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A concise stereoselective total synthesis of Botryolide B

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ABSTRACT

The first total synthesis of Botryolide B is described from easily accessible starting materials. The synthetic strategy involves Jacobsen resolution, Sharpless epoxidation, Swern oxidation, Yamaguchi reaction, and ring closing metathesis (RCM).

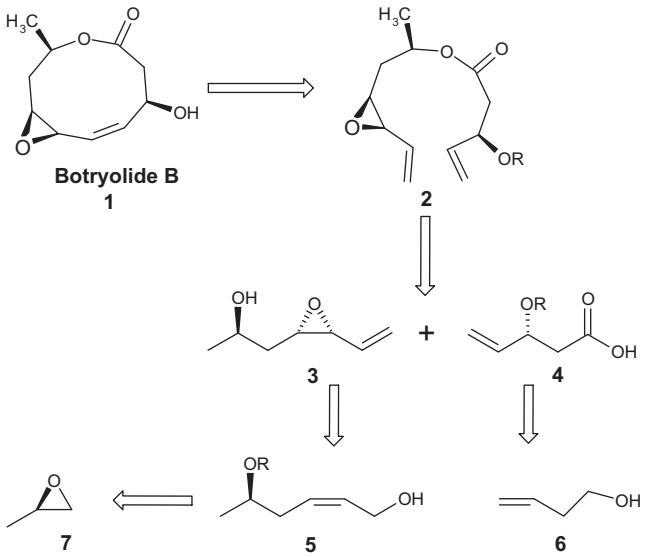
1. Introduction

Natural products containing 10-member framework are found in plants, insects (pheromones), and bacteria (antibiotics). Natural products having medium size lactone[1] ring possess wide range of biological activities such as antibacterial and antifungal activities.[2] They originate from terrestrial, fungal, or marine sources. Botryolide B was first isolated[3] by Gloer and co-workers in 2007 from the cultures of a fungicolous isolate of *Botryotrichum* sp. (NRRL 38180). Botryolide B is a 10-membered lactone having a hydroxyl group, methyl group, epoxide, and cis double bond. During the course of our studies on asymmetric synthesis for the development of simple synthetic routes,[4] herein we wish to report total synthesis of Botryolide B, and its retrosynthetic analysis is depicted in Scheme 1.

As outlined retrosynthetically in Scheme 1, it could be prepared efficiently by RCM protocol from bis-olefin **2**, which in turn could be realized by Yamaguchi esterification of alcohol **3** and acid **4**. Intermediate **3** can be envisaged from (*R*)-propylene oxide **7**, while chiral vinyl alcohol **4** could be produced from 3-butene-1-ol **6.**

The synthesis of fragment **3** began by the kinetic resolution of **8** (Scheme 2) under Jacobsen reaction conditions[5] using the (*R,R*)-catalyst **A** to give chiral epoxide **7** (42%, 99% ee) and diol **9**. Epoxide **7** on treatment with protected 1-methoxy-4-((prop-2-ynyloxy)methyl)benzene **10** in the presence of *n*-BuLi and $BF_3{\cdot}Et_2O$ in THF at −78 °C for 3 h afforded **11** (64%). The protection of homopropargyl alcohol with TBDPSCl in CH_2Cl_2 at room temperature gave TBDPS ether **12**. Deprotection of PMB with DDQ in a mixture of CH_2Cl_2–H_2O (9:1) resulted in primary alcohol **13** in high yield. Treatment of propargyl alcohol **13** with $Ni(OAc)_2$,[6] $NaBH_4$, and ethylenediamine in ethanol at rt under H_2 (atm) for 4 h afforded allylic alcohol **5** in 81% yield, which was then transformed into epoxy alcohol **14** (90%, >20:1 dr) under Sharpless conditions.[7] Conversion of epoxy alcohol **14** into **15** was accomplished in good yield by Swern oxidation followed by one-carbon homologation[8] with PPh_3CH_3I (60% overall yield after two steps). Removal of TBDPS group with HF–pyridine gave fragment **3** (92%).

The journey for the synthesis of segment **4** began from the known but-3-en-1-ol **6**. Thus, protection of the hydroxyl group with BnBr in the presence of NaH in THF at 0 °C gave benzyl ether in 95% yield, which on further epoxidation with *m*-CPBA in CH_2Cl_2 gave **16** in 88% yield. A kinetic resolution of racemic epoxide with (*R,R*)-Jacobsen catalyst **A** furnished the optically active epoxide **17** (42%, 99% ee). Treatment of epoxide **17** with trimethylsulfonium iodide and *n*-BuLi cleanly afforded secondary allylic alcohol **18** in 85% yield.[9] Vinyl alcohol **18** was treated with TBDPSCl to afford protected TBDPS ether (92%), which was subjected to debenzylation with DDQ–CH_2Cl_2 to give **19** (84%).[10] Primary alcohol **19** was



Scheme 1. Retrosynthetic analysis of Botryolide B **1**.

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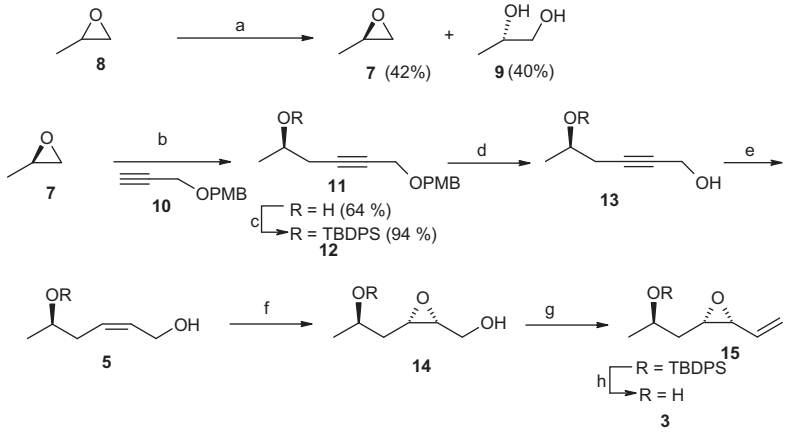
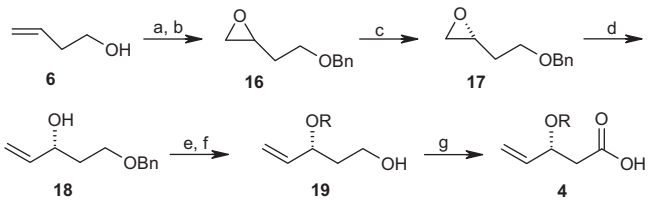
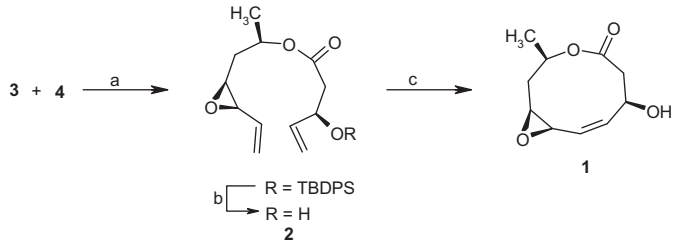


Scheme 2. Reagents and conditions: (a) (*R*,*R*)-Jacobsen catalyst, H_2O, rt, 12 h; (b) *n*-BuLi, $BF_3{\cdot}OEt_2$, THF, −78 °C, 3 h; (c) TBDPSCl, Imidazole, CH_2Cl_2, rt, 2 h; (d) DDQ, CH_2Cl_2–H_2O (9:1), 82%; (e) $Ni(OAc)_2$, $(H_2NCH_2)_2$, $NaBH_4$, EtOH, rt, H_2 (1 atm), 4 h, 88%; (f) (−)-DIPT, $Ti(iOPr)_4$, TBHP, CH_2Cl_2, 4AO MS, -20 °C, 90% ; (g) (i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C, 1 h, 80%; (ii) PPh_3CH_3I, *t*-BuOK, THF, −25 °C, 2 h, 75%; (h) HF–pyridine, THF, rt, 12 h, 92%.



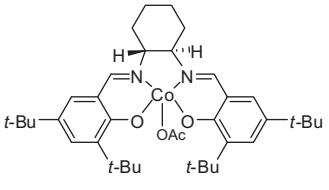
Scheme 3. Reagents and conditions: (a) NaH, BnBr, THF, 0 °C, rt 3 h, 95%; (b) *m*-CPBA, CH_2Cl_2, rt, 88%; (c) (*R*,*R*)-Jacobsen catalyst, H_2O, rt, 12 h, 42%; (d) $(CH_3)_3S{+}I^-$, *n*-BuLi, THF, −10 °C to rt, 85%; (e) TBDPSCl, Imidazole, CH_2Cl_2, rt, 92%; (f) DDQ, CH_2Cl_2–H_2O (19:1) reflux, 4 h, 84%; (g) (i) DMP, CH_2Cl_2, 0 °C to rt, 84%, (ii) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, 0 °C to rt, 82%.



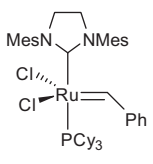
Scheme 4. Reagents and conditions: (a) 2,4,6-trichlorobenzoyl chloride, THF, Et_3N, rt, 6 h, DMAP, toluene, rt, 14 h, 83%; (b) TBAF, THF, rt, 10 h, 91%; (c) 2nd generation Grubbs catalyst, CH_2Cl_2, 25 °C, 65%.

oxidized with Dess–Martin periodinane[11] (DMP) to afford the corresponding aldehyde which on further treatment with $NaClO_2$[12] in the presence of NaH_2PO_4 and 2-methyl-2-butene as a scavenger gave the required acid **4** in 82% overall yield (Scheme 3).

The esterification of two fragments **3** and **4** was achieved under Yamaguchi reaction conditions[13] using 2,4,6-trichlorobenzoyl chloride to furnish diene ester **2** (83%). The removal of TBDPS group with TBAF followed by RCM reaction[14] with Grubb's second-generation catalyst **B** (10 mol %) afforded the target molecule **1** as the sole product in 65%. The prepared synthetic Botryolide B **1** is identical (IR, ^1H NMR, ^{13}C NMR, and Mass) with the natural product and also has an optical rotation ($[\alpha]_D^{25}$ −142.1 (*c* 0.69, $CHCl_3$)) which is in good agreement with the literature value ($[\alpha]_D^{25}$ −144 (*c* 0.23, $CHCl_3$))[3] (Scheme 4).



(*R*,*R*) Jacobsen catalyst (**A**)



2nd generation Grubbs Catalyst (**B**)

In summary, a concise first total synthesis of Botryolide B was achieved using inexpensive and commercially available starting materials. The synthesis is highlighted by Jacobsen resolution, Sharpless epoxidation, Swern oxidation Yamaguchi reaction, and RCM reactions as key steps.

2. Spectral data for selected compounds

2.1. (*R*)-6-(4-Methoxybenzyloxy)hex-4-yn-2-ol 11

$[\alpha]_D^{25}$ −5.8 (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 1.26 (d, J = 6.04 Hz, 3H), 2.40 (m, 2H), 3.80 (s, 3H), 3.95 (qt, J = 6.04 Hz, 1H), 4.10 (m, 2H), 4.50 (s, 2H), 6.82 (d, J = 9.06 Hz, 2H), 7.2 (d, 2H, J = 9.06 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.2, 30.3, 55.2, 57.2, 66.2, 71.3, 83.2, 87.1, 113.7, 129.3, 133.1, 159.2; IR (KBr): 3420, 2935, 2855, 1380, 1272, 1208, 1165, 1120 cm^{-1}; EI-MS: m/z 234 [M^+]; ESI-HRMS: calcd for $C_{14}H_{18}O_3$: 234.1255. Found: 234.1250.

2.2. (*R*)-*tert*-Butyl(6-(4-methoxybenzyloxy)hex-4-yn-2-yloxy)-diphenylsilane 12

$[\alpha]_D^{25}$ +12.1 (*c* 2.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 1.09 (s, 9H), 1.20 (d, J = 6.04 Hz), 2.3–2.4 (m, 2H), 3.8 (s, 3H), 3.92 (qt, J = 6.04 Hz, 1H), 4.05 (t, J = 2.22 Hz, 2H), 4.45 (s, 2H), 6.80 (d, J = 8.30 Hz), 7.2 (d, J = 8.04 Hz, 2H), 7.3–7.4 (m, 6H), 7.62–7.7 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.2, 23.0, 27.0, 29.5, 55.1, 55.3, 66.7, 70.7, 73.0, 83.9, 113.7, 127.5, 129.5, 129.6, 134.0, 134.8, 135.8, 159.2; IR (KBr): 3068, 2929, 2857, 1592, 1428, 1260, 1108 cm^{-1}; EI-MS: m/z 495 [M^+Na]; ESI-HRMS: calcd for $C_{30}H_{36}O_3Si$: 472.2433. Found: 472.2435.

2.3. (*R*)-5-(*tert*-Butyldiphenylsilyloxy)hex-2-yn-1-ol 13

$[\alpha]_D^{25}$ +26.1 (*c* 2.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 1.09 (s, 9H), 1.20 (d, J = 6.04 Hz), 2.3–2.4 (m, 2H), 3.92 (qt, J = 6.04 Hz,

1H), 4.05 (t, J = 2.07 Hz, 2H), 7.31–7.45 (m, 6H), 7.65–7.7 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.0, 22.8, 26.4, 29.2, 50.9, 68.1, 79.9, 83.1, 127.4, 129.4, 131.9, 134.6; IR (KBr): 3422, 3069, 2928, 2857, 1643, 1222, 1107 cm^{-1}; EI-MS: m/z 375 [M$^+$Na]; ESI-HRMS: calcd for $C_{22}H_{28}O_2Si$: 352.1858. Found: 352.1850.

2.4. ((2*R*,3*S*)-3-((*R*)-2-(*tert*-Butyldiphenylsilyloxy)propyl)oxiran-2-yl)methanol 14

$[\alpha]_D^{25}$ +0.5 (c 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.05 (s, 9H), 1.1 (d, J = 6.04 Hz, 3H), 2.0 (m, 2H), 2.87–2.96 (m, 2H), 4.05 (m, 1H), 4.4 (d, J = 6.79 Hz, 2H), 7.3–7.42 (m, 6H), 7.6–7.7 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.1, 24.8, 26.8, 41.2, 50.9, 53.0, 61.3, 66.8, 128.4, 129.4, 130.2, 132.6, 132.4; IR (KBr): 3440, 1590, 1450, 1257, 1050 cm^{-1}; EI-MS: m/z 371 [M$^+$]; ESI-HRMS: calcd for $C_{22}H_{30}O_3Si$: 370.1964. Found: 370.1965.

2.5. (*R*)-1-((2*S*,3*R*)-3-Vinyloxiran-2-yl)propan-2-ol 3

$[\alpha]_D^{25}$ −8.8 (c 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.2 (d, J = 6.20 Hz, 3H), 2.1 (m, 2H), 3.21 (m, 1H), 3.48 (m, 1H), 4.1 (m, 1H), 5.39 (d, J = 9.78 Hz, 1H), 5.48 (d, J = 17.60 Hz, 1H), 5.7 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.6, 42.1, 57.1, 66.2, 85.8, 118.0, 133.5; IR (KBr): 3377, 2930, 2858, 1641, 1463, 1253, 1100, 837 cm^{-1}; EI-MS: m/z 129 [M$^+$1]; ESI-HRMS: calcd for $C_7H_{12}O_2$: 128.0837. Found: 128.0842.

2.6. (*R*)-5-(Benzyloxy)pent-1-en-3-ol 18

$[\alpha]_D^{25}$ −9.50 (c 2.0, $CHCl_3$); ^{1}H NMR (300 MHz,$CDCl_3$): δ 1.63–1.90 (m, 2H), 2.79 (br s, 1H), 3.50–3.74 (m, 2H), 4.20–4.37 (m, 1H), 4.49 (s, 2H), 5.06 (d, J = 10.57 Hz, 1H), 5.23 (d, J = 16.61 Hz, 1H), 5.72–5.93 (m, 1H), 7.20–7.50 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 36.2, 68.1, 71.5, 73.1, 114.2, 127.5, 128.3, 137.8, 140.4; IR (KBr): 3424, 3031, 2920, 2863, 1454, 1364, 1098, 740 cm^{-1}; EI-MS: m/z 215 [M$^+$Na]; ESI-HRMS: calcd for $C_{12}H_{16}O_2$ 192.1150. Found: 192.1149.

2.7. (*R*)-3-(*tert*-Butyldiphenylsilyloxy)pent-4-enoic acid 8

$[\alpha]_D^{25}$ + 12.1 (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.05 (s, 9H), 2.42 (dd, 1H, J = 3.5, 7.00 Hz), 2.61 (dd, 1H, J = 3.0, 6.50 Hz), 4.55 (q, 1H, J = 6.50 Hz), 5.0–5.20 (m, 2H), 5.80–5.90 (m, 1H), 7.35 (m, 6H), 7.65 (m, 4H); IR (neat): 3546, 3070, 2934, 2858, 1780, 1589, 1428, 1240 cm^{-1}; EI-MS: m/z 353 [M$^+$1]; ESI-HRMS: calcd for $C_{21}H_{26}O_3Si$: 354.1651. Found: 354.1652.

2.8. Botryolide B 1

$[\alpha]_D^{25}$ -142.1 (c 0.69, $CHCl_3$) ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.3 (d, J = 6.00 Hz, 3H), 1.3 (m, 2H), 2.5 (d, J = 4.30 Hz, 2H), 3.4–3.5 (m, 2H), 4.7–4.8 (m, 2H), 6.15–6.25 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.5, 38.1, 43.4, 53.7, 57.2, 67.7,67.9, 127.9, 135.1, 170.1; IR (KBr): 3542, 3071, 2990, 2857, 1759, 1428, 1260, 1108, 1050 cm^{-1}; EI-MS: m/z 221 [M$^+$Na]; ESI-HRMS: calcd for $C_{10}H_{14}O_4$: 198.0892. Found: 198.0890.

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References and notes

1. (a) Rousseau, G. *Tetrahedron* **1995**, *51*, 2777; (b) Longo, L. S., Jr.; Bombonato, F. I.; Ferraz, H. M. C. *Quim. Nova* **2007**, *30*, 415; (c) Shiina, I. *Chem. Rev.* **2007**, *107*, 239; (d) Ferraz, H. M. C.; Bombonato, F. I.; Sano, M. K.; Longo, L. S., Jr. *Quim. Nova* **2008**, *31*, 885.
2. (a) Drager, G.; Kirschning, A.; Thiericke, R.; Zerlin, M. *Nat. Prod. Rep.* **1996**, *13*, 365; (b) Ferraz, M. C.; Bombonato, F. I.; Longo, L. S., Jr. *Synthesis* **2007**, 3261; (c) Riatto, V. B.; Pilli, R. A.; Victor, M. M. *Tetrahedron* **2008**, *64*, 2279.
3. Sy, A. A.; Swenson, D. C.; Gloer, J. B.; Wicklow, D. T. *J. Nat. Prod.* **2008**, *71*, 415.
4. Meshram, H. M.; Kumar, D. A.; Ramesh, P. *Helv. Chim. Acta*. In press.
5. (a) Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307; (b) Louis, J. T.; Nelson, W. L. *J. Org. Chem.* **1987**, *52*, 1309.
6. Falck, J. R.; Reddy, L. M.; Byun, K.; Campbell, W. B.; Yi, X. Y. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 2634.
7. (a) Sharpless, K. B.; Katsuki, T. *J. Am. Chem. Soc* **1980**, *102*, 5974; (b) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am Chem. Soc* **1987**, *109*, 5765.
8. Corey, E. J.; Martaf, A.; Laguzza, B. C. *Tetrahedron Lett.* **1981**, *22*, 3339.
9. Alcaraz, L.; Harnett, J. J.; Mioskowski, C.; Martel, J. P.; Le Gall, T.; Shin, D. S.; Falck, J. R. *Tetrahedron Lett.* **1994**, *35*, 5449.
10. Sharma, G. V. M.; Reddy, K. L. *Tetrahedron: Asymmetry* **2006**, *17*, 3197.
11. (a) Dess, B. D.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155; (b) Dess, B. D.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277.
12. (a) Kolar, J. J.; Lindgren, B. O. *Acta Chem. Scand.* **1982**, *36*, 599; (b) Dalcanale, E.; Montanari, F. *J. Org. Chem.* **1986**, *51*, 567.
13. (a) Inanga, J.; Hirata, K.; Sacki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989; (b) Okino, T.; Qi, S.; Matsuda, H.; Murakami, M.; Yamaguchi, K. *J. Nat. Prod.* **1997**, *60*, 158.
14. Mohapatra, D. K.; Ramesh, D. K.; Giardello, M. A.; Chorghade, M. S.; Gurjar, M. K.; Grubbs, R. H. *Tetrahedron Lett.* **2007**, *48*, 2621.