Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters 45 (2004) 8111–8113
Tetrahedron Letters

Stereoselective synthesis of the styryllactones, 7-*epi*-goniodiol and leiocarpin A, isolated from *Goniothalamus leiocarpus*

Jian Chen, Guo-Qiang Lin* and Han-Quan Liu

Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, PR China

Received 9 August 2004; revised 16 August 2004; accepted 20 August 2004
Available online 17 September 2004

Abstract—Two novel styryllactones, 7-*epi*-goniodiol and leiocarpin A, isolated from *Goniothalamus leiocarpus*, were stereoselectively synthesized in a short and efficient route from cinnamyl alcohol based on the asymmetric epoxidation and the palladium-catalyzed cross-coupling of vinyl epoxide with vinyltributylstannane.

Styryl lactones are a series of natural products, exhibiting moderate to significant biological activity including antitumour and antifungal properties, as well as antibiotic potential. Up to now, more than twenty styryl lactones have been isolated from plants and fungi.[1,2] Because of their unique and intriguing structures as well as their antitumour activities, much effort has been centered on the development of methodology for the synthesis of these substrates.[3,4] Among them, leiocarpin A and 7-*epi*-goniodiol are two new styryllactones, recently isolated from the ethanolic extract of stem barks of *Goniothalamus leiocarpus* (Annonaceae), a tropical plant wide spread in the south of the Yunnan province in China.[5] 7-*epi*-Goniodiol displayed selective activities in test of trypan blue dye exclusion method, and showed strong inhibition against HL-60 in concentration as low as 1 μg/mL. Their structures and relative configurations were determined by NMR spectra studies and X-ray crystallographic analysis. The structure assigned to 7-*epi*-goniodiol was similar to (+)-goniodiol except for the configuration at the C_7 chiral center. The same structural relationship was found between leiocarpin A and 9-deoxygoniopypyrone (Fig. 1).

In our previous paper,[6] we described a facile synthetic approach to (+)-goniodiol and 9-deoxygoniopypyrone, by employing Sharpless asymmetric dihydroxylation as the key step to secure the *syn*-configuration between C_6-OH and C_7-OH in both structures. Because a *trans*-configuration between C_6-OH and C_7-OH is the common feature between 7-*epi*-goniodiol and leiocarpin A, we wish to describe herein a short and efficient synthetic access to these compounds, by using an asymmetric epoxidation followed by a intramolecular acid-catalyzed ring-opening reaction as the key steps to control their *trans* configuration.

Our synthesis began with the Sharpless epoxidation of cinnamyl alcohol **1** to give **2** in high yield and high ee (>98% ee).[7] Swern oxidation of the resulting epoxide **2**, followed by Wittig methylenation provided the vinyl epoxide **3** in 74% yield over two steps without loss of optical purity (Scheme 1).

As shown in our previous report that the palladium-catalyzed cross-coupling of allylic cyclic carbonate **4** with vinyltributylstannane **5** afforded the diene.[6] We decided to extend this approach to vinyl epoxide **3** (Scheme 2). The reaction of **3** with **5** occurred under mild neutral condition and provided diene **6** in higher yield and stereoselectivity, however, with a little lower geometric selectivity on the newly formed double bond. The results are listed in Table 1.

Next, our attention was focused on the asymmetric epoxidation of alcohol **6** and its C_7-OH protected compound **7** (Scheme 3). Three epoxidation conditions were conducted, which led to leading to moderate

Keywords: Styryllactones; 7-*epi*-Goniodiol; Leiocarpin A; Synthesized; Epoxidation.
* Corresponding author. Tel.: +86 21 64163300; fax: +86 21 64166128; e-mail: lingq@pub.sioc.ac.cn

0040-4039/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2004.08.132

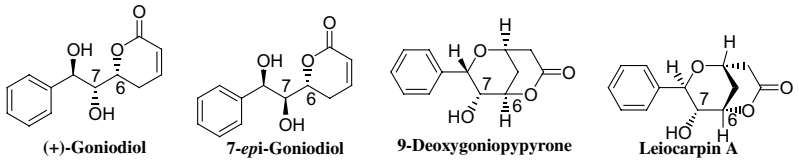
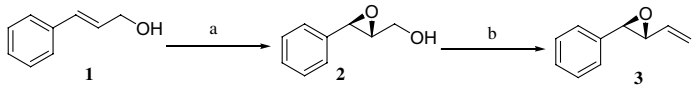
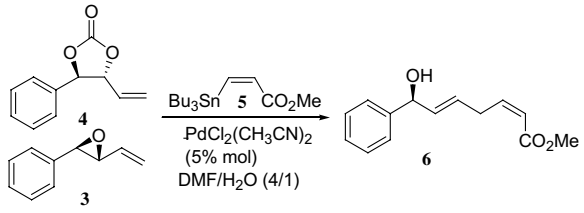


Figure 1.



Scheme 1. Reagents and conditions: (a) TBHP, $Ti(OiPr)_4$, L-DIPT, 4′ sieves, CH_2Cl_2, −15 °C to 0 °C, 90%y, 98%ee; (b), (1) 1.05 equiv $(COCl)_2$, 2 equiv DMSO, Et_3N, −78 °C–rt, 89%, (2) *t*-BuOK, Ph_3PCH_3 I, THF, 0 °C, 1 h, 86%.



Scheme 2.

Table 1. The Pd(0)-catalyzed reaction for substrates **3** and **4**

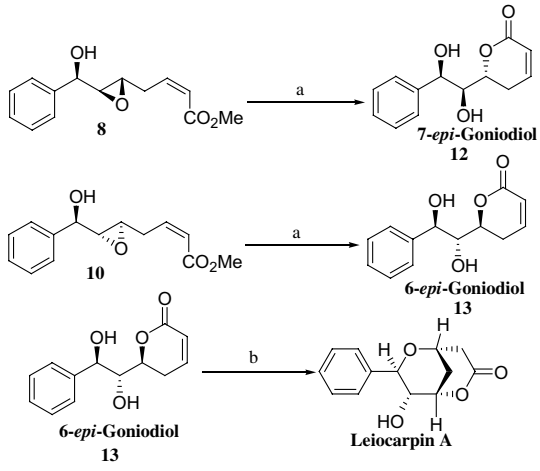
Substrate	Yield (%)	ee (%)	*E*/*Z*
4	71	95	98.2:1.8
3	83	>98	95:5

diastereoselectivities, as shown in Table 2. The *threo* epoxides **8** or **9** were obtained as major products when *m*-CPBA was used, whereas the *erythro* epoxide **10** became the main product when using TBHP/VO(acac)$_2$. Fortunately, the two diastereomers can be completely separated by flash column chromatography, however, their diastereoselectivities remained moderate.

Then, we intended to take advantage of the acid-catalyzed epoxide ring opening reaction to control the *trans*-configuration between C_6 and C_7 found in both 7-*epi*-goniodiol and leiocarpin A. Epoxide **8** was lactonized by treatment of 30% $HClO_4$ in methanol[8] to give 7-*epi*-goniodiol **12**[9] in 71% yield with inversion of the configuration at C_6. The same reaction converted epoxide **10** into 6-*epi*-goniodiol **13** in 74% yield. Finally, reacting 6-*epi*-goniodiol led to leiocarpin A,[10] another natural product, through an intramolecular heteroatom-Michael addition[11] in 94% yield (Scheme 4).

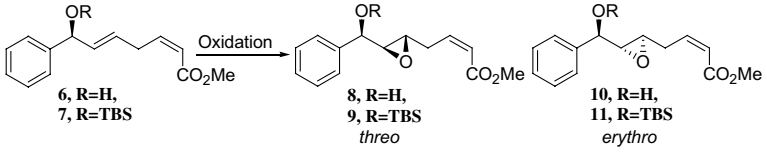
Table 2. Asymmetric epoxidation of **6**, **7**

Substrate	Conditions	Yield (%)	*threo*/*erythro*
6	a	82	2.5:1
6	b	87	1:1.7
7	a	90	2.2:1



Scheme 4. Reagents and conditions: (a) 30% $HClO_4$ in MeOH, 0 °C, 74% for **12**, 71% for **13**; (b) DBU, CH_2Cl_2, 0 °C, 94%.

In summary, we have shown herein that the combination of the asymmetric epoxidation with the palladium-catalyzed coupling of vinyl epoxide with vinyltributylstannane opens an efficient and versatile access to styryllactones such as 7-*epi*-goniodiol and leiocarpin A.



Scheme 3. Reagents and conditions: (a) *m*-CPBA (1.1 equiv), $NaHCO_3$, CH_2Cl_2, −20 °C; (b) cat $VO(acac)_2$, TBHP, (1.1 equiv), CH_2Cl_2, −30 °C.

Acknowledgements

We acknowledge the financial assistance of The National Natural Science Foundation of China. The Major State Basic Research Development Program (Grant No. 2000077506). We also thank Dr. Xin-Sheng Lei and Dr. Hong-Feng Luo for ^{1}H NMR spectra.

References and notes

1. (a) Wu, Y. C.; Duh, C. Y.; Chang, F. R.; Wang, S. K.; Chang, J. J.; McPhail, D. R.; McPhail, A. T.; Lee, K. H. *J. Nat. Prod.* **1991**, *54*, 1077–1081; (b) Sam, T. W.; Saw-Yeu, C.; Matsjeh, S.; Gan, E. K.; Razak, D.; Mohamed, A. L. *Tetrahedron Lett.* **1987**, *28*, 2541–2544; (c) Talapatra, S. K.; Basu, D.; Goaiwami, S.; Talapatra, B. *Indian J. Chem. B* **1985**, *24*, 29–34.
2. (a) Fang, X. P.; Anderson, J. E.; Qui, X. X.; Kozlowski, J. F.; McLaughlin, J. L. *Tetrahedron* **1993**, *49*, 1563–1570, and references cited therein; (b) Fang, X. P.; Anderson, J. E.; Chang, C. J.; McLaughlin, J. L. *J. Nat. Prod.* **1991**, *54*, 1034–1043.
3. (a) Tsubiki, M.; Kanai, K.; Honda, T. *J. Chem. Soc., Chem. Commun.* **1992**, 1640–1641; (b) Yang, Z.-C.; Zhou, W.-S. *Heterocycles* **1997**, *45*, 367–383; (c) Mukai, C.; Hirai, S.; Hanaoka, M. *J. Org. Chem.* **1997**, *62*, 6619–6626; (d) Surivet, J. P.; Goré, J.; Vatèle, J. M. *Tetrahedron* **1996**, *37*, 14877–14890; (e) Gillhouly, J. G.; Shing, T. K. M. *J. Chem. Soc., Chem. Commun.* **1988**, 976; (f) Tsubuki, M.; Kanai, K.; Nagase, H.; Honda, T. *Tetrahedron* **1999**, *55*, 2493–2514; (g) Surivet, J. P.; Vatèle, J. M. *Tetrahedron Lett.* **1998**, *39*, 7299–7300.
4. (a) Gesson, J. P.; Jacquesy, J. C.; Mondon, M. *Tetrahedron Lett.* **1987**, *28*, 3949; (b) Somfai, P. *Tetrahedron* **1994**, *50*, 11315.
5. Mu, Q.; Tang, W.; Li, C.; Lu, Y.; Sun, H.; Zheng, X.; Wu, N.; Lou, B.; Xu, B. *Heterocycle* **1999**, *12*, 2969.
6. Chen, J.; Lin, G. Q.; Wang, Z. M.; Liu, H. Q. *Synlett* **2002**, *8*, 1265–1268.
7. Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237.
8. Zhou, W. S.; Jiang, B.; Pan, X. F. *Tetrahedron* **1990**, *46*, 3173–3188.
9. For 7-*epi*-goniodiol: $[\alpha]_D^{20}$ +83.5 (*c* 0.4, MeOH), {lit. $[\alpha]_D^{20}$ +85.4 (*c* 0.3, MeOH)}, IR (film): 3400, 2930, 1717, 1388, 1259, 1076; ESIMS *m/z*: 257.1 (M + Na); ^{1}H NMR (300 MHz, C_5D_5 N); δ 7.20–7.75 (m, 5H), 6.82 (ddd, J = 9.5 Hz, J = 5.9 Hz, J = 2.9 Hz), 5.95 (ddd, J = 9.5 Hz, J = 2.2 Hz, J = 1.1 Hz, 1H), 5.35 (d, J = 3.7 Hz, 1H), 4.80–5.80 (br s, 1H), 4.90 (dt, J = 10.8 Hz, J = 5.4 Hz, 1H), 4.30 (dd, J = 5.9 Hz, J = 3.8 Hz, 1H), 2.78 (m, 1H), 2.72 (m, 1H).
10. For leiocarpin A: $[\alpha]_D^{20}$ −97.6 (*c* 0.5, $CHCl_3$) {lit. $[\alpha]_D^{20}$ − 98.42 (*c* 0.6, $CHCl_3$)}, IR(KBr) ν_{max} (cm^{-1}): 3360, 1720, 1666, 1180; EIMS (*m/z*): 234 (60), 216 (M − 18, 7), 188 (10), 177 (17), 144 (15), 107 (100), 91 (40), 77 (43); HRMS for $C_{13}H_{14}O_4$: found: 234.0890, calcd: 234.0892; ^{1}H NMR (400 MHz, C_5D_5N): δ 4.8 (br s, 1H), 2.81 (dd, J = 5.2, 17.9, 1H), 2.9 (d, J = 19.5, 1H), 4.35 (br s, 1H), 4.41 (d, J = 8.8, 1H), 3.45 (d, J = 8.8, 1H), 2.11(br s, 1H), 7.25–7.43 (m, 5H).
11. Gillhouley, J. G.; Shing, T. K. M. *J. Chem. Soc., Chem. Commun.* **1988**, 976.