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Total synthesis of (*R*)-(+)-goniothalamin and (*R*)-(+)-goniothalamin oxide: first application of the sulfoxide-modified Julia olefination in total synthesis

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Abstract—A short and efficient synthesis of (*R*)-(+)-goniothalamin **1** and (*R*)-(+)-goniothalamin oxide **2** is described. During this approach, the sulfoxide-modified Julia olefination was used as a key step to connect aldehyde **5** to sulfoxide **6**. The desired styryl-containing adduct is obtained in good yield and with excellent *E*/*Z* selectivity.

Chiral lactones are commonly present in a number of natural and synthetic products, including various pheromones and medicinal compounds. Interestingly, these small exogenous molecules exert powerful effects on the cell functions, making them useful tools for understanding life processes and for treating life-threatening diseases.

Styryl lactones are a group of secondary metabolites commonly isolated from the genus Goniothalamus.[1] Recent studies have demonstrated that these compounds display cytotoxic and antitumour properties. (*R*)-(+)-Goniothalamin **1** is a typical representative of this class of compounds (Fig. 1).

(*R*)-(+)-Goniothalamin **1** was isolated in 1967 from the dried bark of *Cryptocarya caloneura*[2] and given the (*S*)-configuration. A decade later, the configuration of the stereocentre was revised and established as being (*R*).[3] Later on, (*R*)-(+)-**1** was isolated from *Cryptocarya moschata*,[4] *Bryonopsis laciniosa*[5] and various other species of *Goniothalamus*[6] (115 species[7] distributed throughout the tropics and subtropics). Some of the isolated goniothalamin-based derivatives are shown in Figure 1.

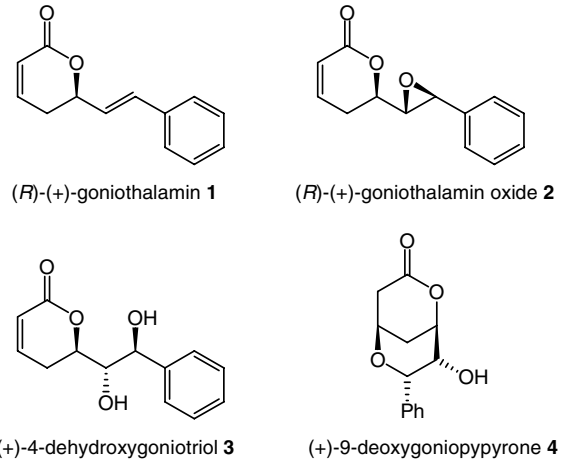

Figure 1. Some of the isolated goniothalamin-based derivatives.

(*R*)-(+)-Goniothalamin **1** displays in vitro cytotoxic effects on different cell lines, including MCF-7, T47D and MDA-MB-231 (breast carcinoma), HeLa cells (human cervical carcinoma), gastric carcinoma (HGC-27), leukemia carcinoma (HL-60) and ovarian carcinoma (Caov-3).[1a,8,9b] This cytotoxic activity, which results from the selective induction of apoptosis[9] on the cancer cell lines, was shown to be surprisingly low on nonmalignant cells.

In vivo studies revealed that (*R*)-(+)-**1** possessed tumouricidal and tumouristatic properties on Sprague–Dawley

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rats with 7,12-dimethylbenzanthracene (DMBA)-induced mammary tumours.[10]

Due to the interesting biological activity of (*R*)-**1**, several successful approaches to this natural product have been reported.[11] Even though the most commonly used antithetic approach to **1** is based on the C2–C3 and/or C6–C7 double bond disconnections (Fig. 2), other methods, such as asymmetric hetero-Diels–Alder cycloadditions and intramolecular nucleophilic additions to ketenes, have been employed.

Our interest in the total synthesis of (*R*)-(+)-**1** arose from the observation that all previous syntheses, that relied upon various olefination methods to establish the C6–C7 double bond, provided the styryl lactone either in poor yields and/or with mediocre selectivity.[11a,1] It was surmised that our recently developed sulfoxide-modified Julia olefination might serve as an ideal method to accomplish the desired olefination in high yield and selectivity.[12] The successful implementation of this approach will also enable us to prepare rapidly a varied library of goniothalamin **1** analogues from a common precursor, aldehyde **5**.

Our retrosynthesis of (*R*)-(+)-**1** is presented in Scheme 1. (*R*)-(+)-Goniothalamin **1** was disconnected at the C6–C7 bond, leading to aldehyde **5** and sulfoxide **6**. It was envisioned that aldehyde **5** might be easily assembled from the optically pure glycidol ether **8** via a ring opening/acylation/metathesis sequence. The benzylic sulfoxide **6** would be readily prepared by oxidation of the corresponding, commercially available, sulfide.

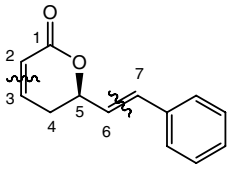
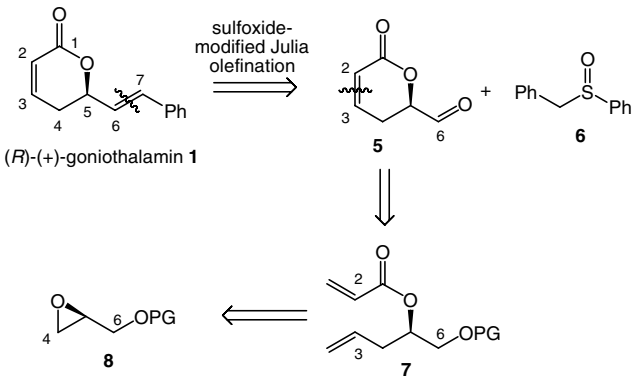


Figure 2. Most common (*R*)-(+)-goniothalamin **1** retrosynthetic disconnections.



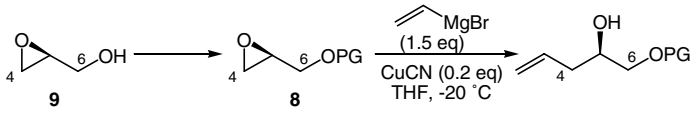
Scheme 1. Retrosynthesis of (*R*)-(+)-goniothalamin **1**.

To test the generality of our approach, it was decided to also evaluate the influence of four commonly used protecting groups (Bn, PMB, TBS and TBDPS) on the yields and selectivity of this sequence.

Our synthesis began with commercially available (*R*)-glycidol **9**, which was protected with PMB, TBS and TBDPS-groups, yielding the corresponding epoxy ethers **8b–d** (Scheme 2).[13] Copper-catalyzed opening of epoxides **8** with vinyl magnesium bromide furnished the optically enriched homoallylic alcohols **10a–d** in excellent yields and purities.

Acylation of alcohols **10a–d**, using either acryloyl chloride or acrylic acid, afforded smoothly the metathesis precursors **7a–d** (Scheme 3).

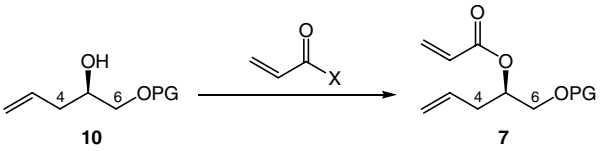
Finally, the metathesis step was evaluated. It was observed that the nature of the protecting group in substrate **7** had a significant influence on the reaction rate (Table 1). Indeed, when the benzyl protected ester **7a** was treated with the 1st generation Grubbs' catalyst (**GC-1**), only poor conversion of **7a** into **11a** was observed (Table 1, entry 1). It was thought that the lone pairs of the oxygen present in the benzyl ether function[14] could compete with the olefins for the vacant coordination sites present in **GC-1**. Even though this process is reversible, it decreases the reaction rate by sequestering



Entry	Product	PG	Conditions	Yield[a] [%]
1	**8a**	Bn	-	-[b]
2	**8b**	PMB	NaH, PMBCl TBAI, DMF	86
3	**8c**	TBS	TBSCl, Im, CH_2Cl_2	99
4	**8d**	TBDPS	TBDPSCl, Im, CH_2Cl_2	99

[a] Refers to pure isolated compounds
[b] Commercially available compound

Scheme 2. Synthesis of homoallylic alcohols **10**.

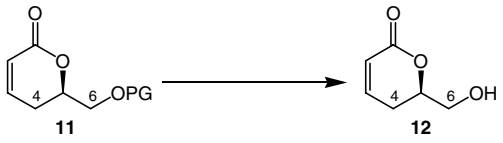


Entry	PG	X	Conditions	Product	Yield[a] [%]
1	Bn	OH	DCC, CH_2Cl_2, r.t.,12 h	**7a**	94
2	PMB	OH	DCC, CH_2Cl_2, r.t.,12 h	**7b**	91
3	TBS	Cl	TEA, CH_2Cl_2, 0 °C, 30 min	**7c**	89
4	TBDPS	Cl	TEA, CH_2Cl_2, 0 °C, 30 min	**7d**	91

[a] Refers to pure isolated compounds

Scheme 3. Synthesis of metathesis precursors **7**.

Table 2. Deprotection of alcohol **11**



Entry	PG	Conditions	Yield[a] (%)
1	Bn	$FeCl_3$, CH_2Cl_2, rt, 5 min	80
2	Bn	BCl_3, CH_2Cl_2, −78 °C, 2 h	83
3	PMB	DDQ, CH_2Cl_2, rt, 2.5 h	92
4	TBS	TBAF, THF, 0 °C, 3 h	43
5	TBS	TBAF, DMF, 0 °C, 12 h	87
6	TBDPS	TBAF, DMF, 0 °C, 12 h	88

[a] Refers to pure, isolated compounds.

the catalyst, resulting in a competitive thermal decomposition of the ruthenium species and therefore requiring a higher catalyst loading.

To overcome this problem, and as originally proposed by Fürstner, $Ti(OPr^i)_4$ was added as an additive[15] with the aim of preferentially blocking the ether oxygen lone pairs. In the event, treatment of substrate **7a** with **GC-1**/$Ti(OPr^i)_4$ resulted in the smooth formation of the desired lactone **11a** in 92% yield (Table 1, entry 2).

A similar situation was encountered with the PMB-protected derivative **11b** (Table 1, entries 3–5), though in this case, even the use of **GC-1**/$Ti(OPr^i)_4$ did not lead to complete conversion of **7b** to **11b**. Therefore, the more reactive 2nd generation Grubbs' catalyst (**GC-2**)/$Ti(OPr^i)_4$ had to be employed (Table 1, entry 5).

As for the TBS and TBPDS-containing substrates **7c** and **d**, the addition of $Ti(OPr^i)_4$ was unnecessary since the steric bulk of these protecting groups effectively inhibits any undesired interaction between the ether and Grubbs' catalyst (Table 1, entries 6 and 7).

Having obtained lactones **11a–d**, we next investigated their selective deprotection (Table 2). Initially, removal of the benzyl group was efficiently accomplished, in the presence of the activated olefins, by treatment of **11a** with $FeCl_3$ (Table 2, entry 1).[16] Unfortunately, this reaction proved to be temperamental[17] and an alternative method, using BCl_3, was employed (Table 2, entry 2).

Pleasingly, DDQ-mediated deprotection of the PMB group proceeded smoothly, yielding alcohol **12** in 92% yield (Table 2, entry 3).

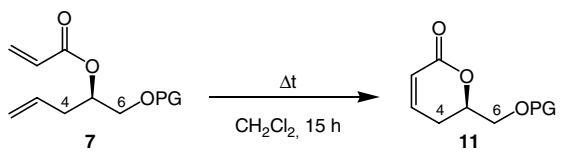
The unravelling of both silicon-containing substrates was achieved using TBAF. Interestingly, it was observed that the polarity of the solvent strongly influenced the product distribution (Table 2, entries 4–6). Indeed, when THF was used as a solvent, a large amount of nonidentified side products were generated, accompanied by the desired alcohol **12**, which was isolated in only 43% yield (Table 2, entry 5). On the other hand, if DMF was employed as the solvent,[18] TBAF-mediated deprotection of **11c** and **d** cleanly furnished alcohols **12** in 87% and 88% yields, respectively.

Swern oxidation of alcohol **12** yielded the unstable aldehyde **5**, which was immediately reacted with sulfoxide **6** under our standard sulfoxide-modified Julia olefination sequence, producing (*R*)-(+)-goniothalamin **1**[19] in 78% yield (starting from alcohol **12**) and with excellent *E*/*Z*-selectivity (Scheme 4).

It is important to note that our sulfoxide-modified Julia olefination afforded the natural product (*R*)-(+)-**1** with both an excellent yield and nearly perfect control of the C6–C7 double bond geometry. Such an observation stands in sharp contrast to the results obtained using alternative olefination methods, such as Wittig, classical Julia and Kociensky–Julia protocols, which accomplished this transformation either in low yields and/or modest selectivity (Table 3).

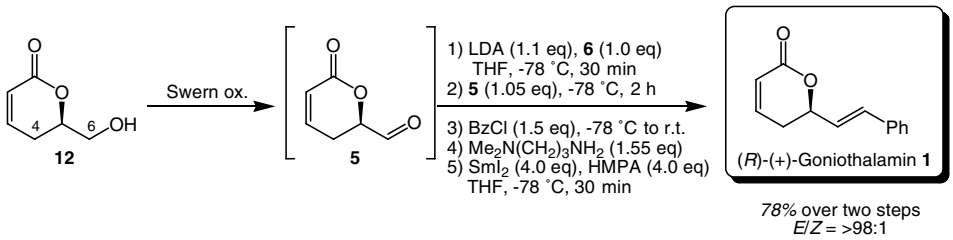
Since it is known that (*R*)-(+)-goniothalamin **1** is a precursor to other related natural products,[20] its stereoselective conversion to (*R*)-(+)-goniothalamin oxide **2** was attempted. After brief optimization of the reaction conditions, (*R*)-(+)-goniothalamin oxide **2** was isolated in 98% yield in a satisfactory 19:1 diastereomeric ratio (Table 4).

Table 1. Optimization of the metathesis reaction



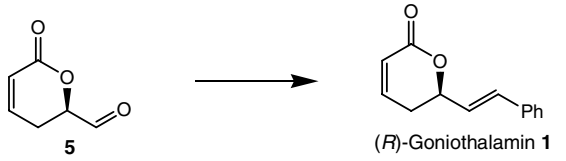
Entry	PG	Grubb's cat. (equiv)	Additive	Product	Yield[a] (%)
1	Bn	**GC-1** (0.1)	—	**11a**	45
2	Bn	**GC-1** (0.1)	$Ti(OPr^i)_4$	**11a**	92
3	PMB	**GC-1** (0.1)	—	**11b**	<10
4	PMB	**GC-1** (0.1)	$Ti(OPr^i)_4$	**11b**	78
5	PMB	**GC-2** (0.05)	$Ti(OPr^i)_4$	**11b**	99
6	TBS	**GC-1** (0.1)	—	**11c**	96
7	TBDPS	**GC-1** (0.1)	—	**11d**	89

[a] Refers to pure, isolated compounds.



Scheme 4. Sulfoxide-modified Julia olefination.

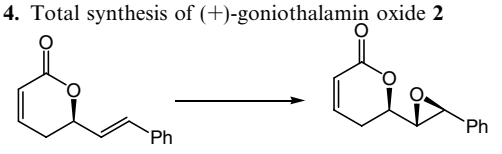
Table 3. Comparison of the various olefination methods in the context of the synthesis of (*R*)-(+)-goniothalamin



Entry	Olefination	Conditions	Yield (%)	*E*/*Z*
1[a]	Wittig	$BnPPh_3^+Cl^-$, *n*-BuLi	53	1:3
2[b]	Wittig	$BnPPh_3^+Br^-$, *n*-BuLi	57	1:9
3[a]	Kociensky–Julia	$PTSO_2Bn$, KHMDS	18	>98:1
4	Julia	$BnSO_2Ph$	<5	n.d.
5	Sulfoxide–Julia	BnS(O)Ph	78	>98:1

[a] Ref. 11l.
[b] Ref. 11a.

Table 4. Total synthesis of (+)-goniothalamin oxide **2**



Entry	Conditions	Yield (%)	dr
1	*m*-CPBA[a] (4.0 equiv), CH_2Cl_2, Δ, 4 h	69	3:2
2	*m*-CPBA[b] (4.0 equiv), CH_2Cl_2, rt, 24 h	97	10:1
3	*m*-CPBA[b] (4.0 equiv), CH_2Cl_2, 0 °C, 24 h	98	19:1

[a] Commercially available 70% *m*-CPBA was used.
[b] Purified acid and H_2O-free *m*-CPBA was used.

In summary, we have demonstrated that the sulfoxide-modified Julia olefination is a powerful method for the selective and connective formation of alkenes previously difficult to access by standard olefination protocols (Table 3). Moreover, we have shown that this reaction could be successfully employed in the context of natural product synthesis and have prepared (*R*)-(+)-goniothalamin **1** in six steps (51–55% overall yield) or five steps (55% overall yield) starting from commercially available (*R*)-glycidol **9** or (*R*)-benzyl glycidol **8a**, respectively.

In contrast to the previous total syntheses of **1**, the styryl subunit was efficiently introduced during the final step. Since it is known that changes in electronic and steric properties of the phenyl group strongly influence the biological activity of this family of natural products, our approach enables the efficient assembly of a variety of goniothalamin **1** analogues by uniting the common intermediate **5** with a range of different sulfoxides **6**.

Finally, (*R*)-(+)-goniothalamin oxide **2** has been obtained in excellent yield by diastereoselective epoxidation of (*R*)-(+)-**1**.

Acknowledgements

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.06.054.

References and notes

1. (a) Ali, A.; Mackeen, M. M.; Hamid, M.; Aun, Q. B.; Zauyah, Y.; Azimahtol, H. L. P.; Kawazu, K. *Planta Med.* **1997**, *63*, 81–83; (b) Cao, S. G.; Wu, X. H.; Sim, K. Y.; Tan, B. K. H.; Pereira, J. T.; Goh, S. H. *Tetrahedron* **1998**, *54*, 2143–2148; (c) Bermejo, A.; Leonce, S.; Cabedo, N.; Andreu, I.; Caignard, D. H.; Atassi, G.; Cortes, D. *J. Nat. Prod.* **1999**, *62*, 1106–1109; (d) Mossadik, M. A.; Haque, M. E. *Phytother. Res.* **2003**, *17*, 1155–1157; (e) Lan, Y. H.; Chang, F. R.; Yu, J. H.; Yang, Y. L.; Chang, Y. L.; Lee, S. J.; Wu, Y. C. *J. Nat. Prod.* **2003**, *66*, 487–490.
2. Hlubucek, J. R.; Robertson, A. V. *Aust. J. Chem.* **1967**, *20*, 2199–2206.
3. Meyer, H. H. *Liebigs Ann. Chem.* **1979**, 484–487.
4. Cavalheiro, A. J.; Yoshida, M. *Phytochemistry* **2000**, *53*, 811–819.
5. Kabir, K. E.; Khan, A. R.; Mosaddik, M. A. *J. Appl. Ent.* **2003**, *127*, 112–115.
6. Goniothalamin was also isolated from: (a) *Goniothalamus giganteus*: El-Zayat, A. E.; Ferrigni, N. R.; McCloud, T. G.; McKenzie, A. T.; Byrn, S. R.; Cassady, J. M.; Chang, C.; McLauglin, J. L. *Tetrahedron Lett.* **1985**, *26*, 955–956; (b) *Goniothalamus uvaroids*: Ahmad, F. B.; Tukol, W. A.; Omar, S.; Sharif, A. M. *Phytochemistry* **1991**, *30*, 2430–2431; (c) *Goniothalamus malayanus, G. andersonni, G.*

macrophyllus and *G. velutinus*: Jewers, K.; Blunden, G.; Wetchapinan, S.; Dougan, J.; Manchada, A. H.; Davis, J. B.; Kyi, A. *Phytochemistry* **1972**, *11*, 2025–2030; (d) *Goniothalamus dolichocarpus*: Goh, S. H.; Ee, G. C. L.; Chuah, C. H.; Wei, C. *Aust. J. Chem.* **1995**, *48*, 199–205.

7. Some of the species are widely used as traditional medicines. See: (a) Kan, W. S. *Pharmaceutical Botany*; National Research Institute of Chinese Medicine: Taipei, 1979; p 247; (b) Surivet, J. P.; Vatele, J.-M. *Tetrahedron* **1999**, *55*, 13011–13028.
8. (a) Inayat-Hussain, S. H.; Osman, A. B.; Din, L. B.; Ali, A. M.; Snowden, R. T.; MacFarlane, M.; Cain, K. *FEBS Lett.* **1999**, *456*, 379–383; (b) Pihie, A. H. L.; Stanslas, J.; Bin Din, L. *Anticancer Res.* **1998**, *18*, 1739–1744; (c) Chien, A. L. T.; Pihie, A. H. L. *J. Biochem. Mol. Biol.* **2003**, *36*, 269–274; (d) Teoh, P. L.; Azimahtol, H. L. P. *Malays. Appl. Biol.* **1999**, *28*, 107–111; (e) de Fátima, A.; Kohn, L. K.; Antonio, M. A.; de Carvalho, J. E.; Pilli, R. A. *Bioorg. Med. Chem.* **2005**, *13*, 2927–2933.
9. (a) Inayat-Hussain, S. H.; Annuar, B. O.; Din, L. B.; Ali, A. M.; Ross, D. *Toxicol. in Vitro* **2003**, *17*, 433–439; (b) Hengartner, M. O. *Nature* **2000**, *12*, 770–776; (c) Zamzami, N.; Marchetti, P.; Castedo, M.; Decaudin, D.; Macho, A.; Hirsch, T.; Susin, S.; Petit, P. X.; Mignotte, B.; Kroemer, G. *J. Exp. Med.* **1995**, *182*, 367–377; (d) Liu, X.; Kim, C. N.; Yang, J.; Jemmerson, R.; Wang, X. *Cell* **1996**, *12*, 147–157; (e) Kluck, R. M.; Bossy-Wetzel, E.; Green, D. R.; Newmeyer, D. D. *Science* **1997**, *275*, 1132–1136; (f) Yang, J.; Liu, X.; Bhalla, K.; Kim, C. N.; Ibrado, A. M.; Cai, J.; Peng, T. I.; Jones, D. P.; Wang, X. *Science* **1997**, *275*, 1129–1132; (g) Li, P.; Nijhawan, D.; Budihardjo, I.; Srinivasula, I. M.; Ahmad, M.; Alnemri, E. S.; Wang, X. *Cell* **1997**, *91*, 479–489; (h) Zou, H.; Henzel, W. J.; Liu, X.; Lutschg, A.; Wang, X. *Cell* **1997**, *90*, 405–413; (i) Srinivasula, S. M.; Ahmad, M.; Fernandes-Alnemri, T.; Alnemri, E. S. *Mol. Cell* **1998**, *1*, 949–957; (j) Nicholson, D. W.; Ali, A.; Thornberry, N. A.; Vaillancourt, J. P.; Ding, C. K.; Gallant, M.; Gareau, Y.; Griffin, P. R.; Labelle, M.; Lazebnik, Y. A.; Munday, N. A.; Raju, S. M.; Smulson, M. E.; Yamin, T.-T.; Yu, V. L.; Miller, D. K. *Nature* **1995**, *376*, 37–43; (k) Kothakota, S.; Azuma, T.; Reinhard, C.; Klippel, A.; Tang, J.; Chu, K.; McGarry, T. J.; Kirschner, M. W.; Koths, K.; Kwiatkowski, D. J.; Williams, L. T. *Science* **1997**, *278*, 294–298.
10. Meenakshii, N.; Lee, A.; Azimahtol, H. L. P.; Hasidah, S. *Malays. Appl. Biol.* **2000**, *29*, 121–126.
11. Selected examples: (a) O'Connor, B.; Just, G. *Tetrahedron Lett.* **1986**, *27*, 5201–5202; (b) Bennet, F.; Knight, D. W. *Tetrahedron Lett.* **1988**, *29*, 4625–4828; (c) Bennett, F.; Knight, D. W.; Fenton, G. *J. Chem. Soc., Perkin Trans. 1* **1991**, 519–523; (d) Rahman, S. S.; Wakefield, B. J.; Roberts, S. M.; Dowle, M. D. *Chem. Commun.* **1989**, 303–304; (e) Honda, T.; Kametani, T.; Kanai, K.; Tatsuzaki, Y.; Tsubuki, M. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1733–1737; (f) Takano, S.; Tamikubo, T.; Sugihara, T.; Ogasawara, K. *Tetrahedron: Asymmetry* **1992**, *3*, 853–856; (g) Fuganti, C.; Perdrochi-Fantoni, G.; Sarra, A.; Servi, S. *Tetrahedron: Asymmetry* **1994**, *5*, 1135–1138; (h) Ramachandran, P. V.; Reddy, M. V. R.; Brown, H. C. *Tetrahedron Lett.* **2000**, *41*, 583–586; (i) Job, A.; Wolberg, M.; Müller, M.; Enders, D. *Synlett* **2001**, 1796–1798; (j) Sundby, E.; Perk, L.; Anthonsen, T.; Aasen, A. J.; Hansen, T. V. *Tetrahedron* **2004**, *60*, 521–524; (k) de Fátima, A.; Pilli, R. A. *Tetrahedron Lett.* **2003**, *44*, 8721–8724; (l) de Fátima, Â.; Pilli, R. A. *ARKIVOC* **2003**, *10*, 118–126.
12. (a) Pospíšil, J.; Pospíšil, T.; Markó, I. E. *Collect. Czech. Chem. Commun.* **2005**, *70*, 1953–1969; (b) Pospíšil, J.; Pospíšil, T.; Markó, I. E. *Org. Lett.* **2005**, *7*, 2373–2376.
13. Benzyl glycidol **8a** is commercially available.
14. Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413–4450.
15. (a) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012–3043; (b) Fürstner, A.; Langemann, K. *J. Am. Chem. Soc.* **1997**, *119*, 9130–9136.
16. Padrón, J. I.; Vázquez, J. T. *Tetrahedron: Asymmetry* **1995**, *6*, 857–858.
17. It was observed that the quality of $FeCl_3$ is extremely important for the reproducibility of the reaction. Traces of humidity present in $FeCl_3$ diminish the yields of the reaction. In these experiments, $FeCl_3$ from Aldrich was employed.
18. For similar observations, see: Mizutani, H.; Watanabe, M.; Honda, T. *Tetrahedron* **2002**, *58*, 8929–8936.
19. Experimental data for (*R*)-(+)-goniothalamin **1**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.56 (m, 2H), 5.12 (1H, dq, $J = 6.5$ Hz, $J = 1.2$ Hz), 6.10 (dt, 1H, $J = 9.7$ Hz, $J = 1.7$ Hz), 6.29 (dd, 1H, $J = 16.1$ Hz, $J = 6.5$ Hz), 6.74 (d, 1H, $J = 15.8$ Hz), 6.94 (dt, 1H, $J = 9.7$ Hz, $J = 4.4$ Hz), 7.30–7.42 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 30.1, 78.1, 121.9, 125.8, 133.3, 144.8, 126.9–136.0 (arom. CH and Cq), 164.1. Mp = 82–83 °C; lit.[111] 81–82 °C. MS (APCI), *m*/*z* (%): 201.0 (39) [M^++H], 183.1 (100), 155.2 (66), 130.1 (41). $[\alpha]_D^{20}$ +169.8 (*c* 1.45, $CHCl_3$); lit.[6c] $[\alpha]_D^{25}$ +170.3 (*c* 1.38, $CHCl_3$).
20. Lan, Y.-H.; Chang, F.-R.; Yu, J.-H.; Yang, Y.-L.; Chang, Y.-L.; Lee, S.-J.; Wu, Y.-C. *J. Nat. Prod.* **2003**, *66*, 487–490.