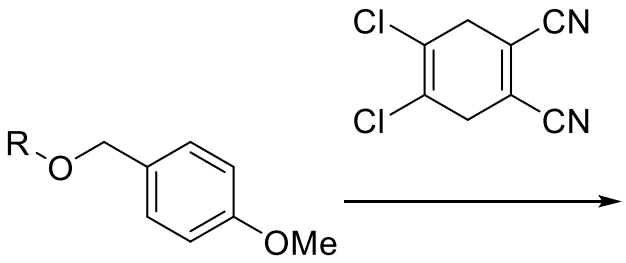
Alcohol protection with TBSOTf



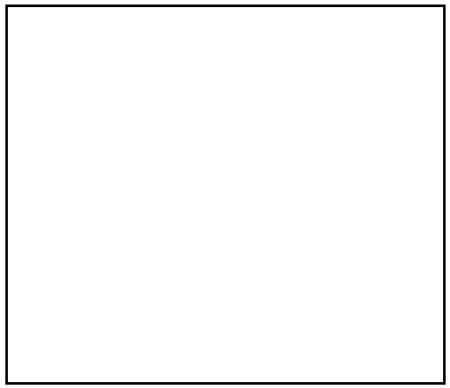
Enolate addition



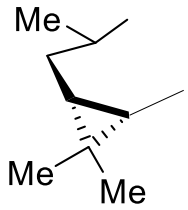
p-OMe Benzyl Deprotection

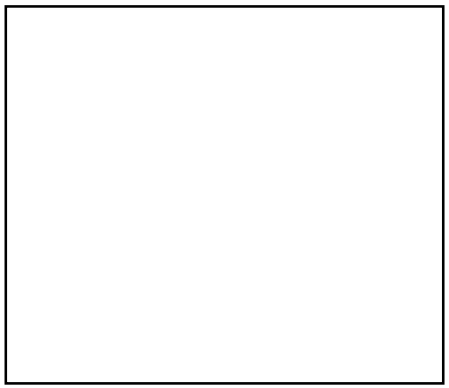


Parikh-Doering Oxidation

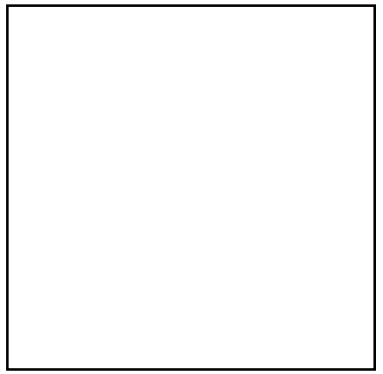


Umpolung Cyclization via Reduction with SmI2 ï Undesired Stereoisomer

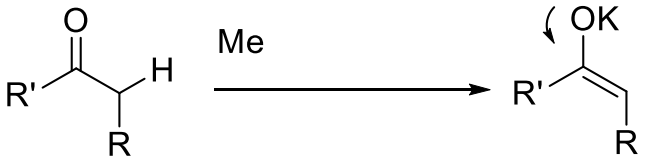




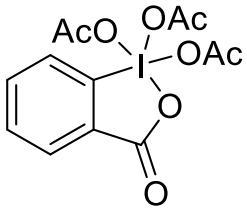
TBS Deprotection

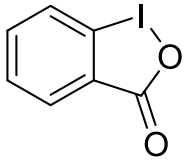


Davis Oxidation ï DMP Oxidation



Dess-Martin Oxidation





Metallation ï 1,2-addition