Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron Letters
Tetrahedron Letters 46 (2005) 8279–8283

Synthesis of the C42–C52 part of ciguatoxin CTX3C

Daisuke Domon, Kenshu Fujiwara,* Yuko Ohtaniuchi, Akihiro Takezawa, Sayaka Takeda, Hidekazu Kawasaki, Akio Murai, Hidethoshi Kawai and Takanori Suzuki

Division of Chemistry, Graduate School of Science, Hokkaido University, Sapporo 060-0810, Japan

Received 2 September 2005; revised 22 September 2005; accepted 28 September 2005
Available online 17 October 2005

Abstract—The C42–C52 part of ciguatoxin CTX3C (**1**) was synthesized from tri-*O*-acetyl D-glucal. The synthetic segment had a tetrahydropyran ring corresponding to the 'C49-reduced' L-ring of **1**, designed to avoid side reactions due to acid-labile C49 acetal carbon during acidic reductive conditions planned in further synthesis toward **1**. The vicinal dimethyl part at C47–C48 was constructed by a stepwise conjugate addition/methylation procedure. The C50–C52 unit was installed by Grignard addition of the C_3 unit followed by spirocyclization and reductive cleavage of the spirocyclic acetal. Stereoselective assembly of the C42–C44 part was achieved by Brown's asymmetric crotylboration.

Ciguatoxin CTX3C (**1**) (Fig. 1), isolated as a causative toxin of ciguatera fish poisoning from cultured dinoflagellate *Gambierdiscus toxicus* by Yasumoto, has potent neurotoxicity and a complex *trans*-fused polycyclic ether structure.[1–3] The remarkable features of **1** prompted us to start our program toward total synthesis of **1**.[4] Here, the synthesis of the C42–C52 part (**5**) of **1** is described.

In our program, the C42–C52 part was planned to be connected with the C32–C41 part (**3**) to construct the IJKLM-ring part (**2**) of **1** by our method based on anion-coupling and reductive etherification reactions (Scheme 1).[4g] Although spirocyclic acetal **4** was initially designed as a straightforward synthetic intermediate for the synthesis of **2**, the predictable instability of its spirocyclic acetal part (C49) under the reductive conditions during the JK ring formation compelled us to revise the design of the C42–C52 part.[5] Therefore, tetrahydropyran **5** was selected as a stable C42–C52 part and was envisaged to be synthesized from spirocyclic acetal **6**, which would be prepared from **7** via a stepwise Grignard addition/spiroacetalization process, by an asymmetric aldol or crotylboration reaction constructing the C42–C44 part and by reductive cleavage of the spirocyclic acetal part. Tri-*O*-acetyl D-glucal (**9**) was selected as the starting material for the preparation of **7**, where inversion of stereochemistry at C46 and C47, lactone formation, and introduction of two methyl groups at C47 and C48 were intended.

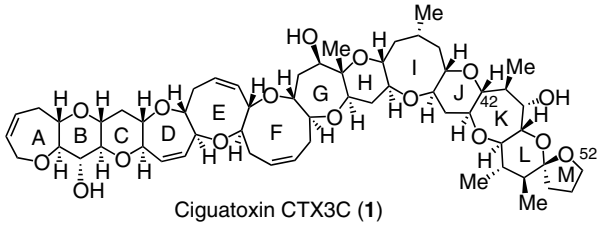
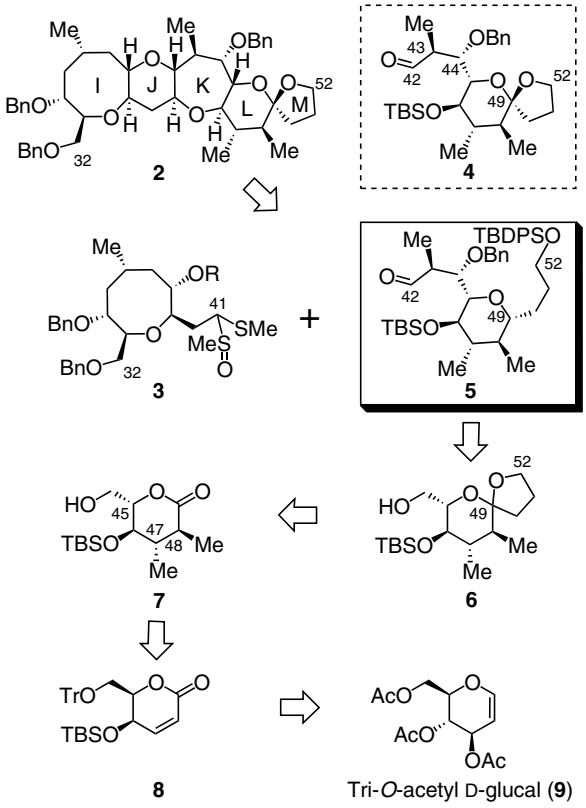


Figure 1.

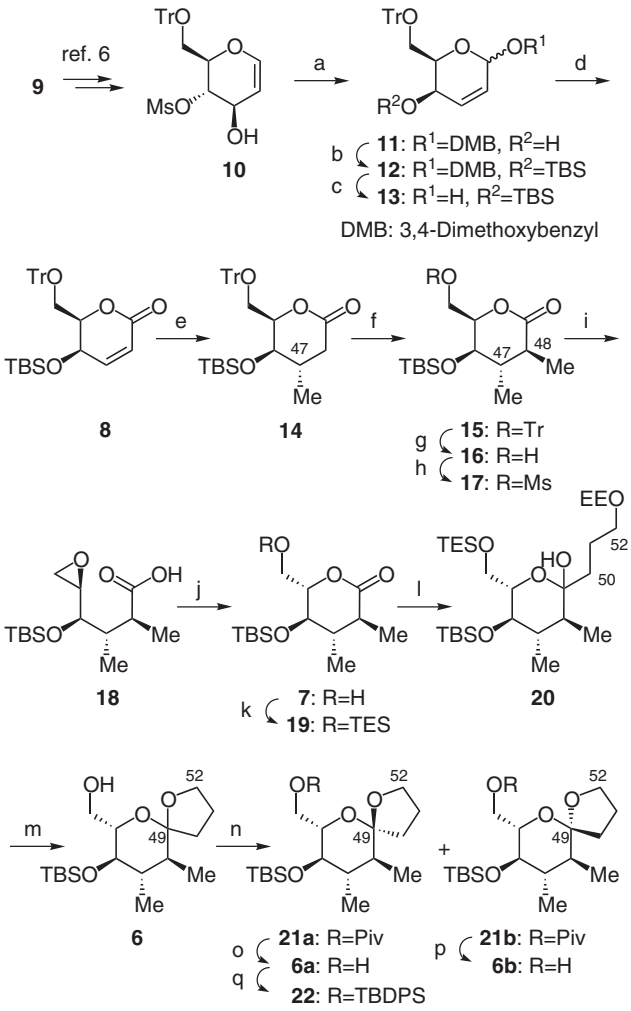
First, spirocyclic acetal **6** was synthesized as shown in Scheme 2. After the starting **9** was transformed into **10** by known procedure,[6] the alcohol **10** was treated with 3,4-dimethoxybenzyl (DMB) alcohol and *t*-BuOK to give **11** (80%) in accordance with Crotti's method.[6] Protection of **11** as a TBS ether followed by removal of the DMB group provided hemiacetal **13** (overall 79%), which was oxidized with TEMPO under basic conditions to afford α,β-unsaturated lactone **8** (93%).[7] The lactone **8** was reacted with Me_2CuLi to produce **14** as a single isomer (98%). Deprotonation of **14** with NHMDS followed by the addition of MeI resulted in the exclusive formation of **15** (98%).[8] The trityl group of **15** was detached with BCl_3 in CH_2Cl_2 to afford **16** in good yield (86%).[9] After mesylation of the alcohol

Keywords: Ciguatoxin CTX3C; Natural product synthesis; Reductive ring-opening; Oxidative cyclization.
* Corresponding author. Tel.: +81 11 706 2701; fax: +81 11 706 4924; e-mail: fjwkn@sci.hokudai.ac.jp

0040-4039/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2005.09.163



Scheme 1.



Scheme 2. Reagents and conditions: (a) *t*-BuOK, DMBOH, PhH, 23 °C, 2 h, 80%; (b) TBSCl, imidazole, DMF, 23 °C, 2 h, 99%; (c) DDQ, CH_2Cl_2–pH 7 buffer (10:1), 23 °C, 30 min, 80%; (d) TEMPO, Bu_4NCl, NCS, CH_2Cl_2–pH 8.6 buffer (1:1), 23 °C, 2 h, 93%; (e) Me_2CuLi, Et_2O, −40 °C, 2 h, 98%; (f) NaHMDS, MeI, THF, −78 °C, 30 min, 98%; (g) BCl_3, CH_2Cl_2, −20 °C, 2 h, 86%; (h) MsCl, Et_3N, CH_2Cl_2, −20 °C, 1 h; (i) 1 M LiOH, THF, 23 °C, 3 h; (j) CSA, CH_2Cl_2, 23 °C, 7 h, 91% from **16**; (k) TESCl, imidazole, DMF, 23 °C, 30 min, 98%; (l) $EEO(CH_2)_3MgBr$, THF, −20 °C, 30 min, 100%; (m) CSA, CH_2Cl_2, 23 °C, 30 min, 89%; (n) PivCl, pyridine, DMAP, CH_2Cl_2, 23 °C, 12 h, **21a**: 67%, **21b**: 22%; (o) DIBALH, CH_2Cl_2, −78 °C, 1 h, 98%; (p) DIBALH, CH_2Cl_2, −78 °C, 30 min, 100%; (q) TBDPSCl, imidazole, DMAP, DMF, 23 °C, 15 min, 50%.

16 followed by basic treatment, the resulting epoxide **18** was cyclized by a catalytic amount of CSA into lactone **7** (overall 91%), which was protected with TESCl to give **19** (98%). Installation of an ethoxyethyl-protected three-carbon unit[10] corresponding to the C50–C52 part as a Grignard reagent at C49 of **19** produced **20** (100%). When the hemiacetal **20** was treated with CSA in CH_2Cl_2, detachment of the ethoxyethyl and TES groups as well as the subsequent spirocyclization took place to give **6** as an inseparable 3:1 mixture of diastereomers (89%). After pivaloate ester formation from **6**, the resulting diastereomers **21a** and **21b** were separated (**21a**: 67%, **21b**: 22%) and transformed into **6a** (98%) and **6b** (100%), respectively. Stereochemistry of **6a** was determined by X-ray crystallographic analysis of its crystalline TBDPS ether **22** (colorless needles, mp 83–84 °C) (Fig. 2).[11] Thus, the spirocyclic acetal **6a** having the same stereochemistry at C49 as **1** was obtained as a major product.

Next, stereoselective construction of the C44–C42 part was examined. After several attempts to apply aldol or crotylboration reaction to aldehyde **23**, prepared from **6a** by Swern oxidation,[12] we found that Brown's asymmetric crotylboration using **24**, prepared from (−)-*B*-methoxydiisopinocampheylborane,[13] exclusively gave **25** in good yield (90% from **6a**) (Scheme 3).[14] Stereochemistry of **25** was determined by NMR analysis of its acetonide derivatives **26** and **28** as follows: the relationship between C45 and C44 was confirmed by large $J_{H44–H45}$ (9.5 Hz) of **26** showing diaxial coupling; the relative configurations at C44 and C43 were verified by the presence of NOE between H44 and H42ax in **28** displaying the axial orientation of these protons and by the small values of $J_{H43–H44}$, $J_{H42ax–H43}$, and $J_{H42eq–H43}$ in **28** exhibiting the equatorial orientation of H43.

During the search for appropriate conditions for direct benzyl protection of the hydroxy group at C44 of **25**, we encountered a problem of TBS migration from O46 to O44. Since the strong basic conditions with K^+ were found to accelerate and complete the migration, a three-step protection/deprotection sequence [(i) the TBS migration to O44 and (2-naphthyl)methyl (NAP)[15] protection at O46, (ii) removal of the TBS group from O44 (overall 71%), and (iii) Bn protection at O44 (∼100%)]

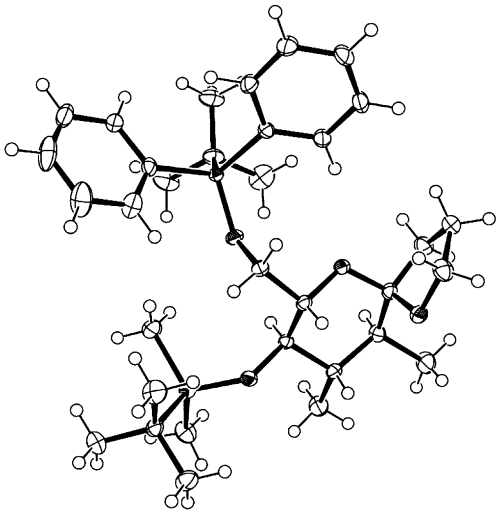
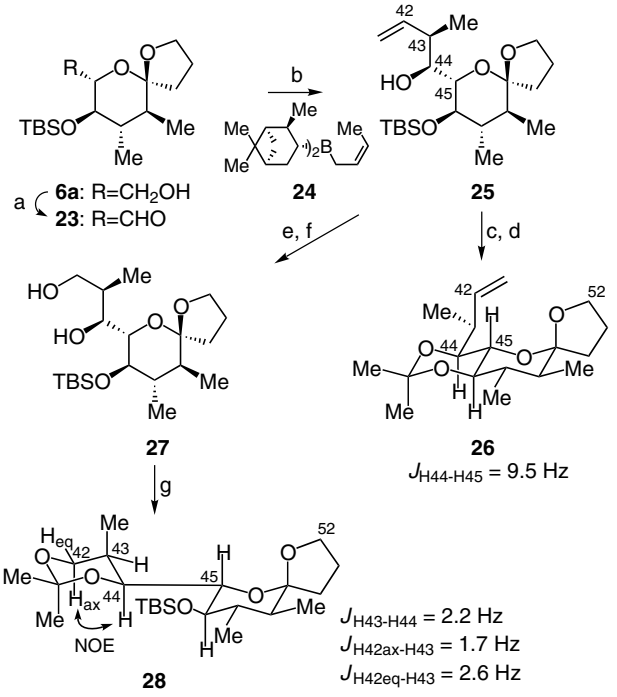


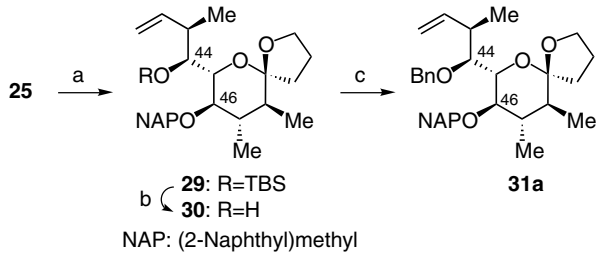
Figure 2. ORTEP diagram of **22**.



Scheme 3. Reagents and conditions: (a) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C, 10 min; (b) **24**, THF, −78 °C, 2 h, then 2 N NaOH, H_2O_2, THF, 23 °C, 12 h, 90% from **6a**; (c) Bu_4NF, THF, 23 °C, 1 h, 69%; (d) 2,2-dimethoxypropane, PPTS, DMF, 23 °C, 2 h, 85%; (e) OsO_4, NMO, 1,4-dioxane–H_2O (1:1), 23 °C, 6 h, then $NaIO_4$, 12 h; (f) $NaBH_4$, MeOH, 23 °C, 20 min; (g) 2,2-dimethoxypropane, PPTS, DMF, 23 °C, 5 h, 51% from **25**.

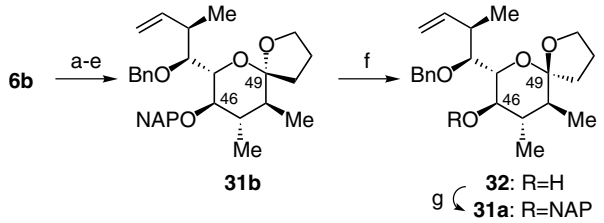
was performed for the benzyl protection of O44 to produce **31a** in good yield (Scheme 4).

At this stage, conversion of **6b** to a natural type spirocyclic acetal was investigated. Since **6b** could not be isomerized into **6a** even after several attempts, advanced synthetic intermediate **31b**, prepared from **6b** in a similar manner as **31a** (overall 43%), was examined for the isomerization into **31a** under acidic conditions (Scheme 5). Although several Brønsted acids did not induce the isomerization, $Et_2O{\cdot}BF_3$ promoted the inversion at C49 with detachment of the NAP group to give an inseparable ~3:1 mixture of **32a** and **32b**, which was protected again with NAPBr to provide the desired **31a** (overall 53%) and recovered **31b** (overall 19%). Thus, the minor component **6b** was converted to the natural type spiroacetal **31a** in overall 23% yield in seven steps.

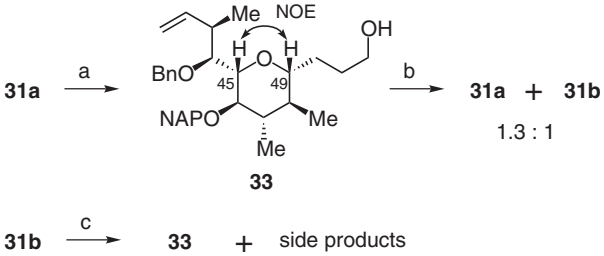


Scheme 4. Reagents and conditions: (a) NAPBr, *t*-BuOK, Bu_4NI, THF, 23 °C, 30 min; (b) Bu_4NF, THF, 23 °C, 20 h, 71% from **25**; (c) BnBr, *t*-BuOK, Bu_4NI, THF, 23 °C, 30 min (~100%).

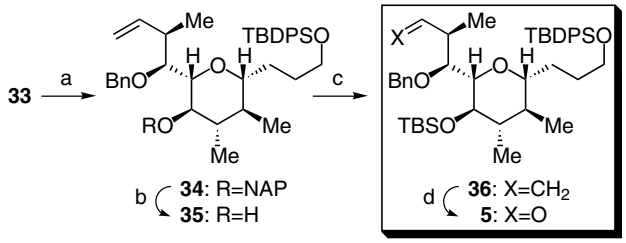
Then, reduction of the spirocyclic acetals **31a** and **31b** was examined (Scheme 6). Treatment of **31a** with large excess of Et_3SiH in the presence of TMSOTf at −78 °C in CH_2Cl_2 exclusively produced **33** (99%).[16,17] The configuration at C49 of **33** was determined by the presence of NOE between H45 and H49. On the other



Scheme 5. Reagents and conditions: (a) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C, 10 min; (b) **24**, THF, −78 °C, 2 h, then 2 N NaOH, H_2O_2, THF, 23 °C, 12 h, 58% for two steps; (c) NAPBr, *t*-BuOK, Bu_4NI, THF, 23 °C, 30 min; (d) Bu_4NF, THF, 23 °C, 24 h, 74% for two steps; (e) BnBr, *t*-BuOK, Bu_4NI, THF, 23 °C, 30 min, ~100%; (f) $Et_2O{\cdot}BF_3$, CH_2Cl_2, 0 °C, 3 h, (**32a**:**32b** = ~3:1); (g) NAPBr, NaH, Bu_4NI, DMF, 23 °C, 5 h, **31a**: 53% for two steps, **31b**: 19% for two steps.



Scheme 6. Reagents and conditions: (a) TMSOTf, Et_3SiH–CH_2Cl_2 (1:1), −78 °C, 15 h, **33**: 99%; (b) iodobenzene diacetate, I_2, hν (a 500 W tungsten lamp), cyclohexane, 23 °C, 1 h, 70% (**31a**:**31b** = 1.3:1); (c) TMSOTf, Et_3SiH–CH_2Cl_2 (1:1), −78 °C, 5 h, **33**: 16%.



Scheme 7. Reagents and conditions: (a) TBDPSCl, imidazole, DMF, 23 °C, 30 min, 96%; (b) DDQ, CH_2Cl_2–pH 7 buffer (10:1), 23 °C, 10 min, 93%; (c) TBSOTf, 2,6-lutidine, CH_2Cl_2, 23 °C, 10 h, 91%; (d) OsO_4, NMO, 1,4-dioxane–H_2O (1:1), 23 °C, 20 h, then $NaIO_4$, 1 h, 88%.

hand, reduction of **31b** under the same conditions gave **33** in low yield (16%) along with unknown side products. The alcohol **33** could return to **31** by a photo-induced radical process using iodobenzene diacetate and I_2 (70%, **31a**:**31b** = 1.3:1),[18] thereby establishing the final M-ring forming process, planned in the synthesis of **2**.

The final process in the synthesis of **5** is illustrated in Scheme 7. Protection of **33** with TBDPSCl followed by removal of the NAP group with DDQ and protection of the resulting hydroxy group with TBSOTf produced **36** (overall 81%), which was converted to **5**[19] through a two-step dihydroxylation/oxidative cleavage process (88%). Thus the C42–C52 part **5** was synthesized from known alcohol **10** in 25 steps in 11% overall yield.[20]

In conclusion, the C42–C52 part (**5**) of **1** was synthesized from **10**, prepared from tri-*O*-acetyl D-glucal by Crotti's method. The tetrahydropyran ring of **5** corresponding to the 'C49-reduced' L-ring of **1** was designed to avoid side reactions due to acid-labile C49 acetal carbon during acidic reductive conditions planned in further synthesis toward **1**. The vicinal dimethyl part at C47–C48 was constructed by a stepwise conjugate addition/methylation procedure. The C50–C52 unit was installed by Grignard addition of the C_3 unit followed by spirocyclization and reductive cleavage of the resulting spirocyclic acetal. Stereoselective assembly of the C42–C44 part was achieved by Brown's asymmetric crotylboration. Further studies toward total synthesis of **1** are in progress in this laboratory.

Supplementary data

Crystallographic data (excluding structure factors) of **22** have been deposited with the Cambridge Crystallographic Data Center as supplementary publication numbers CCDC 282747. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

Acknowledgements

We thank Mr. Kenji Watanabe and Dr. Eri Fukushi (GC–MS and NMR Laboratory, Graduate School of Agriculture, Hokkaido University), for the measurements of mass spectra. This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology of Japanese Government.

References and notes

1. Isolation: Satake, M.; Murata, M.; Yasumoto, T. *Tetrahedron Lett.* **1993**, *34*, 1975.
2. Total synthesis of CTX3C: (a) Hirama, M.; Oishi, T.; Uehara, H.; Inoue, M.; Maruyama, M.; Oguri, H.; Satake, M. *Science* **2001**, *294*, 1904; (b) Inoue, M.; Uehara, H.; Maruyama, M.; Hirama, M. *Org. Lett.* **2002**, *4*, 4551; (c) Maruyama, M.; Inoue, M.; Oishi, T.; Oguri, H.; Ogasawara, Y.; Shindo, Y.; Hirama, M. *Tetrahedron* **2002**, *58*, 1835; (d) Uehara, H.; Oishi, T.; Inoue, M.; Shoji, M.; Nagumo, Y.; Kosaka, M.; Le Brazidec, J.-Y.; Hirama, M. *Tetrahedron* **2002**, *58*, 6493; (e) Kobayashi, S.; Takahashi, Y.; Komano, K.; Alizadeh, B. H.; Kawada, Y.; Oishi, T.; Tanaka, S.-i.; Ogasawara, Y.; Sasaki, S.-y.; Hirama, M. *Tetrahedron* **2004**, *60*, 8375; (f) Inoue, M.; Yamashita, S.; Tatami, A.; Miyazaki, K.; Hirama, M. *J. Org. Chem.* **2004**, *69*, 2797; Reviews: (g) Inoue, M.; Hirama, M. *Synlett* **2004**, 57; (h) Inoue, M.; Miyazaki, K.; Uehara, H.; Maruyama, M.; Hirama, M. *Proc. Natl. Sci. Acad. U.S.A.* **2004**, *101*, 12013; (i) Inoue, M.; Hirama, M. *Acc. Chem. Res.* **2004**, *37*, 961.
3. Recent synthetic studies on ciguatoxins by other groups: (a) Kobayashi, S.; Alizadeh, B. H.; Sasaki, S.-y.; Oguri, H.; Hirama, M. *Org. Lett.* **2004**, *6*, 751; (b) Baba, T.; Takai, S.; Sawada, N.; Isobe, M. *Synlett* **2004**, 603; (c) Baba, T.; Huang, G.; Isobe, M. *Tetrahedron* **2003**, *59*, 6851; (d) Fuwa, H.; Fujikawa, S.; Tachibana, K.; Takakura, H.; Sasaki, M. *Tetrahedron Lett.* **2004**, *45*, 4795; (e) Takakura, H.; Sasaki, M.; Honda, S.; Tachibana, K. *Org. Lett.* **2002**, *4*, 2771; (f) Bond, S.; Perlmutter, P. *Tetrahedron* **2002**, *58*, 1779; (g) Candenas, M. L.; Pinto, F. J.; Cintada, C. G.; Morales, E. Q.; Brouard, I.; Díaz, M. T.; Rico, M.; Rodríguez, E.; Rodríguez, R. M.; Pérez, R.; Pérez, R. L.; Martín, J. D. *Tetrahedron* **2002**, *58*, 1921.
4. Our synthetic studies on ciguatoxins: (a) Oka, T.; Fujiwara, K.; Murai, A. *Tetrahedron* **1996**, *52*, 12091; (b) Atsuta, H.; Fujiwara, K.; Murai, A. *Synlett* **1997**, 307; (c) Oka, T.; Murai, A. *Tetrahedron* **1998**, *54*, 1; (d) Oka, T.; Fujiwara, K.; Murai, A. *Tetrahedron* **1998**, *54*, 21; (e) Fujiwara, K.; Saka, K.; Takaoka, D.; Murai, A. *Synlett* **1999**, 1037; (f) Fujiwara, K.; Tanaka, H.; Murai, A. *Chem. Lett.* **2000**, 610; (g) Fujiwara, K.; Takaoka, D.; Kusumi, K.; Kawai, K.; Murai, A. *Synlett* **2001**, 691; (h) Fujiwara, K.; Koyama, Y.; Doi, E.; Shimawaki, K.; Ohtaniuchi, Y.; Takemura, A.; Souma, S.; Murai, A. *Synlett* **2002**, 1496; (i) Fujiwara, K.; Koyama, Y.; Kawai, K.; Tanaka, H.; Murai, A. *Synlett* **2002**, 1835; (j) Tanaka, H.; Kawai, K.; Fujiwara, K.; Murai, A. *Tetrahedron* **2002**, *58*, 10017; (k) Fujiwara, K.; Goto, A.; Sato, D.; Ohtaniuchi, Y.; Tanaka, H.; Murai, A.; Kawai, H.; Suzuki, T. *Tetrahedron Lett.* **2004**, *45*, 7011; (l) Takemura, A.; Fujiwara, K.; Murai, A.; Kawai, H.; Suzuki, T. *Tetrahedron Lett.* **2004**, *45*, 7567; (m) Takemura, A.; Fujiwara, K.; Shimawaki, K.; Murai, A.; Kawai, H.; Suzuki, T. *Tetrahedron* **2005**, *61*, 7392.
5. Hirama reported the reductive etherification reaction forming the C41–O(C46) bond in **2**, where the spirocyclic LM-ring remained intact.[2d,f] However, our preliminary experiments toward the construction of **2** via our original route, shown in Scheme 1, displayed significant problems due to the spirocyclic acetal part. The details will be described elsewhere.

6. Bussolo, V. D.; Caseli, M.; Pineschi, M.; Crotti, P. *Org. Lett.* **2002**, *4*, 3695.
7. Einhorn, J.; Einhorn, C.; Ratajczak, F.; Pierre, J. L. *J. Org. Chem.* **1996**, *61*, 7452.
8. The Isobe group reported a similar approach to the dimethyl part of the L-ring part of ciguatoxin.[3c]
9. Jones, G. B.; Chapman, B. J.; Huber, R. S.; Beaty, R. *Tetrahedron: Asymmetry* **1994**, *5*, 1199.
10. (a) Descoins, C.; Samain, D.; Lalanne-Casson, B.; Gollois, M. *Bull. Soc. Chim. Fr.* **1977**, 941; (b) Leyendecker, F.; Drouin, J.; Debegge, J. J.; Conia, J. M. *Tetrahedron Lett.* **1977**, *18*, 1591; (c) Shea, K. J.; Wise, S.; Burke, L. D.; Davis, P. D.; Gilman, J. W.; Greeley, A. C. *J. Am. Chem. Soc.* **1982**, *104*, 5708.
11. Crystal data of **22**: $C_{33}H_{52}O_4Si_2$, M 568.94, monoclinic $P2_1$ (No. 4), $a = 12.136(4)$ Å, $b = 10.699(3)$ Å, $c = 12.758(4)$ Å, $\beta = 96.935(4)$, $U = 1644.4(9)$ Å^3, D_c ($Z = 2$) = 1.149 g/cm^3, $T = 153$ K, $\mu = 1.41$ cm^{-1}. The final R value is 0.028 for 5469 independent reflections with $I > 2\sigma I$ and 353 parameters.
12. Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2048.
13. Brown, H. C.; Bhat, K. S. *J. Am. Chem. Soc.* **1990**, *108*, 5919.
14. Although both Evans' asymmetric aldol reaction and Roush's crotylboration gave excellent selectivities in this system, both production yields were modest, cf. Ref. 4g and 2d.
15. (a) Gaunt, M. J.; Yu, J.; Spencer, J. B. *J. Org. Chem.* **1998**, *63*, 4172–4173; (b) Xia, J.; Abbas, S. A.; Locke, R. D.; Piskorz, C. F.; Alderfer, J. L.; Matta, K. L. *Tetrahedron Lett.* **2000**, *41*, 169–173; (c) Wright, J. A.; Yu, J.; Spencer, J. B. *Tetrahedron Lett.* **2001**, *42*, 4033–4036.
16. When the reduction was performed at 0 °C, the yield of **33** decreased and considerable amounts of unknown side products were given.
17. Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1979**, *20*, 4679.
18. (a) Concepción, J. I.; Francisco, C. G.; Hernández, R.; Salazar, J. A.; Suárez, E. *Tetrahedron Lett.* **1984**, *25*, 1953; Reviews involving the oxidative formation of spiroacetals, see: (b) Perron, F.; Albizati, K. F. *Chem. Rev.* **1989**, *89*, 1617; (c) Brimble, M. A.; Farès, F. A. *Tetrahedron* **1999**, *55*, 7661; See, also: (d) Čeković, Ž. *Tetrahedron* **2003**, *59*, 8073.
19. Selected spectral data of **5**: $[\alpha]_D^{23}$ −3.1 (c 0.48, $CHCl_3$); ^{1}H NMR (300 MHz, C_6D_6, C_6HD_5 as 7.15 ppm): δ 0.02 (6H, s), 0.58 (3H, d, $J = 6.4$ Hz), 0.84 (3H, d, $J = 6.2$ Hz), 0.91 (9H, s), 0.95–1.34 (3H, m), 1.10 (9H, s), 1.25 (3H, d, $J = 7.2$ Hz), 1.56–1.74 (2H, m), 1.77–1.85 (1H, m), 2.55 (1H, m), 2.74 (1H, br dt, $J = 2.2$, 8.4 Hz), 2.98 (1H, t, $J = 9.4$ Hz), 3.47 (1H, br d, $J = 9.4$ Hz), 3.65 (2H, br dd, $J = 6.1$, 5.9 Hz), 4.14 (1H, br d, $J = 4.4$ Hz), 4.41 (1H, d, $J = 11.9$ Hz), 4.52 (1H, d, $J = 11.9$ Hz), 7.04–7.24 (11H, m), 7.69–7.72 (4H, m), 9.80 (1H, br s); ^{13}C NMR (75 MHz, C_6D_6, $^{13}CC_5D_6$ as 128.0 ppm): δ −3.1 (CH_3), −2.3 (CH_3), 10.9 (CH_3), 14.5 (CH_3), 16.6 (CH_3), 18.7 (C), 19.5 (C), 26.4 (CH_3) × 3, 27.1 (CH_3) × 3, 28.6 (CH_2), 29.7 (CH_2), 41.3 (CH), 45.5 (CH), 47.5 (CH), 64.2 (CH_2), 71.4 (CH_2), 74.3 (CH), 77.5 (CH), 82.0 (CH), 83.3 (CH),127.56 (CH) × 2, 127.59 (CH), 128.0 (CH) × 4, 128.5 (CH) × 2, 129.9 (CH) × 2, 134.5 (C) × 2, 136.0 (CH) × 4, 139.3 (C), 202.9 (CH); IR (film) ν_{max} 3070, 2929, 2857, 2711, 1725, 1589, 1472, 1462, 1428, 1388, 1361, 1258, 1216, 1187, 1111, 1028, 1006, 939, 921, 867, 835, 775, 757, 738, 701, 665, 614 cm^{-1}; LR-EIMS, m/z 659 (6.2%, [M −t-Bu]$^+$), 551 (47%, [M−(t-Bu+BnOH)]$^+$), 91 (bp); HR-EIMS, calcd for $C_{39}H_{55}O_5Si_2$ [M−t-Bu]$^+$: 659.3588, found: 659.3594.
20. The total yield was based on the linear route from **10** to **5** excluding the isomerization process from **6b** to **31a**.