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New construction of the bicyclo[3.3.1]nonane system via Lewis acid promoted regioselective ring-opening reaction of the tricyclo[4.4.0.0^{5,7}]dec-2-ene derivative

Masahito Abe and Masahisa Nakada*

Department of Chemistry, Faculty of Science and Engineering, Waseda University, 3-4-1 Ohkubo, Shinjuku-ku, Tokyo 169-8555, Japan

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Abstract—A new access to the bicyclo[3.3.1]nonane system, which is a common structure in a number of polyisoprenylated phloroglucinol derivatives (phloroglucins), has been developed via the Lewis acid promoted regioselective ring-opening reaction of the cyclopropane, a tricyclo[4.4.0.0^{5,7}]dec-2-ene derivative.

Hyperforin (Fig. 1) was isolated as a metabolite from St. John's wort (*Hypericum perforatum* L.), a medicinal plant traditionally used to treat depression and superficial wounds, burns, and dermatitis.[1] To date it has been reported that hyperforin shows antibacterial,[1a,2] antitumor,[3] apoptotic,[4] and some other interesting biological activities.[5–7] Recently, a number of polyisoprenylated phloroglucinol derivatives (phloroglucins) from diverse plant sources have been reported,[8] and synthetic studies on members of this class of natural products have been carried out.[9,10]

In addition to its wide-ranging biological activities, hyperforin possesses a trioxygenated bicyclo[3.3.1]nonane system, bearing a homoprenyl group and a methyl group at C6, three prenyl groups at C1, C3, and C7, and an isobutyryl function at the bridgehead C5, giving us a synthetic challenge.

The potent bioactivity and complex structural features make hyperforin an attractive synthetic target; hence, we commenced synthetic studies on hyperforin, and report herein a new construction of the bicyclo-[3.3.1]nonane system, a core structure of hyperforin.

As outlined in Scheme 1, we expected that Lewis acid promoted regioselective ring-opening reaction of the cyclopropane **1**, a tricyclo[4.4.0.0^{5,7}]dec-2-ene derivative, via the intramolecular attack of the benzyl carbonate would afford the cyclic carbonate **2**,[12] which was a potentially viable intermediate for the synthesis of phloroglucins because **2** was oxygenated at its C9

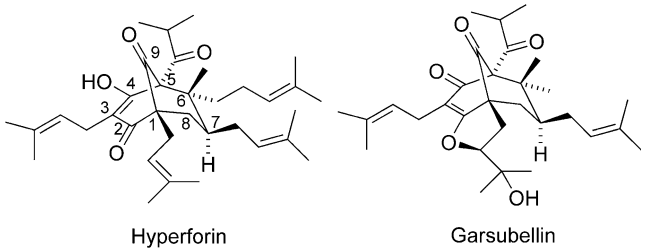
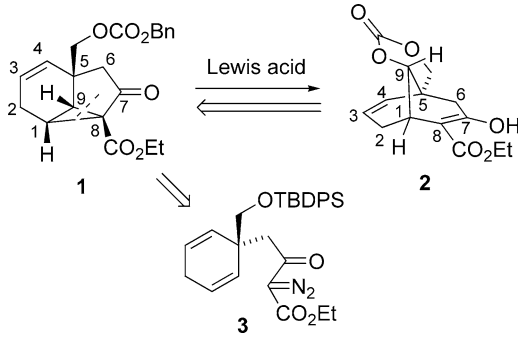


Figure 1.



Scheme 1. Retrosynthetic analysis of **1**.[11]

* Corresponding author. Tel./fax: +81 3 5286 3240; e-mail: mnakada@waseda.jp

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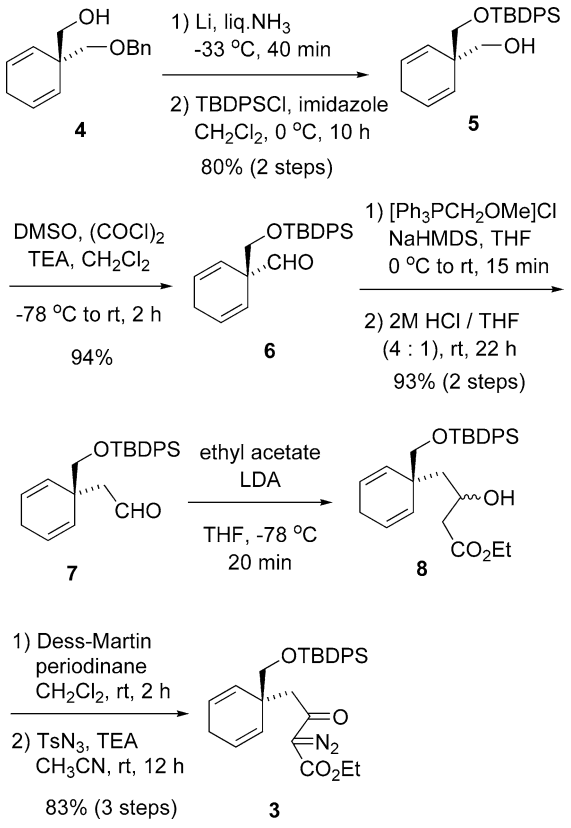
position. Hence, **2** was suitable for preparing the bicyclo[3.3.1]nonane-9-one system, which had been successfully alkylated at its bridgehead position.[13]

The Lewis acid promoted ring-opening reaction of cyclopropane **1** was challenging because no precedent for this type of ring-opening reaction forming cyclic carbonate had been reported so far as we know. In addition, two diastereomers could be produced by the possible bond cleavage between either C1 and C8 or C8 and C9 of **1**. We expected that, however, this ring-opening reaction would take place because the Lewis acid promoted ring-opening reaction of cyclopropyl ketone with oxygen nucleophile had been reported.[12] Furthermore, formation of cyclic carbonate by the Lewis acid promoted ring-opening reaction of the epoxide of allylic benzyl carbonate had been reported, too.[14] We also expected that the bicyclo[3.3.1]nonane derivative **2** would be the major product, because the intramolecular attack of the benzyl carbonate group at C9 would be favorable due to the limited length of the carbonate.

Since we have succeeded in preparing some chiral tricyclo[4.4.0.0^{5,7}]dec-2-ene derivatives via the catalytic asymmetric intramolecular cyclopropanation,[15] we expected that **1** would be easily prepared according to the similar procedure, that is, the intramolecular cyclopropanation of α-diazo-β-keto ester **3**.

Thus, we commenced the preparation of **3** from alcohol **4**[15b,16] as shown in Scheme 2. To introduce a benzyl carbonate group at the later stage, the benzyl group in **4** was replaced with a readily removable TBDPS group. The benzyl group was easily removed by Birch reduction, and the resulting diol was converted to TBDPS ether **5** under carefully controlled conditions to avoid formation of the bis-TBDPS ether (80%, 2 steps). Swern oxidation of **5** cleanly afforded aldehyde **6** (94%), which was reacted with methoxymethylidene phosphorane, followed by acidic hydrolysis to afford the one-carbon homologated aldehyde **7** (93%, 2 steps). Aldol reaction of a lithium enolate of ethyl acetate with **7** proceeded smoothly to produce **8** as a mixture of diastereomers; hence, this mixture was used for the next step without purification. Dess–Martin oxidation of **8** cleanly produced the corresponding ketone, which was successfully converted to the α-diazo-β-keto ester **3**[17] (83%, 3 steps).

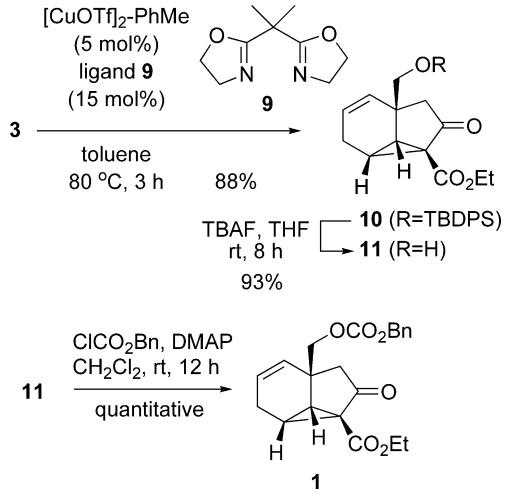


Scheme 2. Synthesis of **3**.

The intramolecular cyclopropanation of **3** with CuOTf (10 mol %) was sluggish, but the reaction using the catalyst in situ formed from CuOTf (10 mol %) and ligand **9**[18] (15 mol %) affected to produce the desired **10**[19] (88%) (Scheme 3). The TBDPS group in **10** was removed with TBAF (93%) to afford the alcohol **11**, which was converted to **1**[20] (quantitative) under conventional conditions.

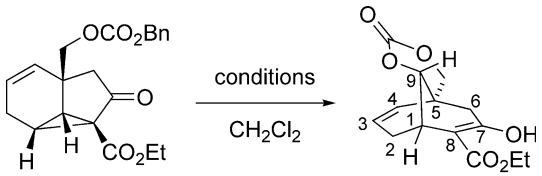
Now, the stage was set for the Lewis acid promoted ring-opening reaction of **1**. Among various Lewis acids screened, we found that TESOTf promoted the ring-opening reaction of **1** (Table 1, entries 1–3), however, use of TESOTf (1.0 equiv) produced the desired product **2** in only 33% yield (at 50% conversion) (entry 1). Although an excess amount of TESOTf slightly increased the yield (entries 2 and 3), the starting material remained under these reaction conditions. Furthermore, the reaction carried out at elevated reaction temperature resulted in decreased yield, so another Lewis acid effective for this ring-opening reaction was investigated.

Fortunately, $BF_3{\cdot}OEt_2$ was found to be most suitable for this ring-opening reaction. Thus, 1 equiv of $BF_3{\cdot}OEt_2$ produced **2** in rather low yield (quantitative at 34% conversion), but use of 6 equiv of $BF_3{\cdot}OEt_2$



Scheme 3. Synthesis of **1**.

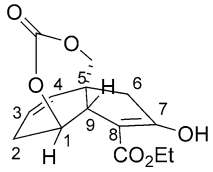
Table 1. Lewis acid promoted ring-opening reaction of cyclopropane **1**



1 **2**

Entry	Lewis acid (equiv)	Temperature (°C)	Time[a] (h)	Yield[b] (%)
1	TESOTf (1.0)	−78, −78 to −10	4, 11.5	33 (at 50% conv)
2	TESOTf (3.0)	−78, −60, −60 to −20	0.75, 1, 13	44 (at 14% conv)
3	TESOTf (6.0)	−78, −20	0.2, 36	73 (at 29% conv)
4	$BF_3{\cdot}OEt_2$ (1.0)	−78, −78 to −10	4, 11.5	Quantitative (at 34% conv)
5	$BF_3{\cdot}OEt_2$ (6.0)	−78, −50, −20	0.2, 1.5, 6.5	61 (at 84% conv)
6	$BF_3{\cdot}OEt_2$ (6.0)	−78, −20	0.2, 47	**93**

[a] Time at the corresponding reaction temperature. That is, 4 h for −78 °C (entry 1) is the reaction time at −78 °C, and 11.5 h for −78 to −10 °C (entry 1) is the time required for raising the reaction temperature from −78 to −10 °C.
[b] Isolated yields.



2'

Figure 2.

increased the yield to 61% (at 84% conversion), and, finally, prolonged reaction time (47 h) at −20 °C successfully increased the yield up to 93% without recovering the starting material. It should be noted that no formation of **2′** (Fig. 2), which could be produced via another bond-cleavage of the cyclopropane **1**, was observed in all entries in Table 1.

The product **2** was fully characterized by ^{1}H NMR, ^{13}C NMR, IR, and HRMS spectra.[21] Detailed analysis of its H–H and C–H COSY spectra clearly disclosed the correlations (H-4/H-3; H-3/H-2; H-2/H-1; H-1/H-9) to establish the structure of **2** as shown in Table 1. The characteristic enol form of **2** was supported by ^{1}H NMR, ^{13}C NMR, and IR spectra.

In summary, a new access to the bicyclo[3.3.1]nonane system, which is a common structure in a number of polyisoprenylated phloroglucinol derivatives (phloroglucins), has been developed. The key reaction is the Lewis acid promoted regioselective ring-opening reaction of cyclopropane **1**, a tricyclo[4.4.0.0^{5,7}]dec-2-ene derivative, by the intramolecular attack of the benzyl carbonate to produce the desired product **2** as a sole product. The chiral tricyclo[4.4.0.0^{5,7}]dec-2-ene derivative **1** is expected to be readily prepared by the catalytic asymmetric intramolecular cyclopropanation of **3** by use of a chiral ligand, so the chiral bicyclo[3.3.1]nonane system, which would be a key intermediate for the asymmetric synthesis of phloroglucins, would be produced via this ring-opening reaction. Therefore, further studies on the asymmetric synthesis of hyperforin are now underway in this laboratory.

Acknowledgments

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References and notes

1. (a) Gurevich, A. I.; Dobrynin, V. N.; Kolosov, M. N.; Popravko, S. A.; Ryabova, I. D.; Chennov, B. K.; Derbentseva, N. A.; Aizenman, B. E.; Garagulya, A. D. *Antibiotiki* **1971**, *6*, 510–513; (b) Bystrov, N. S.; Chernov, B. K.; Dobrynin, V. N.; Kolosov, M. N. *Tetrahedron Lett.* **1975**, *16*, 2791–2794; (c) Erdelmeier, C. A. J. *Pharmacopsychiatry* **1998**, *31*, 2–6; (d) Barnes, J.; Anderson, L. A.; Phillipson, J. D. *J. Pharm. Pharmacol.* **2001**, *53*, 583–600; (e) Schempp, C. M.; Windeck, T.; Hezel, S.; Simon, J. C. *Phytomedicine* **2003**, *10*, 31–37.
2. Schempp, C. M.; Pelz, K.; Wittmer, A.; Schopf, E.; Simon, J. C. *Lancet* **1999**, *353*, 2129.
3. (a) Schempp, C. M.; Winghofer, B.; Lüdtke, R.; Simon-Haarhaus, B.; Schöpff, E.; Simon, J. C. *Br. J. Dermatol.* **2000**, *142*, 979–984; (b) Schempp, C. M.; Kirkin, V.; Simon-Haarhaus, B.; Kersten, A.; Kiss, J.; Termeer, C. C.; Gilb, B.; Kaufmann, T.; Borner, C.; Sleeman, J. P.; Simon, J. C. *Oncogene* **2002**, *21*, 1242–1250; For the derivative of hyperforin, see: (c) Gartner, M.; Müller, T.; Simon, J. C.; Giannis, A.; Sleeman, J. P. *ChemBioChem* **2005**, *6*, 171–177.
4. Hostanska, K.; Reichling, J.; Bommer, S.; Weber, M.; Saller, R. *Eur. J. Pharm. Biopharm.* **2003**, *56*, 121–132.
5. Inhibition of inflammatory enzymes (cyclooxygenase-1 and 5-lipoxygenase): Albert, D.; Zündorf, I.; Dingermann, T.; Müller, W. E.; Steinhilber, D.; Werz, O. *Biochem. Pharmacol.* **2002**, *64*, 1767–1775.
6. Interference with radical chain oxidation processes: Heilmann, J.; Winkelmann, K.; Sticher, O. *Planta Med.* **2003**, *69*, 202–206.
7. Action as a nuclear factor that regulates expression of the cytochrome P450 3A4 monooxygenase: (a) Watkins, R.

E.; Maglich, J. M.; Moore, L. B.; Wisely, G. B.; Noble, S. M.; Davis-Searles, P. R.; Lambert, M. H.; Kliewer, S. A.; Redinbo, M. R. *Biochemistry* **2003**, *42*, 1430–1438; (b) Moore, L. B.; Goodwin, B.; Jones, S. A.; Wisely, G. B.; Serabjit-Singh, C. J.; Willson, T. M.; Collins, J. L.; Kliewer, S. A. *Proc. Natl. Acad. Sci. U.S.A.* **2000**, *97*, 7500–7502.

8. (a) Karanjgoakar, C. G.; Rama Rao, A. V.; Venkataraman, K.; Palmer, K. J. *Tetrahedron Lett.* **1973**, *14*, 4977–4980; (b) Rama Rao, A. V.; Venkatswamy, G.; Pendse, A. D. *Tetrahedron Lett.* **1980**, *21*, 1975–1978; (c) Krishnamurthy, N.; Lewis, Y. S.; Ravindranath, B. *Tetrahedron Lett.* **1981**, *22*, 793–796; (d) Maisenbacher, P.; Kovar, K. A. *Planta Medica* **1992**, *58*, 291–293; (e) Fukuyama, Y.; Kuwayama, A.; Minami, H. *Chem. Pharm. Bull.* **1997**, *45*, 947–949; (f) Fukuyama, Y.; Minami, H.; Kuwayama, A. *Phytochemistry* **1998**, *49*, 853–857; (g) de Oliveira, C. M. A.; Porto, A. L. M.; Bittrich, V.; Marsaioli, A. J. *Phytochemistry* **1999**, *50*, 1073–1079; (h) Henry, G. E.; Jacobs, H.; Carrington, C. M. S.; McLean, S.; Reynolds, W. F. *Tetrahedron* **1999**, *55*, 1581–1596; (i) Verotta, L.; Appendino, G.; Belloro, E.; Jakupovic, J.; Bombardelli, E. *J. Nat. Prod.* **1999**, *62*, 770–772; (j) Grossman, R. B.; Jacobs, H. *Tetrahedron Lett.* **2000**, *41*, 5165–5169; (k) Lokvam, J.; Braddock, J. F.; Reichardt, P. B.; Clausen, T. P. *Phytochemistry* **2000**, *55*, 29–34; (l) Porto, A. L. M.; Machado, S. M. F.; de Oliveira, C. M. A.; Bittrich, V.; Amaral, M. d. C. E.; Marsaioli, A. J. *Phytochemistry* **2000**, *55*, 755–768; (m) Verotta, L.; Appendino, G.; Jakupovic, J.; Bombardelli, E. *J. Nat. Prod.* **2000**, *63*, 412–415; (n) Cuesta-Rubio, O.; Velez-Castro, H.; Frontana-Uribe, B. A.; Cárdenas, J. *Phytochemistry* **2001**, *57*, 279–283; (o) Shan, M. D.; Hu, L. H.; Chen, Z. L. *J. Nat. Prod.* **2001**, *64*, 127–130; (p) Winkelmann, K.; Heilmann, J.; Zerbe, O.; Rali, T.; Sticher, O. *J. Nat. Prod.* **2001**, *64*, 701–706; (q) Cuesta-Rubio, O.; Frontana-Uribe, B. A.; Ramírez-Apan, T.; Cárdenas, J. *Z. Naturforsch.* **2002**, *57c*, 372–378; (r) Matsuhisa, M.; Shikishima, Y.; Takaishi, Y.; Honda, G.; Ito, M.; Takeda, Y.; Shibata, H.; Higuti, T.; Kodzhimatov, O. K.; Ashurmetov, O. *J. Nat. Prod.* **2002**, *65*, 290–294; (s) Chaturvedula, V. S. P.; Schilling, J. K.; Kingston, D. G. I. *J. Nat. Prod.* **2002**, *65*, 965–972; (t) Weng, J.-R.; Lin, C.-N.; Tsao, L.-T.; Wang, J.-P. *Chem. Eur. J.* **2003**, *9*, 1958–1963; (u) Weng, J.-r.; Lin, C.-n.; Tsao, L.-t.; Wang, J.-p. *Chem. Eur. J.* **2003**, *9*, 5520–5527; (v) Wu, J.; Cheng, X.-F.; Harrison, L. J.; Goh, S.-H.; Sim, K.-Y. *Tetrahedron Lett.* **2004**, *45*, 9657–9659; (w) Verotta, L.; Lovaglio, E.; Sterner, O.; Appendino, G.; Bombardelli, E. *J. Org. Chem.* **2004**, *69*, 7869–7874; (x) Trusheva, B.; Popova, M.; Naydenski, H.; Tsvetkova, I.; Gregorio Rodriguez, J.; Bankova, V. *Fitoterapia* **2004**, *75*, 683–689; (y) Šavikin-Fodulović, K.; Aljančić, I.; Vajs, V.; Menković, N.; Macura, S.; Gojgić, G.; Milosavljević, S. *J. Nat. Prod.* **2003**, *66*, 1236–1238; (z) Weng, J.-R.; Tsao, L.-T.; Wang, J.-P.; Wu, R.-R.; Lin, C.-N. *J. Nat. Prod.* **2004**, *67*, 1796–1799; (aa) Cruz, F. G.; Teixeira, J. S. R. *J. Brz. Chem. Soc.* **2004**, *15*, 504–508; (bb) Wu, J.; Cheng, X.-F.; Harrison, L. J.; Goh, S.-H.; Sim, K.-Y. *Tetrahedron Lett.* **2004**, *45*, 9657–9659; (cc) Wu, C.-C.; Weng, J.-R.; Won, S.-J.; Lin, C.-N. *J. Nat. Prod.* **2005**, *68*, 1125–1127; (dd) Gartner, M.; Müller, T.; Simon, J. C.; Giannis, A.; Sleeman, J. P. *ChemBioChem* **2005**, *6*, 171–177; (ee) Herath, K.; Jayasuriya, H.; Ondeyka, J. G.; Guan, Z.; Borris, R. P.; Stijfhoorn, E.; Stevenson, D.; Wang, J.; Sharma, N.; Macnaul, K.; Menke, J. G.; Ali, A.; Schulman, M. J.; Singh, S. B. *J. Nat. Prod.* **2005**, *68*, 617–619; (ff) Baggett, S.; Protiva, P.; Mazzola, E. P.; Yang, H.; Ressler, E. T.; Basile, M. J.; Weinstein, I. B.; Kennelly, E. J. *J. Nat. Prod.* **2005**, *68*, 354–360; (gg) Massoit, G.; Long, C.; David, B.; Serrano, M. J.; Daubie, F.; Alby, F.; Ausseil, F.; Knibiehler, M.; Moretti, C.; Hoffmann, J. S.; Cazaux, C.; Lavaud, C. *J. Nat. Prod.* **2005**, *68*, 979–984; (hh) Hernandez, I. M.; Fernandez, M. C.; Cuesta-Rubio, O.; Piccinelli, A. N.; Rastrelli, L. *J. Nat. Prod.* **2005**, *68*, 931–934; Taher, M.; Idris, M. S.; Ahmad, F.; Arbain, D. *Phytochemistry* **2005**, *66*, 723–726; (ii) Teixeira, J. S. R.; Cruz, F. G. *Tetrahedron Lett.* **2005**, *46*, 2813–2816; (jj) Wu, C.-C.; Weng, J.-R.; Won, S.-J.; Lin, C.-N. *J. Nat. Prod.* **2005**, *68*, 1125–1127; (kk) Cao, S.; Low, K.-N.; Glover, R. P.; Crasta, S. C.; Ng, S.; Buss, A. D.; Butler, M. S. *J. Nat. Prod.* **2006**, *69*, 707–709.

9. (a) Nicolaou, K. C.; Pfefferkorn, J. A.; Kim, S.; Wei, H. X. *J. Am. Chem. Soc.* **1999**, *121*, 4724–4725; (b) Nicolaou, K. C.; Pfefferkorn, J. A.; Cao, G.-Q.; Kim, S.; Kessabi, J. *Org. Lett.* **1999**, *1*, 807–810; (c) Usuda, H.; Kanai, M.; Shibasaki, M. *Org. Lett.* **2002**, *4*, 859–862; (d) Spessard, S. J.; Stoltz, B. M. *Org. Lett.* **2002**, *4*, 1943–1946; (e) Young, D. G. J.; Zeng, D. X. *J. Org. Chem.* **2002**, *67*, 3134–3147; (f) Usuda, H.; Kanai, M.; Shibasaki, M. *Tetrahedron Lett.* **2002**, *43*, 3621–3624; (g) Kraus, G. A.; Nguyen, T. H.; Jeon, I. *Tetrahedron Lett.* **2003**, *44*, 659–661; (h) Ciochina, R.; Grossman, R. B. *Org. Lett.* **2003**, *5*, 4619–4621; (i) Klein, A.; Miesch, M. *Tetrahedron Lett.* **2003**, *44*, 4483–4485; (j) Srikrishna, A.; Kumar, P. P.; Reddy, T. J. *ARKIVOC* **2003**, *3*, 55–66; (k) Mehta, G.; Bera, M. K. *Tetrahedron Lett.* **2004**, *45*, 1113–1116; (l) Usuda, H.; Kuramochi, A.; Kanai, M.; Shibasaki, M. *Org. Lett.* **2004**, *6*, 4387–4390; (m) Nicolaou, K. C.; Carenzi, G. E. A.; Jeso, V. *Angew. Chem., Int. Ed.* **2005**, *44*, 3895–3899.

10. For total synthesis of garsubellin, see: (a) Kuramochi, A.; Usuda, H.; Yamatsugu, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2005**, *127*, 14200–14201; (b) Siegel, D. R.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2006**, *128*, 1048–1049.

11. Numbering for hyperforin was applied to **2** for clarity, and numbering for **1** and **2′** corresponds to that of **2**.

12. Wong, H. N. C.; Hon, M.-Y.; Tse, C.-W.; Yip, Y.-C.; Tanko, J.; Hudlicky, T. *Chem. Rev.* **1989**, *89*, 165–198.

13. (a) Giblin, G. M. P.; Kirk, D. T.; Mitchell, L.; Simpkins, N. S. *Org. Lett.* **2003**, *5*, 1673–1675; (b) Blake, A. J.; Giblin, G. M. P.; Kirk, D. T.; Simpkins, N. S.; Wilson, C. *Chem. Commun.* **2001**, *24*, 2668–2669.

14. Minami, N.; Ko, S. S.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 1109–1111.

15. (a) Honma, M.; Sawada, T.; Fujisawa, Y.; Utsugi, M.; Watanabe, H.; Umino, A.; Matsumura, T.; Hagihara, T.; Takano, M.; Nakada, M. *J. Am. Chem. Soc.* **2003**, *125*, 2860–2861; (b) Honma, M.; Nakada, M. *Tetrahedron Lett.* **2003**, *44*, 9007–9011.

16. Zutterman, F.; De Wilde, H.; Mijngheer, R.; De Clercq, P.; Vandewalle, M. *Tetrahedron* **1979**, *35*, 2389–2396.

17. Compound **3**: R_f 0.28 (hexane/ethyl acetate = 10/1); mp = 45–47 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.67$ (4H, m), 7.38 (6H, m), 5.80 (2H, m), 5.75 (2H, d, $J = 10.5$ Hz), 4.28 (2H, q, $J = 7.1$ Hz), 3.59 (2H, s), 3.17 (2H, s), 2.60 (2H, m), 1.32 (3H, t, $J = 7.1$ Hz), 1.07 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 191.0$, 161.3, 135.6, 133.6, 129.4, 129.2, 127.5, 125.3, 71.2, 61.2, 45.9, 42.6, 26.9, 26.6, 19.5, 14.4; IR (neat) ν_{max}: 2848, 2129, 1707, 1656, 1335, 1316, 1177, 1140, 1114, 1051, 833, 744, 704 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{29}H_{35}N_2O_4Si$: 503.2366, found: 503.2363.

18. Asymmetric catalysis of this reaction using a chiral bisoxazoline ligand was not pursued at this point because we thought that the key ring-opening reaction of **1** should be examined first.

19. Compound **10**: R_f 0.30 (hexane/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.66$ (4H, m), 7.41 (6H, m), 5.79 (1H, m), 5.68 (1H, dd, $J = 9.7$, 2.9 Hz), 4.20 (2H, q,

$J = 7.1$ Hz), 3.78 (2H, s), 3.03 (1H, d, $J = 17.1$ Hz), 2.65 (3H, m), 2.10 (1H, m), 1.99 (1H, d, $J = 17.1$ Hz), 1.28 (3H, t, $J = 7.1$ Hz), 1.07 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 207.0$, 168.8, 135.5, 135.4, 132.9, 132.8, 131.7, 129.8, 129.7, 127.7, 126.6, 68.5, 61.3, 53.7, 44.2, 39.6, 38.5, 30.5, 26.8, 21.2, 19.3, 14.2; IR (neat) ν_{max}: 2860, 1738, 1266, 1238, 1114, 736, 704 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{29}H_{35}O_4Si$: 475.2305, found: 475.2295.

20. Compound **1**: R_f 0.70 (hexane/ethyl acetate = 1/1);^{1}H NMR (400 MHz, $CDCl_3$) $\delta = 7.38$ (5H, m), 5.86 (1H, m), 5.75 (1H, dd, 9.9, 2.7 Hz), 5.19 (2H, s), 4.39 (1H, d, 10.5 Hz), 4.31 (1H, d, 10.5 Hz), 4.19 (2H, q, 7.1 Hz), 2.66 (4H, m), 2.10 (1H, m), 2.08 (1H, d, 17.1 Hz), 1.27 (3H, t, 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 205.1$, 168.4, 154.9, 134.7, 130.9, 128.6, 128.5, 128.3, 127.2, 72.5, 70.0, 61.5, 54.1, 43.7, 38.3, 36.0, 30.6, 20.8, 14.1; IR (neat) ν_{max}: 2980, 1750, 1398, 1266, 1040, 952, 734, 700 cm^{-1}; FAB MS $[M+H]^+$ calcd for $C_{21}H_{23}O_6$: 371.1495, found: 371.1495.
21. Compound **2**: R_f 0.33 (hexane/ethyl acetate = 1/1); mp = 134–136 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 12.4$ (1H, s), 5.98 (1H, dd, 10.0, 4.9 Hz), 5.45 (1H, d, 10.0 Hz), 4.54 (1H, d, 4.4 Hz), 4.27 (4H, m), 3.22 (1H, dd, 4.4, 2.2 Hz), 2.54 (1H, dd, 18.6, 2.2 Hz), 2.36 (1H, d, 17.8 Hz), 2.27 (1H, d, 17.8 Hz), 2.04 (1H, dd, 18.6, 4.9 Hz), 1.33 (3H, t, 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 171.1$, 168.8, 147.7, 130.6, 124.9, 99.5, 77.7, 74.0, 60.8, 36.1, 31.5, 30.2, 25.7, 14.1; IR (neat) ν_{max}: 3446, 2908, 1750, 1643, 1608, 1231, 742 cm^{-1}; FAB HRMS $[M+H]^+$ calcd for $C_{14}H_{17}O_6$: 281.1025, found: 281.1062.