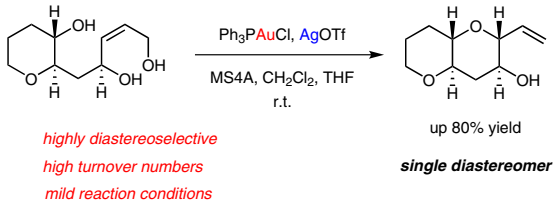
Synlett H. Yokoyama et al. Letter

Stereoselective Construction of Polyether *trans*-Pyran Ring System by Gold(I)-Catalyzed Cyclization

Hajime Yokoyama*
Megumi Matsuo
Masahiro Miyazawa
Yoshiro Hirai

Graduate School of Science and Engineering, University of Toyama, Gofuku, Toyama 930-8555, Japan
hyokoyam@sci.u-toyama.ac.jp



Received: 26.05.2016
Accepted after revision: 04.07.2016
Published online: 01.08.2016
DOI: 10.1055/s-0035-1562525; Art ID: st-2016-u0363-l

Abstract Many natural polyether toxins contain the *trans*-pyran ladder structure. We describe a synthesis of the polyether *trans*-pyran ring system by using cationic gold(I)-catalyzed cyclization. This gold(I)-catalyzed cyclization provided high diastereoselectivity and high turnover. This method is expected to be applicable to the synthesis of polyethers.

Key words gold catalyst, cyclization, polyether, stereoselective, *trans*-fused pyran system

Many polyether toxins have been isolated from marine origin. Their interesting ladder structures have attracted the attention of synthetic chemists. Many reports and reviews were accumulated for a few years.[1,2] For example, yessotoxin, which was isolated from digestive glands of the scallops *Patinopecten yessoensis* (Figure 1),[3] has a typical *trans*-pyran ladder system. The key issue for synthetic studies is stereoselective ether construction, especially the consecutive *trans*-pyran ring system. We have been studying the palladium(II)-catalyzed cyclization of allylic alcohols with oxygen and nitrogen nucleophiles.[4,5] In 2009, we reported the novel synthesis of a *trans*-pyran ring system by using palladium(II)-catalyzed cyclization of allylic alcohol.[5e]

On the other hand, homogeneous gold catalysts are known to activate alkynes, allenes, and alkenes for intramolecular or intermolecular attack of the nucleophile.[6] Aponick's group[6a,b] and Robertson's group[6e] reported the interesting reaction by using gold(I) or gold(III) catalyst. Especially, they show the efficient and simple method by gold(I) catalyst, which enables reduced catalyst loading and provides excellent chiral transfer. Mechanistically, by the estimation of DFT methods, this gold(I)-catalyzed cyclization proceeds via *anti*-addition and *anti*-elimination, and

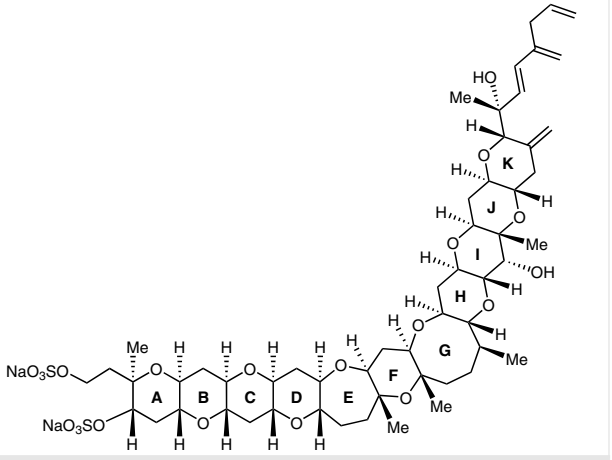
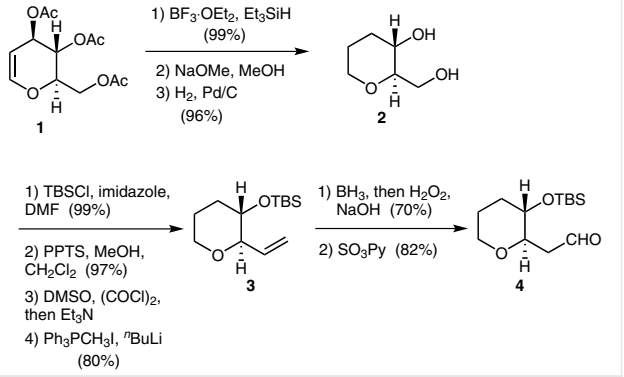


Figure 1 Yessotoxin, a natural polyether

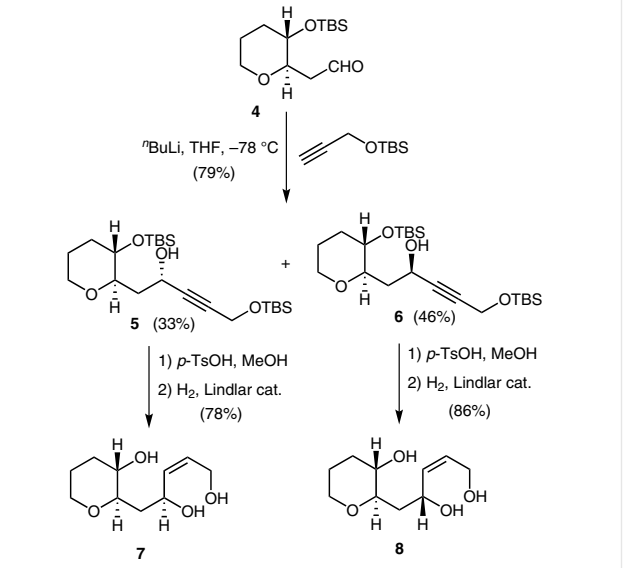
interestingly, it seems to be facilitated by hydrogen bonding.[6d] Recently, Widenhoefer's group also reported gold(I)-catalyzed amination.[7] Therefore we considered the stereoselective construction of the polyether *trans*-pyran ring system might be achieved by gold(I)-catalyzed cyclization.

Aldehyde **4** was obtained from tri-*O*-acetyl D-glucal (**1**) according to the reported method (Scheme 1).[5e] Reduction of this material **1** with Et_3SiH and $BF_3{\cdot}OEt_2$ gave the diacetate in 99% yield. Deprotection of the diacetate with NaOMe, followed by hydrogenation with Pd/C catalyst under a hydrogen atmosphere afforded the diol **2** in 96% yield from the diacetate. Protection of diol **2**, followed by deprotection of primary alcohol, gave the monoalcohol in 96% yield. Oxidation of this hydroxy moiety, followed by Wittig reaction of resulting aldehyde, gave the terminal olefin **3** in 80% yields (two steps). Hydroboration–oxidation of this terminal olefin **3** and oxidation with SO_3Py afforded the aldehyde **4**[5e,8] in 57% yield (two steps).



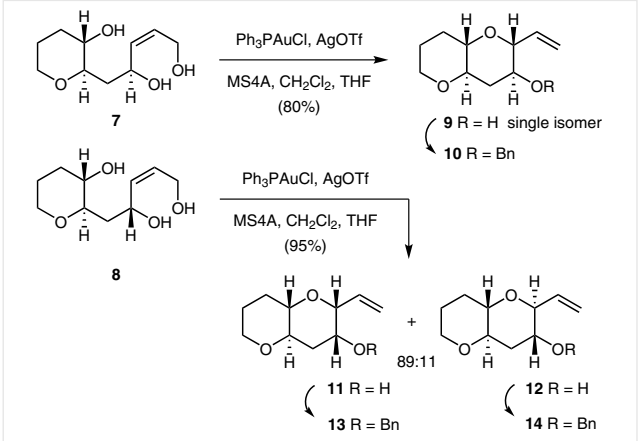
Scheme 1 Preparation of aldehyde **4**

Aldehyde **4** was treated with lithio propargyl derivatives in THF to afford a mixture of adducts **5** (33%) and **6** (46%) in 79% yield (Scheme 2). After acidic workup, careful column chromatography afforded the two pure diastereoisomers. The diastereomer **5** was deprotected and hydrogenation with Lindlar catalyst under a hydrogen atmosphere to give the triol **7** in 78% yields (two steps). The other diastereomer **6** was similarly treated to afford the triol **8** in 86% yields (two steps).



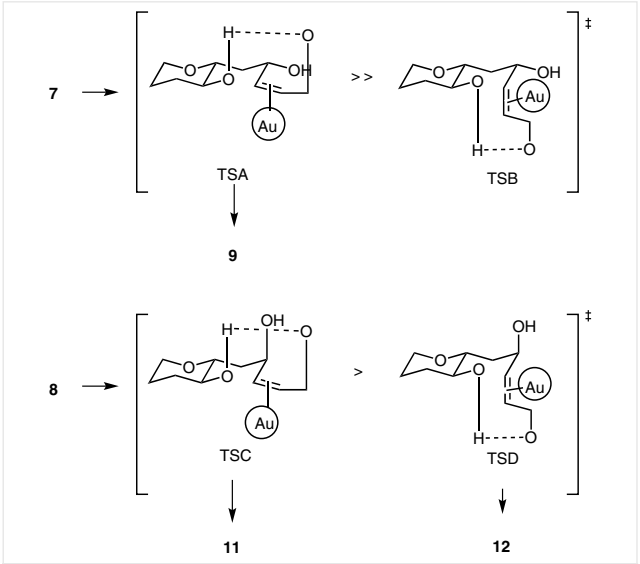
Scheme 2 Synthesis of the precursors **7** and **8**

Next, the triol **7** was treated with 10 mol% Ph_3PAuCl, 10 mol% AgOTf, and 4 Å molecular sieves at room temperature under an argon atmosphere to afford the pyran ring compound **9** in 80% yield as a single isomer (Scheme 3).[9] The other triol **8** afforded the pyran ring compounds in 95% yield as a diastereomeric mixture (**11**/**12** = 89:11).[10] The stereochemistry of the benzyl derivatives **10** and **13** were determined by NMR spectra in comparison with literature data.[11]



Scheme 3 Gold(I)-catalyzed cyclization

The transition structures of this reaction in **7** are considered to be TSA and TSB, if this reaction proceeds via *anti*-addition and *anti*-elimination, as suggested in the literature[6d] and involves a six-membered cyclic transition structure (Scheme 4), TSB suffers the steric repulsion between the gold-catalyst-coordinated alkene moiety and hydroxyl moieties. TSA would lead the desired pyran ring system **9**. On the contrary, in case of **8**, the steric repulsion in TSD is smaller than in TSB and that may be the reason why **11** and **12** are both formed.



Scheme 4 Proposed transition structures of gold(I)-catalyzed cyclization

In conclusion, we have attained the synthesis of *trans*-pyran ring system by using a gold(I)-catalyzed cyclization. We are undergoing the synthesis of natural poylether by using this method.

Acknowledgment

We thank to the University of Toyama, for financial support.

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1562525.

References and Notes

(1) (a) Blunt, J. W.; Copp, B. R.; Munro, M. H. G.; Northcote, P. T.; Prinsep, M. R. *Nat. Prod. Rep.* **2004**, *21*, 1. (b) Faulkner, D. J. *Nat. Prod. Rep.* **2002**, *19*, 1.

(2) (a) Kadota, I.; Yamamoto, Y. *Acc. Chem. Res.* **2005**, *38*, 423. (b) Nakata, T. *Chem. Rev.* **2005**, *105*, 4314. (c) Inoue, M. *Chem. Rev.* **2005**, *105*, 4379. (d) Alvarez, E.; Candenas, M.-L.; Perez, R.; Ravelo, J. L.; Martin, J. D. *Chem. Rev.* **1995**, *95*, 1953.

(3) (a) Murata, M.; Kumagai, M.; Lee, J. S.; Yasumoto, T. *Tetrahedron Lett.* **1987**, *28*, 5869. (b) Scheuer, P. J. *Tetrahedron* **1994**, *50*, 3. (c) Satake, M.; Terasawa, K.; Kadowaki, Y.; Yasumoto, T. *Tetrahedron Lett.* **1996**, *37*, 5955. (d) Takahashi, H.; Kusumi, T.; Kan, Y.; Satake, M.; Yasumoto, T. *Tetrahedron Lett.* **1996**, *37*, 7087. (e) Morohashi, A.; Satake, M.; Oshima, Y.; Yasumoto, Y. *Biosci. Biotechnol. Biochem.* **2000**, *64*, 1761. (f) Yasumoto, T. *Chem. Rec.* **2001**, *1*, 228. (g) Mori, Y.; Hayashi, H. *Tetrahedron* **2002**, *58*, 1789. (h) Suzuki, K.; Nakata, T. *Org. Lett.* **2002**, *4*, 3943. (i) Mori, Y.; Nogami, K.; Hayashi, H.; Noyori, R. *J. Org. Chem.* **2003**, *68*, 9050. (j) Mori, Y.; Takase, T.; Noyori, R. *Tetrahedron Lett.* **2003**, *44*, 2319. (k) Oishi, T.; Watanabe, K.; Murata, M. *Tetrahedron Lett.* **2003**, *44*, 7315. (l) Kadota, I.; Ueno, H.; Yamamoto, Y. *Tetrahedron Lett.* **2003**, *44*, 8935. (m) Watanabe, K.; Suzuki, M.; Murata, M.; Oishi, T. *Tetrahedron Lett.* **2005**, *46*, 3991. (n) Kadota, I.; Ueno, H.; Sato, Y. *Yamamoto Y.* **2006**, *47*, 89. (o) Oishi, T.; Suzuki, M.; Watanabe, K.; Murata, M. *Tetrahedron Lett.* **2006**, *47*, 3975. (p) Kadota, I.; Abe, T.; Sato, Y.; Kabuto, C.; Yamamoto, Y. *Tetrahedron Lett.* **2006**, *47*, 6545. (q) Torikai, K.; Watanabe, K.; Minato, H.; Imaizumi, T.; Murata, M.; Oishi, T. *Synlett* **2008**, *15*, 2368. (r) Akoto, C. O.; Rainier, J. D. *Angew. Chem. Int. Ed.* **2008**, *47*, 8055. (s) Oishi, T.; Imaizumi, T.; Murata, M. *Chem. Lett.* **2010**, *39*, 108. (t) Sakai, T.; Sugimoto, A.; Tatematsu, H.; Mori, Y. *J. Org. Chem.* **2012**, *77*, 11177. (u) Czabaniuk, L. C.; Jamison, T. F. *Org. Lett.* **2015**, *17*, 774. (v) Zhang, Y.; Rainier, J. D. *J. Antibiot.* **2016**, *69*, 259.

(4) (a) Harrington, P. J.; Hegedus, L. S.; McDaniel, K. F. *J. Am. Chem. Soc.* **1987**, *109*, 4335. (b) Saito, S.; Hara, T.; Takahashi, N.; Hirai, M.; Moriwake, T. *Synlett* **1992**, 237. (c) Hirai, Y.; Terada, T.; Amemiya, Y.; Momose, T. *Tetrahedron Lett.* **1992**, *33*, 7893. (d) Hirai, Y.; Nagatsu, M. *Chem. Lett.* **1994**, *23*, 21. (e) Makabe, H.; Kong, L. K.; Hirota, M. *Org. Lett.* **2003**, *5*, 27. (f) Uenishi, J.; Ohmi, M.; Ueda, A. *Tetrahedron: Asymmetry* **2005**, *16*, 1299. (g) Kawai, N.; Lagrange, J.-M.; Ohmi, M.; Uenishi, J. *J. Org. Chem.* **2006**, *71*, 4530. (h) Kawai, N.; Hande, S. M.; Uenishi, J. *Tetrahedron* **2007**, *63*, 9049. (i) Uenishi, J.; Vikhe, Y. S.; Kawai, N. *Chem. Asian J.* **2008**, *3*, 473. (j) Hande, S. M.; Kawai, N.; Uenishi, J. *J. Org. Chem.* **2009**, *74*, 244. (k) Vikhe, Y. S.; Hande, S. M.; Kawai, N.; Uenishi, J. *J. Org. Chem.* **2009**, *74*, 5174. (l) Hande, S. M.; Uenishi, J. *Tetrahedron Lett.* **2009**, *50*, 189. (m) Uenishi, J.; Fujikura, Y.; Kawai, N. *Org. Lett.* **2011**, *13*, 2350. (n) Borrero, N. V.; Aponick, A. *J. Org. Chem.* **2012**, *77*, 8410. (o) Ghebreghiorgis, T.; Kirk, B. H.; Aponick, A.; Ess, D. H. *J. Org. Chem.* **2013**, *78*, 7664.

(5) (a) Yokoyama, H.; Shouji, Y.; Kubo, T.; Miyazawa, M.; Hirai, Y. *Heterocycles* **2015**, *91*, 1752. (b) Yokoyama, H.; Kubo, T.; Matsumura, Y.; Hosokawa, J.; Miyazawa, M.; Hirai, Y. *Tetrahedron* **2014**, *70*, 9530. (c) Yokoyama, H.; Kusumoto, Y.; Sumiyoshi, K.; Miyazawa, M.; Hirai, Y. *Heterocycles* **2014**, *89*, 353. (d) Yokoyama, H.; Hayashi, Y.; Nagasawa, Y.; Ejiri, H.; Miyazawa, M.; Hirai, Y. *Tetrahedron* **2010**, *66*, 8458. (e) Yokoyama, H.; Nakayama, S.; Murase, M.; Miyazawa, M.; Yamaguchi, S.; Hirai, Y. *Heterocycles* **2009**, *77*, 211. (f) Yokoyama, H.; Hirai, Y. *Heterocycles* **2008**, *75*, 2133. (g) Yokoyama, H.; Kobayashi, H.; Miyazawa, M.; Yamaguchi, S.; Hirai, Y. *Heterocycles* **2007**, *74*, 283. (h) Yokoyama, H.; Ejiri, H.; Miyazawa, M.; Yamaguchi, S.; Hirai, Y. *Tetrahedron: Asymmetry* **2007**, *18*, 852. (i) Miyazawa, M.; Hirose, Y.; Narantsetsetseg, M.; Yokoyama, H.; Yamaguchi, S.; Hirai, Y. *Tetrahedron Lett.* **2004**, *45*, 2883. (j) Miyazawa, M.; Narantsetseg, M.; Yokoyama, H.; Yamaguchi, S.; Hirai, Y. *Heterocycles* **2004**, *63*, 1017. (k) Yokoyama, H.; Otaya, K.; Kobayashi, H.; Miyazawa, M.; Yamaguchi, S.; Hirai, Y. *Org. Lett.* **2000**, *2*, 2427. (l) Yokoyama, H.; Otaya, K.; Yamaguchi, S.; Hirai, Y. *Tetrahedron Lett.* **1998**, *39*, 5971. (m) Hirai, Y.; Watanabe, J.; Nozaki, T.; Yokoyama, H.; Yamaguchi, S. *J. Org. Chem.* **1997**, *62*, 776.

(6) (a) Aponick, A.; Li, C-Y.; Biannic, B. *Org. Lett.* **2008**, *10*, 669. (b) Aponick, A.; Biannic, B. *Synthesis* **2008**, 3356. (c) Aponick, A.; Biannic, B. *Org. Lett.* **2011**, *13*, 1330. (d) Ghebreghiorgis, T.; Biannic, B.; Kirk, B. H.; Ess, D. H.; Aponick, A. *J. Am. Chem. Soc.* **2012**, *134*, 16307. (e) Unsworth, W. P.; Stevens, K.; Lamont, S. G.; Robertson, J. *Chem. Commun.* **2011**, *47*, 7659.

(7) Mukherjee, P.; Widenhoefer, R. A. *Org. Lett.* **2010**, *12*, 1184.

(8) Takai, S.; Isobe, M. *Org. Lett.* **2002**, *4*, 1183.

(9) **2-Vinyloctahydropyrano[3,2-*b*]pyran-3-ol (9)**
Dry CH_2Cl_2 (1 mL) was added to an aluminum-foil-covered two-necked flask containing PPh_3AuCl (16 mg, 0.03 mmol), AgOTf (7.9 mg, 0.03 mmol), and activated MS4Å (26 mg). After stirring for 10 min, a solution of triol **7** (51.3 mg, 0.25 mmol) in dry THF (1 mL) was added. After the mixture was stirred for 7 d and 20 h, it was diluted with CH_2Cl_2, and the mixture was filtered through a short plug of silica. The eluent was concentrated and the residue was purified on silica gel column chromatography (hexane–EtOAc = 70:30, v/v) to give the alcohol **9** (36.2 mg, 80%) as a single isomer and a colorless oil.
Analytical Data of 9
^{1}HNMR (600 MHz, $CDCl_3$): δ = 5.82 (ddd, *J* = 17.59, 10.62, 7.33 Hz, 1 H), 5.40 (d, *J* = 17.89 Hz, 1 H), 5.32 (d, *J* = 10.26 Hz, 1 H), 3.90–3.87 (m, 1 H), 3.56–3.54(m, 1 H), 3.44–3.40 (m, 1 H), 3.38–3.31 (m, 1 H), 3.01–2.99 (m, 2 H), 2.38–2.35 (m, 1 H), 2.07–1.92 (m, 2 H), 1.73–1.69 (m, 2 H), 1.45–1.39 (m, 1 H). ^{13}C NMR (150 MHz, CD_3OD): δ = 135.7, 119.7, 83.9, 77.7, 76.8, 69.1, 68.0, 38.0, 29.3, 25.6. IR (nujol): 3395, 2925, 2865, 1460, 1090, 1029 cm^{-1}. MS (EI): *m/z* = 184 [M$^+$]. HRMS (EI): *m/z* calcd for $C_{10}H_{14}O_2$ [M$^+$ – H_2O]: 166.0994; found: 166.1000.

(10) We reported the conversion of **11** into **9** previously: Ref. 5.

(11) Suzuki, Y.; Kuwabara, A.; Koizumi, Y.; Mori, Y. *Tetrahedron* **2013**, *69*, 9086.