Enantioselective Total Synthesis of (+)-Leucascandrolide A Macrolactone

Michael T. Crimmins* and Phieng Siliphaivanh Org. Lett. 2003, 5, 4641

Presented By:
Lan Wang
(+)-Leucascandrolide A

- Isolated by Pietra and coworkers in 1996 from the calcareous sponge *Leucascandra caveolata*
- High *in vitro* cytotoxicity
- Significant antifungal properties
- Full biological potential of the compound has not been established
- The first total synthesis was reported by Leighton and co-workers in 2000
(+)-Leucascandrolide A Macrolactone
Dr. Michael T. Crimmins

- B.A. with Honors (1976) Hendrix College, Conway, Arkansas
- Doctor of Philosophy, Duke University, Durham, North Carolina 1980 - Steven W. Baldwin
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Highlights in the paper

- Diastereoselective reductive opening of a bicyclic ketal
- (-)-DIPCI-mediated diastereoselective aldol addition
- H-W-Z coupling
- Diastereoselective aldol addition
- hetero Micheal addition
- Yamaguchi
Retrosynthesis
Forward synthesis (Fragment 7)


Forward synthesis (Fragment 6)

Forward synthesis (Fragment 4)

Forward synthesis (Fragment 3)

Put them together

Conclusion

- Accomplished in a highly convergent 20 linear steps from propanediol
- Diastereoselective reductive opening of a bicyclic ketal
- A hetero-Michael addition
- (-)-DIPCI-mediated diastereoselective aldol addition