Introduction



 From plankton: Marine
 Dinoflagellate Amphidinium sp (2000)¹



 First enantioselective total synthesis by Fürtsner (2007)²

¹ Kubota, T.; Tsuda, M.; Kobayashi, J. *Tetrahedron Lett.* **2000**, 41, 713. ² Fürstner, A.; Larionov, O.; Flügge, S. *Ang. Chem. Int. Ed.* **2007**, 46, 5545.

Introduction

- 14-membered macrolactone
- 4 exocyclic methylene groups
- 4 asymmetric centers
 (8R, 9S, 10S, 13R)
- An epoxi-alcohol
- An unsaturated-side chain

Fürstner, A.; Larionov, O.; Flügge, S. *Ang. Chem. Int. Ed.* **2007**, 46, 5545. Fürstner, A.; Flügge, S.; Larionov, O.; Takahashi, Y.; Kubota, T.; Kobayashi, J. *Chem.-Eur. J.* **2009**, 15, 4011





First enantioselective total synthesis



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Fürstner, A.; Larionov, O.; Flügge, S. Ang. Chem. Int. Ed. 2007, 46, 5545.

First enantioselective total synthesis



Fürstner, A.; Larionov, O.; Flügge, S. Ang. Chem. Int. Ed. 2007, 46, 5545.

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First enantioselective total synthesis



Fürstner, A.; Larionov, O.; Flügge, S. Ang. Chem. Int. Ed. 2007, 46, 5545.

b

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Retrosynthesis



b





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b

Preparation of substrate 6









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b

Preparation of substrate 7





Preparation of Acceptor Aldehyde u^{\flat}





Preparation of Acceptor Aldehyde $\overset{m{u}^{\scriptscriptstyle b}}{-}$

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3



GII

Preparation of Acceptor Aldehyde u^{\flat}

3





PMPO

11

Preparation of Acceptor Aldehyde $\overset{m{u}^{\scriptscriptstyle b}}{-}$

3

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DIBAL-H THF, -50 °C, 1.5 h 91 %



1/Ti(O*i*-Pr)₄ (10 mol%) (-)-*D*-DIPT (15 mol%), *t*-BuOOH MS (4 Å), DCM, -20 °C, 12h (d.r. = 88 : 12)

2/SO₃•Py, DMSO, Et₃N DCM, 10 °C, 3 h



94%



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Preparation of Donor Aldehyde 4





Completion of the Synthesis



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Completion of the Synthesis





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Completion of the Synthesis



85%



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Completion of the Synthesis





Conclusion



• 22 steps : overall Yield = 3.3 %

 Key steps : ring closing enyne and diene metathesis, allylic transpositions, ring contraction, cross aldol condensation

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Thank you for your attention



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Mechanism of the Dehydrogenative Alcohol Silylation



Ito, H.; Watanabe, A.; Sawamura, M. Org. Lett. 2005, 7, 1869.





b



Volchkov, I; Park, S.; Lee, D. Org. Lett. 2011, 13, 3530

Synthesis of compound 10



Volchkov, I; Park, S.; Lee, D. Org. Lett. 2011, 13, 3530

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Hanawa, H.; Hashimoto, T.; Maruoka, K. J. Am. Chem. Soc. 2003, 125, 1706.

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Volchkov, I; Park, S.; Lee, D. Org. Lett. 2011, 13, 3530

b



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Synthesis of compound 20



Gold-Catalyzed

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b



Park, S.; Lee, D. J. Am. Chem. Soc. 2006, 128, 10664.

Knoevenagel-Mannich Type mechanism



b



Erkkilä, A.; Pihko, P. M. Eur. J. Org. Chem. 2007, 4205.

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Furlàn, R. L.; Mata, E. G.; Mascaretti, O. A. J. Chem. Soc., Perkin Trans. 1 1997, 355.

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 R^1 "R1 R 3 2 R R^1 Ru =₹R¹ R^1 .R¹ ,Ru Ru R Ru ,R1 $\sim R^1$ Ŕ R R

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Route 2



Mori, M. Adv. Synth. Catal. 2007, 349, 121.

Retrosynthesis



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