Cyclization Control of an Ambliofuran Analogue: Effective Total Synthesis of (±)-Baiyunol†

Mugio Nishizawa,* Hidetoshi Yamada, and Yuji Hayashi‡

Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Yamashirocho, Tokushima 770 Japan, and Department of Chemistry, Faculty of Science, Osaka City University, Sumiyoshiku, Osaka 558, Japan

Received May 14, 1987

Cyclization of ambliofuran (**3a**) with mercury(II) triflate/*N,N*-dimethylaniline complex (**2**) is mainly initiated from an internal double bond (Δ^{10}) to give **4** and **5**, whereas the corresponding sulfone **3b** affords terminal cyclization products **16**, **17**, and **18**. On the other hand, the cyclization of 13-oxoambliofuran (**3c**) is effectively controlled to give $\Delta^{8,9}$ bicyclic product **28** in high yield. The carbonyl group at C-13 plays an essential role in controlling not only the initiation but also the termination of this cyclization. The resulting ketone **28** is efficiently converted to (±)-baiyunol (**1a**), an aglycon of a sweet substance.

The sweet substance baiyunoside (**1b**), reported by Tanaka and co-workers as a constituent of *Phlomis betonicoides*,[1] is the glycoside of a furanoditerpene with the labdane skeleton.[2] During our investigations dealing with a biomimetic olefin cyclization using mercury(II) triflate-/*N,N*-dimethylaniline complex (**2**),[3] we have examined the cyclization of some acyclic furanoterpenoids[4] and have observed that the cyclization of ambliofuran (**3a**) is mainly initiated from an internal double bond (Δ^{10}) to give **4** and **5**, whereas the corresponding sulfone **3b** affords only the terminal cyclization products **16**, **17**, and **18**.[5] Product **18** is a mixture of three isomeric olefins ($\Delta^{7,8}$:$\Delta^{8,9}$:$\Delta^{8,17}$ = 9:4:3). Thus, control of the cyclization of ambliofuran analogues not only with respect to initiation but also termination is essential in order to permit a selective total synthesis of (±)-baiyunol (**1a**), an aglycon of the sweet substance **1b** (Chart I). Furano ketone **3c** was found to be the best substrate for our purposes, giving the $\Delta^{8,9}$ bicyclic product **28** in very high yield. The resulting organomercuric ketone **28** was efficiently transformed to **1a**.

Result and Discussion

Synthesis of 3-substituted acyclic furanoterpenoids such as perillene and dendrolasin[6] has been reported by means of a Grignard coupling process,[7] a butenolide route,[8] or a route based on ketone derivatives of *n*-butylthiomethylene epoxide.[9] However, these methods often produce difficult to separate isomeric mixtures. Therefore, we employed Masaki's procedure[10] for the preparation of ambliofuran (**3a**). Condensation of the lithio derivative of 3-furfuryl *p*-tolyl sulfone with (*E,E*)-farnesyl bromide afforded sulfone **3b** in 86% yield along with a dialkylation product (9% yield). Reductive desulfurization with lithium/ammonia afforded ambliofuran (**3a**) as the sole isolable product. The furans **3b** and **3a** thus obtained are stereochemically pure on the basis of HPLC, ^{1}H NMR, and ^{13}C NMR analysis. Furano ketone **3c** was prepared by a condensation of 1,3-dithiane derivative of 3-furan aldehyde[11] and (*E,E*)-farnesyl bromide using lithium diisopropylamide followed by the hydrolysis using thallium(III) nitrate.[12]

When mercury(II) triflate/*N,N*-dimethylaniline complex (**2**) (1.2 equiv), prepared in situ in nitromethane,[3a] was slowly added to a solution of ambliofuran (**3a**) in a 3:1 mixture of nitromethane and dichloromethane at −20 °C, the cyclization was mainly initiated from an internal double bond (Δ^{10}) to give **4** (38% yield) and doubly cyclized product **5** (15% yield) along with terminal cyclization product **6** (13%), after the treatment with saturated sodium chloride solution (Chart II). In order to confirm the structures of **4**–**6**, each product was subjected to a demercuration reaction with sodium borohydride. Generation of four isomeric secondary cyclization products **7a**–**d** from **4** is reasonably explained by a nonstereoselective radical cyclization process. Each isomer was separated by HPLC and structures were established by spectral analysis. The doubly cyclized product **5**[13] was converted to demercuration product **8**[14] and the tetracyclic product **6** was transformed to **9a**. The spectral properties of both products were consistent with the assigned structures. The latter compound **9a** is an example of the relatively new diterpenoid, marginatane, skeleton. The first example, marginatafuran (**9b**), was reported as a constituent of a nudibranch.[15] The formation of **4** and **5** in this study is

† Dedicated to Professor Emeritus Takeo Sakan of Osaka City University on the occasion of his 77th birthday.

‡ Osaka City University.

(1) Tanaka, T.; Tanaka, O.; Lin, Z. W.; Zhou, J.; Ageta, H. *Chem. Pharm. Bull.* **1983**, *31*, 780. Tanaka, T.; Tanaka, O.; Lin, Z. W.; Zhou, J. *Ibid.* **1985**, *33*, 4275.

(2) Faulkner, D. J. *Nat. Prod. Rep.* **1984**, *1*, 551.

(3) (a) Nishizawa, M.; Takenaka, H.; Nishide, H.; Hayashi, Y. *Tetrahedron Lett.* **1983**, *24*, 2581. (b) Nishizawa, M.; Takenaka, H.; Hayashi, Y. *Chem. Lett.* **1983**, 1459. (c) Nishizawa, M.; Takenaka, H.; Hayashi, Y. *Tetrahedron Lett.* **1984**, *25*, 437. (d) Nishizawa, M.; Nishide, H.; Hayashi, Y. *J. Chem. Soc., Chem. Commun.* **1984**, 467. (e) Nishizawa, M.; Takenaka, H.; Hirotu, K.; Higuchi, T.; Hayashi, Y. *J. Am. Chem. Soc.* **1984**, *106*, 4290. (f) Nishizawa, M.; Nishide, H.; Hayashi, Y. *Tetrahedron Lett.* **1984**, *25*, 5071. (g) Nishizawa, M. *Chemistry* **1984**, *39*, 751. (h) Nishizawa, M.; Takenaka, H.; Hayashi, Y. *J. Am. Chem. Soc.* **1985**, *107*, 522. (i) Nishizawa, M. *J. Synth. Org. Chem. Jpn.* **1986**, *44*, 160. (j) Nishizawa, M.; Takenaka, H.; Hayashi, Y. *J. Org. Chem.* **1986**, *51*, 806.

(4) Furan-terminated cationic cyclization has been intensively studied; see: (a) Tanis, S. P.; Chuang, Y. H.; Head, D. B. *Tetrahedron Lett.* **1985**, *26*, 6147. Tanis, S. P.; Herrinton, P. M. *J. Org. Chem.* **1985**, *50*, 3988; **1983**, *48*, 4572. (b) Nasipuri, D.; Das, G. *J. Chem. Soc., Perkin Trans 1* **1979**, 2776. (c) Matumoto, T.; Usui, S. *Chem. Lett.* **1978**, 105. (d) Cimino, G.; De Stefhano, S.; Guerriero, A.; Minale, L. *Tetrahedron Lett.* **1975**, 1425.

(5) Nishizawa, M.; Yamada, H.; Hayashi, Y. *Tetrahedron Lett.* **1986**, *27*, 187.

(6) Walker, R. P.; Faulkner, D. J. *J. Org. Chem.* **1981**, *46*, 1098.

(7) (a) Araki, S.; Butsugan, Y. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1446. (b) Tanis, S. P. *Tetrahedron Lett.* **1982**, *23*, 3115. (c) Kojima, Y.; Wakita, S.; Kato, N. *Tetrahedron Lett.* **1979**, 4577.

(8) Tius, M. A.; Takaki, K. S. *J. Org. Chem.* **1982**, *47*, 3166.

(9) Garst, M. E.; Spencer, T. A. *J. Am. Chem. Soc.* **1973**, *95*, 250.

(10) Masaki, Y.; Hashimoto, K.; Sakuma, K.; Kaji, K. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1289.

(11) Reich, H. J.; Shah, S. K.; Gold, P. M.; Olson, R. E. *J. Am. Chem. Soc.* **1981**, *103*, 3112. Hoppmann, A.; Weyerstahl, P. *Tetrahedron* **1978**, *34*, 1723. Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481.

(12) Fujita, E.; Nagao, Y.; Kaneko, K. *Chem. Pharm. Bull.* **1978**, *26*, 3743.

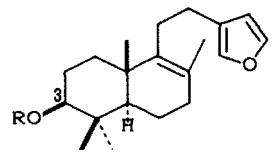
(13) Although we had assigned structure i to the doubly cyclized product in our previous communication (ref 5), it should be corrected to structure **5**.

(14) Ca. 10% of isomeric olefins ($\Delta^{1,10}$ and $\Delta^{10,20}$) was incorporated and these were separated by HPLC.

(15) Gustafson, K.; Andersen, R. J.; Cun-heng, H.; Clardy, J. *Tetrahedron Lett.* **1985**, *26*, 2521.

0022-3263/87/1952-4878$01.50/0

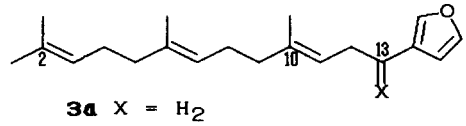
Chart I



1a R = H
1b R = β-D-glc$\frac{2\,1}{}$β-D-xyl

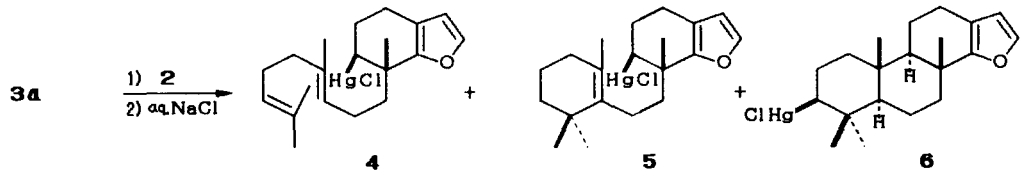
$Hg(OSO_2CF_3)_2 \cdot C_6H_5N(CH_3)_2$

2

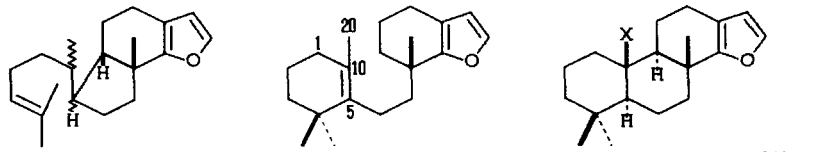


3a X = H_2
3b X = H, $SO_2C_7H_7$
3c X = O
3d X = $S_2C_3H_6$

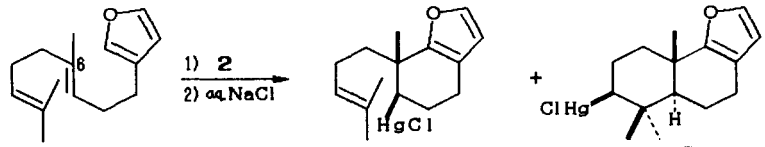
Chart II



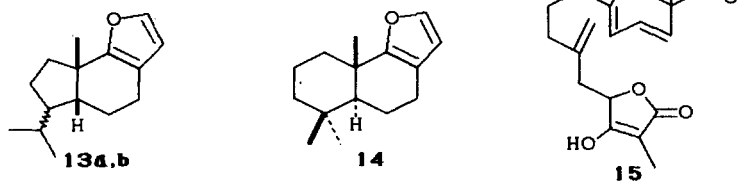
4 **5** **6**



7a~7d **8** **9a** X = CH_3 **9b** X = COOH



10 **11** **12**



13a,b **14** **15**

especially important since this is the first example of the biomimetic olefin cyclization initiated from an internal double bond selectively. Quite recently, the first example of a natural product based upon this unique cyclization mode, hippospongin (**15**), was reported as a constituent of Okinawan marine sponge.[16]

Attempted cyclization of dendrolasin (**10**) with **2** (1.4 equiv) under the same condition described above also initiated at the internal double bond (Δ^6) to give **11** in 53% yield along with tricyclic **12** (10% yield). This result is a striking contrast to the BF_3-induced cyclization of **10** to give pallescesin A (**14**) as the sole product reported by Nasipuri.[4b] Sodium borohydride reduction of **11** also produced an isomeric mixture of radical cyclization products **13a** and **13b**.

Reaction of the sulfone **3b** with **2** at −20 °C was initiated only at the terminal position (Δ^2) to give a mixture of tetracyclic products **16** and **17** in 42% yield (3:1 ratio based on the ^1H NMR analysis of C-15 proton signals; **16** δ 6.52,

(16) Kobayashi, J.; Ohizumi, Y.; Nakamura, H.; Hirata, Y. *Tetrahedron Lett.* **1986**, *27*, 2113.

Chart III

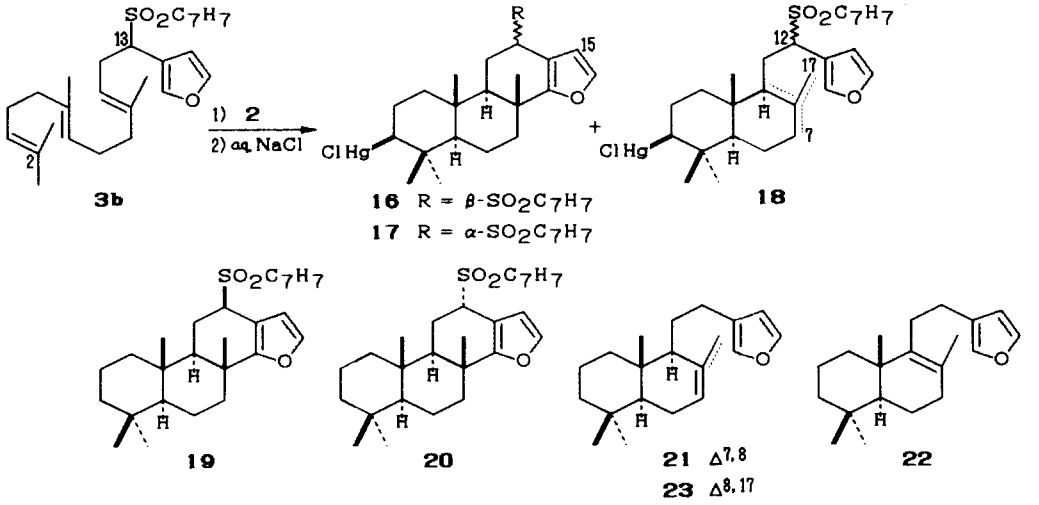
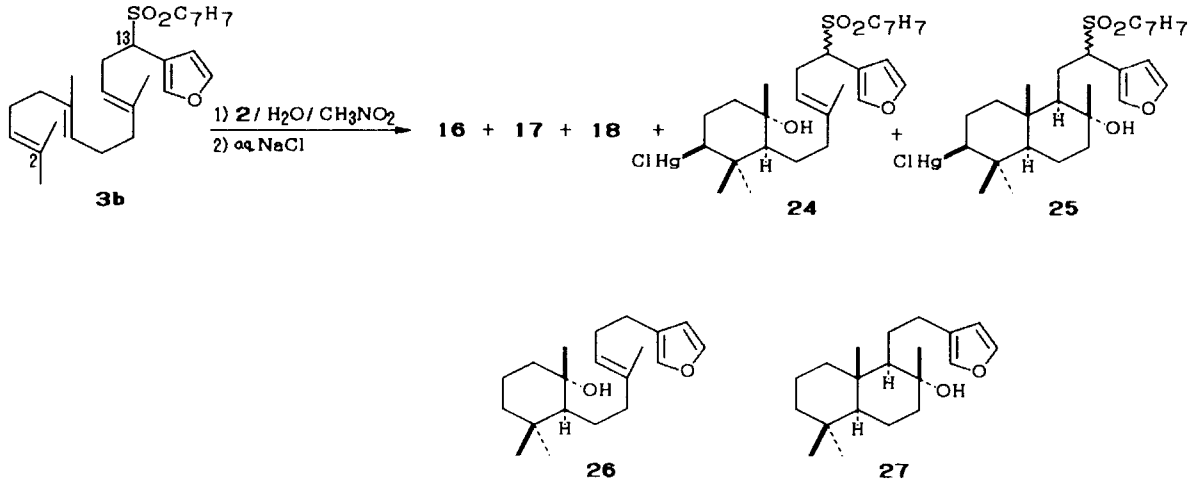


Chart IV



17 δ 6.00) along with a mixture of bicyclic products **18** ($\Delta^{7,8}$:$\Delta^{8,9}$:$\Delta^{8,17}$ = 9:4:3) in 19% yield (Chart III). Pure **16** was isolated by careful crystallization and characterized by spectroscopy. Sodium borohydride reduction of the mixture of **16** and **17** gave **19** and **20** in 74% and 24% yields, respectively. The bicyclic products **18** were subjected to lithium/ammonia reduction followed by HPLC separation, affording **21**, **22**, and **23**.[17] Thus, the *p*-tolylsulfonyl group at C-13 effectively controls the cyclization to start at the terminal position (Δ^2) and partially blocks the third ring formation perhaps due to its steric bulk.

The cyclization of **3b** with **2** was also conducted in the presence of water (30 equiv),[3h] and monocyclic and bicyclic cationic intermediates were stereoselectively trapped to give the diastereomerically mixed tertiary alcohols **24** and **25** in 16% and 18% yields, respectively, together with above-mentioned **16**, **17**, and **18** (Chart III). The alcohols **24** and **25** were subjected to the lithium/ammonia reduction, affording desulfurization products **26** and **27** (Chart IV). The monocyclic alcohol **26** showed entirely superimposable spectral properties (IR, ^{1}H NMR, and ^{13}C NMR) with those of natural ambliol-A.[6]

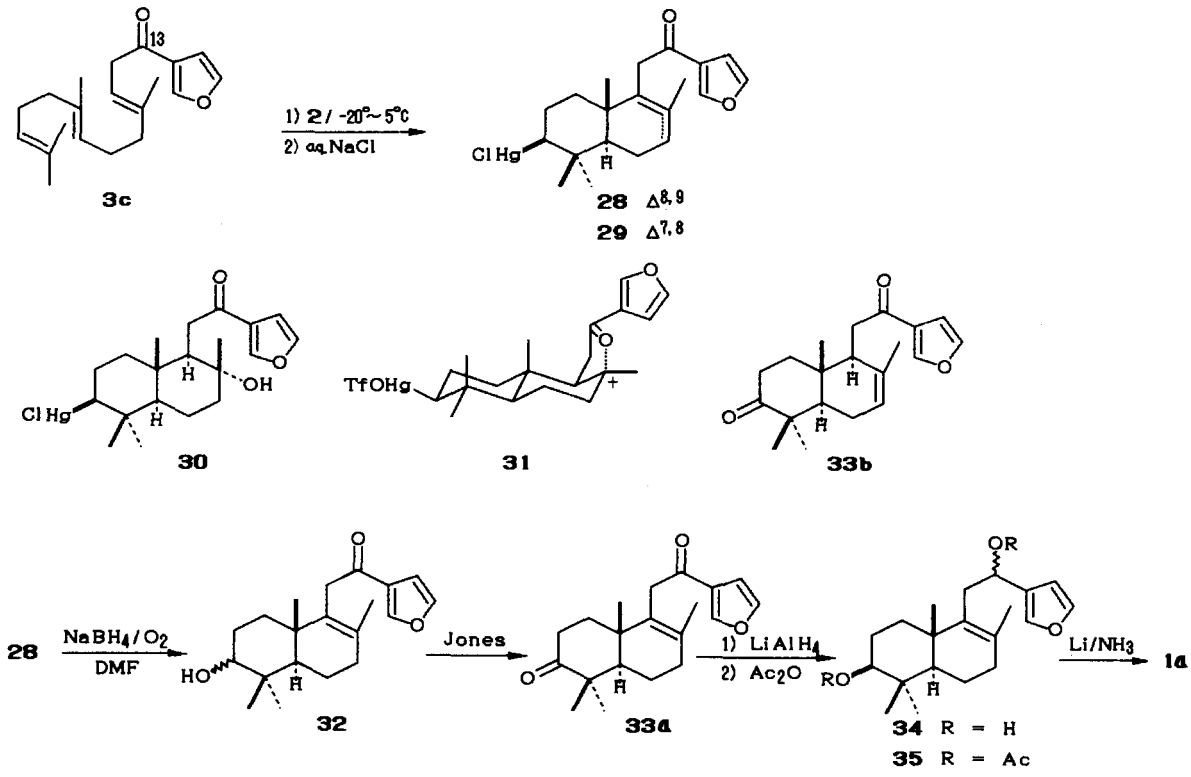
The cyclization of 13-oxoambliofuran (**3c**) is expected to be controlled on both factors, the initiation and the termination due to the electron-withdrawing effect of the carbonyl group from the furan ring. When the reaction of **3c** (Chart V) with **2** (1.4 equiv) was quenched with aqueous sodium chloride solution at −20 °C, keto alcohol **30** was obtained in 33% yield along with the desired ketone **28** (31% yield). This result suggests that the cationic intermediate **31** is stable enough to exist under the reaction conditions. Thus, the reaction mixture was warmed to 5 °C prior to the quenching in order to promote the proton elimination. By the latter procedure, the desired product **28** was obtained in 68% yield along with isomer **29** (8% yield). Although the separation of these isomers at this stage was not easy on a large scale, it was simply achieved in a later step. Neither exocyclic double-bond isomer nor internal double-bond cyclization product or any fully cyclized products were detected. Thus, the cyclization was effectively controlled by the introduction of C-13 carbonyl group. The reason for the selective elimination of the C-9 proton from the intermediate **31** is not clear.

The organomercuric ketone **28** was subjected to Whitesides' hydroxylation[18] ($NaBH_4/O_2$/DMF) to give 3α- and 3β-hydroxylated ketones **32**. The carbonyl moiety at C-12 was entirely inert under this condition. The mixture **32** was oxidized with Jones reagent, affording a single diketone (**33a**) in 86% yield. Recrystallization at this stage eliminated the contaminating $\Delta^{7,8}$ isomer **33b**. The diketone **33a** was transformed in 98% yield to a diastereo-

(17) The ratio of **21** and the mixture of **20** and **22** was determined by the HPLC to be 3:13, and the ratio of **20** and **22** was determined by ^{1}H NMR to be 9:4.

(18) Hill, C. L.; Whitesides, G. M. *J. Am. Chem. Soc.* **1974**, *96*, 870.

Chart V



meric mixture of diacetates **35** through lithium aluminum hydride reduction followed by acetylation. Finally the mixture of diacetates **35** was subjected to a lithium/ammonia reduction and alcohol **1a** was obtained via a simultaneous fragmentation of the acetoxyl moiety from C-12 and the acetyl group from C-3 in 58% yield. The spectral properties (IR, ^{1}H NMR, and ^{13}C NMR) of **1a** were indistinguishable from those of authentic (+)-baiyunol derived from baiyunoside (**1b**).[1] The sole byproduct of the final reaction was the diol **34**, which was easily separated from **1a** and employed for recycling, making the conversion from **35** to **1a** nearly quantitative.

Thus, we have developed a very simple and efficient procedure for the synthesis of (±)-baiyunol utilizing our cyclization agent **2**. This method has allowed us to obtain sufficient quantities of **1a** in order to prepare a variety of sugar derivatives to find more effective artificial sweeteners.[19]

Experimental Section

General. Reactions were run under a positive pressure of argon unless otherwise noted and performed in flame-dried glassware which was cooled under argon. Anhydrous solvents were transferred by an oven-dried syringe. Solvents were distilled before use: nitromethane, dimethylformamide (DMF), hexamethylphosphoric triamide (HMPA), dichloromethane, pyridine, and acetonitrile from calcium hydride and tetrahydrofuran (THF) and diethyl ether from sodium benzophenone ketyl. After workup the organic layers were dried over anhydrous magnesium sulfate. The term "in vacuo" refers to solvent removal via rotary evaporator at water aspirator pressure, followed by evacuation of the flask at 0.1 mmHg for a few hours. Analytical thin-layer chromatography (TLC) was performed on precoated glass plates (5 × 1.5 cm) with silica gel (Merck Kieselgel 60 F_{254} for ordinary phase and Merck RP-18 F_{254} for reverse phase). Column chromatography was performed by using silica gel obtained from Fuji-Devison (BW-820, 60–200 mesh). High performance liquid chromatography (HPLC) was performed on a JASCO trirotor-V instrument with a Gilson 131 refractive index (RI) detector using a Develosil 30-3 column (4 × 250 or 10 × 250 mm for ordinary phase) or a Develosil ODS-5 column (4 × 250 or 10 × 250 mm for reverse phase) supplied from Nomura Chemicals. Melting points were obtained on a Yanagimoto apparatus and are uncorrected. Proton nuclear magnetic resonance (^{1}H NMR) spectra were determined on JEOL GX-400 (400 MHz) or Hitachi R-90H (90 MHz) instruments. Chemical shifts are reported in δ units downfield from tetramethylsilane (TMS). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Coupling constants (J) are reported in herz. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were determined on JEOL GX-400 (100 MHz) or Hitachi R-90H (22.5 MHz) instruments. Chemical shifts are reported in δ units downfield from TMS. Splitting patterns are designed as s, singlet; d, doublet; t, triplet; q, quartet. Infrared spectra (IR) were determined in the indicated solvents in sodium chloride cavity cells on a JASCO A-100 spectrophotometor. Mass spectra (MS) were obtained on an JEOL D-300 instrument at an Ionization voltage of 70 eV.

13-(*p*-Toluenesulfonyl)ambliofuran (3b). To a stirred solution of 3-furfuryl *p*-tolyl sulfone (1.16 g, 5.13 mmol) in THF (14 mL) were added dropwise *n*-butyllithium (1.38 M solution in hexane, 4.09 mL, 5.64 mmol) and HMPA (1.4 mL) at −78 °C, and the mixture was stirred for 20 min at 0 °C. The mixture was again cooled to −78 °C; to it was added a solution of (*E*,*E*)-farnesyl bromide (1.61 g, 5.64 mmol) in THF (15 mL), and the mixture was stirred for an additional 1 h at this temperature. After the addition of aqueous ammonium chloride solution, the mixture was extracted with ether to give the crude product. Column chromatography on silica gel using a 10:1 mixture of hexane and ethyl acetate as an eluant afforded **3b** (1.94 g, 86% yield) as a colorless syrup: IR ($CHCl_3$) 1600, 1310, 1300, 1140, 1085, 1020, 875 cm^{-1}; ^{1}H NMR ($CDCl_3$) 1.50 (3 H, s), 1.54 (6 H, s), 1.64 (3 H, s), 2.37 (3 H, s), 3.90 (1 H, dd, J = 12, 3 Hz), 4.75–5.15 (3 H, m), 6.30 (1 H, d, J = 1 Hz), 7.09 (2 H, d, J = 8 Hz), 7.23 (1 H, s), 7.28 (1 H, t, J = 1 Hz), 7.50 (2 H, d, J = 8 Hz); ^{13}C NMR ($CDCl_3$) 15.9 q, 16.3 q, 17.6 q, 21.6 q, 21.6 q, 25.6 t, 26.3 t, 26.5 t, 26.6 t, 26.8 t, 39.5 t, 39.6 t, 63.0 d, 110.5 d, 117.4 s, 118.5 d, 123.6 d, 124.2 d, 129.0 d, 129.0 d, 129.2 d, 129.2 d, 134.2 s, 138.7 s, 142.4 d, 142.9 d, 144.3 s; HRMS, m/z 440.2356 (M$^+$), calcd for $C_{27}H_{36}O_3S$ 440.2383. The dialkylation product (301 mg, 9% yield) was obtained as a colorless syrup.

(19) Tanaka, O. *Kagaku no Ryoiki* **1985**, *35*, 590.

Ambliofuran (3a). To a stirred solution of excess lithium in liquid ammonia was added dropwise a solution of **3b** (1.99 g, 4.52 mmol) in ether (10 mL) at −78 °C, and the mixture was stirred at the same temperature for 10 min. After the addition of powdered ammonium chloride, liquid ammonia was evaporated in vacuo. The ether extract was subjected to column chromatography of 5D-ODS (60 g) with a mixture of acetonitrile and water (10:1) as an eluant to give ambliofuran (**3a**) (789 mg, 61% yield) as a colorless syrup: IR ($CHCl_3$) 1500, 1160, 1060, 1020, 870 cm^{-1}; ^1H NMR ($CDCl_3$) 1.54 (9 H, s), 1.66 (3 H, s), 4.93–5.25 (3 H, m), 6.22 (1 H, br s), 7.16 (1 H, br s), 7.29 (1 H, t, J = 1 Hz); ^{13}C NMR ($CDCl_3$) 16.0 q, 16.0 q, 17.6 q, 25.1 t, 25.6 q, 26.6 t, 26.8 t, 28.5 t, 39.7 t, 111.0 d, 123.7 d, 124.1 d, 124.3 d, 131.0 s, 134.8 s, 135.6 s, 138.7 d, 142.3 d; HRMS, m/z 286.2269 (M^+), calcd for $C_{20}H_{30}O$ 286.2295.

13-Oxoambliofuran (3c). To a stirred THF (40 mL) solution of 2-(3-furyl)-1,3-dithiane (3.30 g, 17.7 mmol) was added dropwise a solution of lithium diisopropylamide prepared from diisopropylamine (2.15 g, 21.2 mmol) and n-butyllithium (1.23 M hexane solution 16.5 mL, 20.6 mmol) in THF (25 mL) at −78 °C, and the mixture was stirred at this temperature for 10 min. To this was added a solution of (*E,E*)-farnesyl bromide (5.04 g, 17.7 mmol) in THF (20 mL), and the mixture was stirred for an additional 40 min at −78 °C. After being quenched with aqueous ammonium chloride solution, the crude product was obtained by ether extraction. Column chromatography on silica gel with a mixture of hexane and ethyl acetate (40:1) as eluant afforded the alkylated 1,3-dithiane (6.66 g, 96% yield) as a pale yellow syrup: IR ($CHCl_3$) 1500, 1160, 1050, 875 cm^{-1}; ^1H NMR ($CDCl_3$) 1.49 (3 H, s), 1.55 (6 H, s), 1.63 (3 H, s), 1.96 (8 H, br), 5.04 (3 H, br), 6.39 (1 H, br s), 7.30 (1 H, br s), 7.40 (1 H, br s); ^{13}C NMR ($CDCl_3$) 16.1, 16.5, 17.7, 25.5, 25.8, 26.5, 26.8, 27.6, 39.8, 39.9, 42.4, 51.8, 111.3, 117.6, 124.2, 124.5, 128.9, 131.1, 134.9, 139.1, 142.5, 143.2.

The alkylated 1,3-dithiane product (6.62 g, 16.9 mmol) and thallium(III) nitrate trihydrate (7.90 g, 17.8 mmol) were dissolved in THF (50 mL) and methanol (400 mL), and the mixture was stirred for 5 min at room temperature. An inorganic precipitate was removed by filtration through a cotton–Celite pad, and the filtrate was concentrated in vacuo. To this was added water (200 mL), and the solution was extracted with ether. The concentrated extract was subjected to short-path column chromatography using hexane and ethyl acetate to give 13-oxoambliofuran (4.77 g, 94% yield) as a colorless syrup: IR ($CHCl_3$) 3120, 1670, 1560, 1510, 1205, 1160, 875 cm^{-1}; ^1H NMR ($CDCl_3$) 1.56 (6 H, s), 1.65 (6 H, s), 1.94–2.07 (8 H), 3.39 (2 H, d, J = 7 Hz), 5.01 (2 H, br), 5.34 (1 H, t, J = 7 Hz), 6.70 (1 H, dd, J = 2, 1 Hz), 7.37 (1 H, t, J = 2 Hz), 7.97 (1 H, dd, J = 2, 1 Hz); ^{13}C NMR ($CDCl_3$) 16.0 q, 16.6 q, 17.6 q, 25.6 t, 26.4 t, 26.7 t, 39.6 t, 39.6 t, 40.4 t, 108.7 d, 115.9 d, 123.7 d, 124.2 d, 127.3 s, 131.0 s, 135.1 s, 139.1 s, 143.8 d, 147.0 d, 193.0 s; HRMS, m/z 300.2069 (M^+), calcd for $C_{20}H_{28}O_2$ 300.2089.

Cyclization of Ambliofuran (3a). To a stirred suspension of dried mercury(II) oxide yellow (182 mg, 0.84 mmol) in nitromethane (20 mL) was added trifluoromethanesulfonic (triflic) anhydride (236 mg, 0.84 mmol) at room temperature, and the mixture was stirred for 1 h until the orange color disappeared. To the resulting creamy white suspension was added *N,N*-dimethylaniline (102 mg, 0.84 mmol). The mixture turned to a pale yellow clear solution instantaneously, affording mercury(II) triflate/*N,N*-dimethylaniline complex (**2**). The solution of **2** in nitromethane was slowly added to a solution of ambliofuran (200 mg, 0.698 mmol) in dichloromethane (4 mL) and nitromethane (6 mL) over a period of 17 min at −20 °C, and the mixture was stirred for an additional 1 h at this temperature. To it was added brine (30 mL), and the resulting heterogeneous solution was gradually warmed to room temperature and stirred for another 2 h. The insoluble inorganic materials were filtered off through a cotton–Celite pad and the filtrate was extracted with dichloromethane. The crude product was subjected to chromatography on a column of silica gel (60 g) using a mixture of hexane and chloroform (2:1) as an eluant to give **4** (138 mg, 38%) [IR ($CHCl_3$) 1500, 1150, 1130, 1100, 880 cm^{-1}; ^1H NMR ($CDCl_3$) 1.42 (3 H, s), 1.54 (3 H, s), 1.59 (3 H, s), 1.68 (3 H, s), 3.22 (1 H, dd, J = 8, 4 Hz), 5.04 (2 H, m), 6.11 (1 H, d, J = 1 Hz), 7.21 (1 H, d, J = 1 Hz); ^{13}C NMR ($CDCl_3$) 15.9 q, 17.6 q, 23.6 t, 25.0 t, 25.6 q, 26.6 t, 26.9 t, 31.1 q, 39.6 t, 40.9 s, 42.4 t, 65.2 d, 109.9 d, 115.5 s, 123.7 d, 124.1 d, 131.1 s, 135.3 s, 140.5 d, 155.2 s.], **5** (59 mg, 15%) [IR ($CHCl_3$) 1500, 1160, 1140, 1115, 900 cm^{-1}; ^1H NMR ($CDCl_3$) 0.93 (3 H, s), 0.98 (3 H, s), 1.44 (3 H, s), 1.53 (3 H, s), 3.29 (1 H, dd, J = 7.4 Hz), 6.11 (1 H, d, J = 1 Hz), 7.23 (1 H, s); ^{13}C NMR ($CDCl_3$) 19.5 t, 19.8 q, 25.1 t, 25.2 t, 26.9 t, 28.6 q, 28.8 q, 32.8 t, 35.0 s, 39.8 t, 41.1 s, 42.3 t, 65.2 d, 78.4 d, 110.0 d, 115.5 s, 127.2 s, 136.3 s, 140.5 d, 155.3 s.], and tricyclic **6** (48 mg, 13%) [IR ($CHCl_3$) 1140, cm^{-1}; ^1H NMR ($CDCl_3$) 0.94 (3 H, s), 1.04 (6 H, s), 1.17 (3 H, s), 2.76 (1 H, dd, J = 14, 5 Hz), 6.02 (1 H, d, J = 2 Hz), 7.11 (1 H, d, J = 2 Hz); ^{13}C NMR ($CDCl_3$) 16.4 q, 18.7 t, 20.2 t, 22.5 q, 22.9 t, 25.8 q, 26.5 t, 29.8 s, 36.7 t, 37.0 q, 37.2 s, 39.4 s, 42.6 t, 56.6 d, 59.0 d, 74.1 d, 110.0 d, 113.6 s, 140.2 d, 159.4 s.

Sodium Borohydride Reduction of 4. To a stirred solution of **4** (160 mg, 0.307 mmol) in dichloromethane (2 mL) and ethanol (2 mL) was added a solution of sodium borohydride (116 mg, 3.07 mmol) and sodium hydroxide (246 mg, 6.14 mmol) in 0.3 mL of water, and the mixture was stirred for 30 min at room temperature. The inorganic precipitate was filtered off and the filtrate was extracted with dichloromethane. Column chromatography on silica gel (5 g) using hexane and ethyl acetate (10:1) as an eluant afforded a mixture of **7a–d** (41.9 mg, 48% yield). Each of these products was separated by HPLC using the C-30-3 column and hexane as eluant. **7a**: IR ($CHCl_3$) 1245, 1200, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) 0.90 (3 H, d, J = 7 Hz), 1.25 (3 H, s), 1.58 (3 H, s), 1.67 (3 H, s), 5.06 (1 H, t, J = 7 Hz), 6.06 (1 H, d, J = 2 Hz), 7.18 (1 H, d, J = 2 Hz); ^{13}C NMR ($CDCl_3$) 17.8 q, 18.0 q, 19.4 t, 24.1 t, 25.9 t, 26.1 q, 26.4 q, 27.3 t, 33.8 d, 36.6 t, 37.1 t, 43.4 s, 46.2 d, 49.3 d, 109.9 d, 115.5 s, 125.1 d, 131.3 s, 140.4 d, 156.6 s; HRMS, m/z 286.2268 (M^+), calcd for $C_{20}H_{30}O$ 286.2295. **7b**: IR ($CHCl_3$) 1160, 890 cm^{-1}; ^1H NMR ($CDCl_3$) 0.77 (3 H, d, J = 7 Hz), 1.20 (3 H, s), 1.52 (3 H, s), 1.61 (3 H, s), 5.05 (1 H, t, J = 7 Hz), 6.08 (1 H, d, J = 2 Hz), 7.22 (1 H, d, J = 2 Hz); ^{13}C NMR ($CDCl_3$) 15.2, 17.7, 19.1, 23.0, 25.1, 25.7, 26.1, 26.5, 33.8, 34.9, 36.1, 37.0, 44.8, 49.3, 109.7, 114.9, 124.8, 130.9, 140.1, 157.5; HRMS, m/z 286.2299 (M^+). **7c**: ^1H NMR ($CDCl_3$) 0.90 (3 H, d, J = 7 Hz), 1.27 (3 H, s), 1.61 (3 H, s), 1.67 (3 H, s), 5.10 (1 H, t, J = 7 Hz), 6.10 (1 H, d, J = 2 Hz), 7.17 (1 H, d, J = 2 Hz); ^{13}C NMR ($CDCl_3$) 17.7, 18.4, 21.9, 25.4, 25.8, 28.3, 33.7, 35.6, 36.5, 42.8, 47.3, 49.3, 109.9, 125.0, 134.9, 140.2; HRMS, m/z 286.2295 (M^+). **7d**: ^1H NMR ($CDCl_3$) 0.93 (3 H, d, J = 7 Hz), 1.37 (3 H, s), 1.59 (3 H, s), 1.66 (3 H, s), 5.16 (1 H, t, J = 7 Hz), 6.09 (1 H, d, J = 2 Hz), 7.17 (1 H, d, J = 2 Hz); ^{13}C NMR ($CDCl_3$) 17.6 q, 18.2 t, 21.7 q, 21.8 t, 23.2 t, 25.2 q, 25.7 q, 26.8 t, 27.9 d, 33.7 t, 35.8 t, 36.5 s, 47.3 d, 49.5 d, 109.6 d, 114.2 s, 124.9 d, 130.8 s, 140.4 d, 158.2 s; HRMS, m/z 286.2285 (M^+).

Sodium Borohydride Reduction of 5. To a stirred solution of **5** (21 mg, 0.028 mmol) in dichloromethane (1 mL) and ethanol (1 mL) was added a solution of sodium borohydride (10.5 mg, 0.28 mmol) and sodium hydroxide (25 mg, 0.63 mmol) in water (0.05 mL), and the mixture was stirred for 30 min at room temperature. The mixture was filtered through a cotton–Celite pad to remove the inorganic precipitate, and the filtrate was extracted with dichloromethane. The crude product was subjected to column chromatography on silica gel (1.2 g) using hexane as eluant and followed by preparative HPLC with the ODS-5 column using acetonitrile as an eluant to give **8** (3.3 mg, 42%): IR ($CHCl_3$) 1505, 1150, 1100, 895 cm^{-1}; ^1H NMR ($CDCl_3$) 0.93 (3 H, s), 0.96 (3 H, s), 1.21 (3 H, s), 1.53 (3 H, s), 6.07 (1 H, d, J = 2 Hz), 7.16 (1 H, d, J = 2 Hz); ^{13}C NMR ($CDCl_3$) 19.6 q, 19.7 t, 20.4 t, 22.6 t, 23.3 t, 25.5 q, 28.6 q, 28.7 q, 32.8 t, 35.0 s, 35.6 s, 36.0 t, 40.0 t, 40.6 t, 109.9 d, 115.7 s, 126.6 s, 137.0 s, 139.8 d, 156.8 s; HRMS, m/z 286.2284 (M^+), calcd for $C_{20}H_{30}O$ 286.2295.

Cyclization of Dendrolasin (10). To a solution of dendrolasin (**10**) (120 mg, 0.55 mmol) in nitromethane (5 mL) and dichloromethane (3 mL) was added dropwise a solution of **2**, prepared from mercury(II) oxide (143 mg, 0.66 mmol), triflic anhydride (186 mg, 0.66 mmol), and *N,N*-dimethylaniline (80 mg, 0.66 mmol) in nitromethane (12 mL), over a period of 10 min at −20 °C, and the mixture was stirred for 2 h, at this temperature. Brine was added to the reaction mixture, and the resulting heterogeneous solution was stirred for an additional 2 h at room temperature. The inorganic precipitate was filtered through a cotton–Celite pad and the filtrate was extracted with dichloromethane. Column chromatography on silica gel (20 g) using a mixture of hexane and dichloromethane as eluant afforded **11** (131 mg, 53%) [IR ($CHCl_3$) 1510, 1450, 1380, 1130, 1110, 890 cm^{-1}; ^1H NMR ($CDCl_3$) 1.40 (3

H, s), 1.54 (3 H, s), 1.64 (3 H, s), 3.17 (1 H, dd, J = 9, 4 Hz), 5.00 (1 H, br), 6.08 (1 H, d, J = 2 Hz), 7.17 (1 H, d, J = 2 Hz); ^{13}C NMR ($CDCl_3$) 17.7 q, 23.7 t, 25.1 t, 25.7 q, 27.0 t, 31.2 q, 40.9 s, 42.5 t, 65.3 d, 110.0 d, 115.7 s, 124.1 d, 131.5 s, 140.5 d, 155.3 s.] and **12** (24.5 mg, 10%) [^{1}H NMR ($CDCl_3$) 1.11 (6 H, s), 1.21 (3 H, s), 2.78 (1 H, dd, J = 12, 6 Hz), 6.03 (1 H, d, J = 2 Hz), 7.11 (1 H, d, J = 2 Hz); ^{13}C NMR ($CDCl_3$) 21.3 q, 21.4 t, 22.7 t, 25.7 q, 26.4 t, 36.2 s, 36.6 q, 38.1 t, 38.9 s, 54.4 d, 73.0 d, 109.9 d, 113.7 s, 140.2 d, 158.4 s.] along with the recovered starting material **10** (39 mg, 33%).

Sodium Borohydride Reduction of 11. To a stirred solution of **11** (122.4 mg, 0.27 mmol) in dichloromethane (2 mL) and ethanol (2 mL) was added a solution of sodium borohydride (103 mg, 2.7 mmol) and sodium hydroxide (216 mg, 5.4 mmol) in 0.25 mL of water, and the mixture was stirred for 30 min at room temperature. The mixture was filtered through a cotton–Celite pad, and the filtrate was extracted with dichloromethane. Column chromatography on silica gel (5 g) using hexane as an eluant gave a diastereomeric mixture of **13a** and **13b** (34.4 mg, 59%). This mixture was separated by HPLC using the Develosil C-30-3 column with hexane as eluant to give pure **13a** [^{1}H NMR ($CDCl_3$) 0.85 (3 H, d, J = 7 Hz), 0.90, (3 H, d, J = 7 Hz), 1.26 (3 H, s), 6.06 (1 H, d, J = 2 Hz), 7.21 (1 H, d, J = 2 Hz); HRMS, m/z 218.1671 (M^+), calcd for $C_{15}H_{22}O$ 218.1671.] and **13b** [IR ($CHCl_3$) 1780, 1700, 1465, 1380, 1360, 1080, 910 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.91 (3 H, d, J = 7 Hz), 0.95 (3 H, d, J = 7 Hz), 1.29 (3 H, s), 6.15 (1 H, d, J = 2 Hz), 7.22 (1 H, d, J = 2 Hz); HRMS, m/z 218.1677 (M^+), calcd for $C_{15}H_{22}O$ 218.1671.].

Cyclization of 3b. A solution of sulfone **3b** (200 mg, 0.45 mmol) in nitromethane was added to a stirred solution of **2**, prepared from mercury(II) oxide (117 mg, 0.545 mmol), triflic anhydride (154 mg, 0.545 mmol), and *N,N*-dimethylaniline (66 mg, 0.545 mmol) in nitromethane (20 mL), and the mixture was stirred for 2 h at −20 °C. To it was added brine (20 mL), and the mixture was stirred for an additional 3 h at room temperature. The filtrate from a cotton–Celite pad was extracted with dichloromethane. Column chromatography on silica gel (30 g) using a mixture of hexane and ethyl acetate (15:1) as eluant afforded a mixture of tetracyclic products **16** and **17** (126 mg, 42%) and bicyclic products **18** (59 mg, 19%). Pure **16** was isolated by a recrystallization from a mixture of hexane and dichloromethane: mp 205.5–207 °C; IR ($CHCl_3$) 1600, 1310, 1300, 1250, 1140, 1130, 1085, 1040, 980, 905, 810 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.65 (3 H, s), 0.85 (3 H, s), 1.00 (6 H, s), 2.36 (3 H, s), 2.70 (1 H, dd, J = 14, 4 Hz), 4.17 (1 H, dd, J = 8, 7 Hz), 6.52 (1 H, d, J = 1 Hz), 7.15 (1 H, d, J = 1 Hz), 7.19 (2 H, d, J = 8 Hz), 7.55 (2 H, d, J = 8 Hz); ^{13}C NMR ($CDCl_3$) 16.0 q, 19.9 t, 20.4 t, 21.8 q, 21.8 q, 25.8 q, 26.3 t, 36.4 t, 36.7 t, 37.2 s, 39.3 q, 42.4 s, 54.7 d, 58.8 d, 61.2 d, 73.4 d, 107.0 s, 110.4 d, 129.4 d, 129.4 d, 129.8 d, 129.9 d, 132.9 s, 140.9 d, 144.8 s, 163.1 s. Anal. Calcd for $C_{27}H_{35}O_3SHgCl$: C, 48.05; H, 5.21. Found: C, 47.92; H, 5.21.

Sodium Borohydride Reduction of a Mixture of 16 and 17. To a stirred solution of a mixture of **16** and **17** (96 mg, 0.142 mmol) in dichloromethane (2 mL) and ethanol (2 mL) was added a solution of sodium borohydride (54 mg, 1.42 mmol) and sodium hydroxide (120 mg, 3.0 mmol) in water (0.2 mL), and the mixture was stirred for 40 min at room temperature. The filtrate from a cotton–Celite pad was extracted with dichloromethane. Column chromatography on silica gel (7 g) using a mixture of hexane and ethyl acetate (30:1) as eluant gave **19** (44 mg, 74%) [mp 212–213 °C; IR ($CHCl_3$) 1600, 1395, 1390, 1310, 1300, 1140, 1130, 1090, 880, 810 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.68 (3 H, s), 0.81 (9 H, s), 2.36 (3 H, s), 4.19 (1 H, dd, J = 10, 7 Hz), 6.52 (1 H, d, J = 1 Hz), 7.13 (1 H, d, J = 1 Hz), 7.18 (2 H, d, J = 8 Hz), 7.57 (2 H, d, J = 8 Hz); ^{13}C NMR ($CDCl_3$) 16.0 q, 18.0 t, 18.3 t, 20.3 t, 21.3 q, 21.5 q, 21.8 q, 33.2 s, 33.3 q, 36.4 t, 37.4 s, 39.6 t, 41.9 t, 54.9 d, 56.7 d, 61.3 d, 106.8 s, 110.2 d, 129.1 d, 129.6 d, 133.0 s, 140.5 d, 144.3 s, 163.4 s; HRMS, m/z 285.2207 ($M^+ - SO_2C_7H_7$), calcd for $C_{20}H_{29}O$ 285.2217.] and **20** (15 mg, 24%) [mp 190–191 °C; IR ($CHCl_3$) 1600, 1380, 1310, 1300, 1140, 1090, 820 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.82 (9 H, s), 1.07 (3 H, s), 2.41 (3 H, s), 4.10 (1 H, d, J = 7 Hz), 6.16 (1 H, d, J = 1 Hz), 7.17 (1 H, d, J = 1 Hz), 7.25 (2 H, d, J = 8 Hz), 7.63 (2 H, d, J = 8 Hz); ^{13}C NMR ($CDCl_3$) 16.2 q, 18.1 t, 18.4 t, 19.4 t, 21.2 q, 21.6 q, 21.7 q, 33.3 q, 36.1 t, 36.5 s, 37.2 s, 39.1 t, 42.0 t, 49.9 d, 56.6 d, 59.8 d, 106.4 s, 110.7 d, 129.2 d, 129.2 d, 129.3 d, 129.3 d, 135.2 s, 140.5 d, 144.4 s, 163.9 s; HRMS, m/z 285.2188 ($M^+ - SO_2C_7H_7$), calcd for $C_{20}H_{29}O$ 285.2217.

Reduction of a Mixture of Bicyclic Products 18. To a stirred solution of excess lithium in liquid ammonia was added dropwise a solution of **18** (49 mg, 0.0725 mmol) in dry THF (2 mL) at −78 °C, and the mixture was stirred at this temperature for 10 min. After the addition of powdered ammonium chloride, liquid ammonia was evaporated in vacuo, and the residue was extracted with ether. Column chromatography on 5D-ODS (supplied from Fuji-Devison Co. 5 g) using a mixture of acetonitrile and water (19:1) as eluant afforded a reduction product mixture (20 mg, 96%). Further purification with HPLC (ODS-5 column, 19:1 mixture of acetonitrile and water as eluant) afforded pure **22** (1.0 mg) [^{1}H NMR ($CDCl_3$) 0.84 (3 H, s), 0.89 (3 H, s), 0.95 (3 H, s), 1.59 (3 H, s), 6.24 (1 H, br), 7.19 (1 H, br), 7.29 (1 H, br); HRMS, m/z 286.2274 (M^+), calcd for $C_{20}H_{30}O$ 286.2295.] and a mixture of **21** and **23** (10 mg).

Cyclization of 3b in the Presence of Water. To a stirred solution of **3b** (300 mg, 0.681 mmol) and water (0.37 mL, 20.4 mmol) in nitromethane (10 mL) was added a solution of **2**, prepared from mercury(II) oxide (177 mg, 0.82 mmol), triflic anhydride (230 mg, 0.82 mmol), and *N,N*-dimethylaniline (99 mg, 0.82 mmol), in nitromethane (20 mL) at −20 °C, and the mixture was stirred for 2 h at this temperature. After addition of brine (20 mL), the resulting heterogeneous solution was stirred for an additional 2 h at room temperature. The solution was filtered through a cotton–Celite pad and was extracted with dichloromethane. Column chromatography on silica gel (30 g) by a gradient elution with a mixture of hexane and ethyl acetate (15:1 to 3:2) afforded a diastereomeric mixture of **16** and **17** (71 mg, 15%), **18** (125.9 mg, 25%, isomeric mixture based on the double bond), **24** (73.5 mg, 16%, diastereomeric mixture) [IR ($CHCl_3$) 3600, 1595, 1310, 1300, 1140, 1085, 875 cm^{-1}] and **25** (83.9 mg, 18%, diastereomeric mixture) [IR ($CHCl_3$) 3590, 1600, 1305, 1295, 1140, 1080, 1010, 870 cm^{-1}].

Ambliol-A (26). To a stirred solution of excess lithium (6 mg) in liquid ammonia (6 mL) was added dropwise a solution of **24** (93.1 mg, 0.134 mmol) in dry THF (3 mL) at −78 °C, and the mixture was stirred at the same temperature for 10 min. To this was added ammonium chloride, and the liquid ammonia was evaporated under reduced pressure. The ether extract was subjected to column chromatography on silica gel (5 g) using a mixture of hexane and ethyl acetate as eluant to give **26** (21.4 mg, 52% yield) as a colorless syrup: IR ($CHCl_3$) 3600, 1500, 1390, 1160, 1025, 910, 880 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.82 (3 H, s), 0.93 (3 H, s), 1.15 (3 H, s), 1.60 (3 H, s), 5.13 (1 H, br t, J = 6 Hz), 6.22 (1 H, d, J = 1 Hz), 7.17 (1 H, d, J = 1 Hz), 7.29 (1 H, t, J = 1 Hz); ^{13}C NMR (C_6D_6) 16.2 q, 20.8 t, 21.5 q, 23.4 q, 25.2 t, 25.3 t, 28.8 t, 32.9 q, 35.5 s, 41.7 t, 43.2 t, 43.9 t, 56.6 d, 73.5 s, 111.3 d, 124.1 d, 125.2 s, 137.0 s, 139.2 d, 142.8 d; HRMS, m/z 286.2276 ($M^+ - H_2O$), calcd for $C_{20}H_{30}O$ 286.2295.

Bicyclic Alcohol 27. According to the same procedure described above, **25** (13.9 mg, 0.020 mmol) was converted to **27** (3.3 mg, 54% yield): IR ($CHCl_3$) 3580, 1500, 1390, 1160, 1060, 1020, 940, 905, 875 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.78 (6 H, s), 0.86 (3 H, s), 1.12 (3 H, s), 6.22 (1 H, br s), 7.18 (1 H, d, J = 1 Hz), 7.27 (1 H, br s); ^{13}C NMR 15.5 q, 18.5 t, 20.6 t, 21.5 q, 23.9 q, 26.1 t, 28.0 t, 33.2 s, 33.4 q, 39.2 s, 39.9 t, 42.0 t, 44.7 t, 56.1 d, 61.4 d, 74.0 s, 110.9 d, 125.5 s, 138.6 d, 142.4 d; HRMS, m/z 286.2276 ($M^+ - H_2O$), calcd for $C_{20}H_{30}O$ 286.2295.

Cyclization of 13-Oxoambliofuran (3c). To a stirred solution of the mercury(II) triflate/*N,N*-dimethylaniline complex, prepared from mercury(II) oxide (2.34 g, 10.82 mmol), triflic anhydride (3.05 g, 10.82 mmol), and *N,N*-dimethylaniline (1.31 g, 10.82 mmol) in nitromethane (50 mL), was added a solution of ketone **3c** (2.50 g, 8.32 mmol) at −20 °C, and the mixture was stirred for 2 h. After warming up to 5 °C, saturated sodium chloride solution (40 mL) was added and the mixture was stirred for 30 min at room temperature. Inorganic precipitates were removed by a filtration through a cotton–Celite pad, and the filtrate was extracted with chloroform. The concentrated extract was subjected to column chromatography on silica gel (160 g) using hexane and ethyl acetate as eluant to give starting ketone **3c** (320 mg, 13%) and a 10:1 mixture of bicyclic products **28** and **29** (3.40 g, 76% yield): IR ($CHCl_3$) 1680, 1560, 1505, 1160, 1040, 875 cm^{-1}; ^{1}H NMR ($CDCl_3$, peaks due to **28**) 0.99 (3 H, s), 1.04 (3 H, s), 1.09 (3 H,

s), 1.48 (3 H, s), 2.77 (1 H, dd, J = 13.5, 4.0 Hz), 3.47 (2 H, d, J = 4.6 Hz), 6.78 (1 H, dd, J = 2.0, 1.0 Hz), 7.44 (1 H, dd, J = 2.0, 1.5 Hz), 8.07 (1 H, dd, J = 1.5, 1.0 Hz); ^{13}C NMR ($CDCl_3$) 20.2 q, 20.4 q, 21.1 t, 26.4 q, 26.9 t, 33.7 t, 36.5 q, 38.2 s, 39.2 t, 39.6 t, 53.7 d, 73.2 d, 108.7 d, 127.3 s, 130.4 s, 143.8 d, 146.3 d, 192.2 s; HRMS, m/z 536.1137 (M^+), calcd for $C_{20}H_{27}O_2HgCl$ 536.1166.

Organomercuric Keto Alcohol 30. When the above reaction mixture was quenched at −20 °C, the mixture of bicyclic products **28** and **29** was obtained in 31% yield along with keto alcohol **30** (33% yield): IR ($CHCl_3$) 3550, 1680, 1560, 1510, 1390, 1200, 1160, 875 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.88 (3 H, s), 0.98 (3 H, s), 1.06 (3 H, s), 1.13 (3 H, s), 1.56 (3 H, s), 2.73 (2 H, m), 2.86 (1 H, dd, J = 17.3, 4.6 Hz), 6.75 (1 H, dd, J = 1.9, 0.8 Hz), 7.42 (1 H, dd, J = 1.9, 1.4 Hz), 8.08 (1 H, dd, J = 1.4, 0.8 Hz); ^{13}C NMR ($CDCl_3$) 16.0 q, 22.6 t, 23.6 q, 26.1 q, 26.5 t, 36.5 t, 36.8 q, 38.4 s, 39.3 s, 42.2 t, 44.7 t, 55.4 d, 58.0 d, 72.9 s, 73.1 d, 108.7 d, 127.4 s, 143.9 d, 146.7 d, 183.1 s.

Keto Alcohols 32. A solution of the organomercuric ketone **28** (3.40 g, 6.35 mmol) in dry DMF (100 mL) was added dropwise to a stirred solution of sodium borohydride (483 mg, 12.7 mmol) in DMF (35 mL) under vigorous bubbling of oxygen gas during a period of 3.5 h at room temperature, and the mixture was stirred for an additional 5 min. To it was added 1 N sulfuric acid (70 mL) and then the solution was neutralized by the addition of saturated sodium hydrogen carbonate solution. Ether extraction and concentration gave the crude product. Column chromatography on silica gel (60 g) using hexane and ethyl acetate afforded keto alcohols **32** (1.99 g, 81% yield): IR ($CHCl_3$) 3620, 1685, 1560, 1500, 1150, 1030, 870 cm^{-1}.

Diketones 33a and 33b. To a solution of the keto alcohols **32** (1.99 g, 6.34 mmol) in acetone (30 mL) was added Jones reagent (1.67 M solution, 5.50 mL, 9.2 mmol), and the mixture was stirred for 30 min at room temperature. The resulting mixture was diluted with water and extracted with ether to give the crude product. Column chromatography on silica gel (60 g) using hexane and ethyl acetate as eluant afforded a mixture of diketones (1.71 g, 86% yield). Recrystallization from hexane and ether provided pure diketone **33a** (890 mg) as colorless crystals: mp 93–93.5 °C; IR ($CHCl_3$) 1685, 1560, 1510, 1390, 1335, 1160, 1055, 1045, 1005, 880, 820 cm^{-1}; ^{1}H NMR ($CDCl_3$) 1.01 (3 H, s), 1.06 (3 H, s), 1.12 (3 H, s), 1.51 (3 H, s), 1.74 (2 H, m), 1.89 (1 H, dd, J = 12.3, 2.5 Hz), 2.11 (1 H, dd, J = 17.6, 5.6 Hz), 2.44–2.48 (2 H, m), 3.49 (1 H, d, J = 18.3 Hz), 3.56 (1 H, d, J = 18.3 Hz), 6.78 (1 H, dd, J = 1.9, 0.8 Hz), 7.45 (1 H, dd, J = 1.9, 1.4 Hz), 8.09 (1 H, br s); ^{13}C NMR ($CDCl_3$) 19.7 q, 20.0 t, 20.2 q, 20.9 q, 27.1 q, 33.2 t, 34.0 t, 34.5 t, 37.8 s, 39.5 t, 46.9 s, 50.5 d, 108.7 d, 127.3 s, 131.1 s, 131.1 s, 143.9 d, 146.4 d, 192.1 s, 217.2 s. Anal. Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.33. Found: C, 76.44; H, 8.31. The mother liquid of the recrystallization was subjected to medium pressure liquid chromatography (Kusano Kagakukikai Co.) with a Gilson RI detector using an ODS column and an eluant of a 2:1 mixture of acetone and water to give additional **33a** (520 mg) along with $\Delta^{7,8}$ isomer **33b** (155 mg) as a colorless syrup: IR ($CHCl_3$) 1710, 1690, 1560, 1510, 1450, 1390, 1155, 875 cm^{-1}; ^{1}H NMR ($CDCl_3$) 1.01 (3 H, s), 1.09 (3 H, s), 1.12 (3 H, s), 1.49 (3 H, s), 5.49 (1 H, br s), 6.80 (1 H, d, J = 1.7 Hz), 7.46 (1 H, t, J = 1.7, 1.5 Hz), 8.07 (1 H, br s); ^{13}C NMR ($CDCl_3$) 14.6 q, 22.1 q, 22.5 q, 24.3 t, 25.5 q, 30.0 s, 34.7 t, 35.9 s, 38.0 t, 38.6 t, 47.6 d, 51.0 d, 108.7 d, 122.0 s, 127.6 s, 133.9 d, 144.0 d, 146.3 d, 193.6 s, 215.5 s; HRMS, m/z 314.1900, calcd for $C_{20}H_{26}O_3$ 314.1883.

Diacetates 35. To a stirred suspension of lithium aluminum hydride (2.14 g, 56.0 mmol) in anhydrous THF (50 mL) was slowly added a solution of the diketone **33** (8.06 g, 25.6 mmol) in THF (100 mL), and the mixture was stirred for 1 h at room temperature. To it was added ethyl acetate (50 mL) and then water (30 mL) slowly, and the resulting gray suspension was stirred for 10 min until the color changed to white. Addition of anhydrous magnesium sulfate, filtration through a cotton–Celite pad, and concentration provided a mixture of diols **34** (8.10 g) as a colorless syrup: IR ($CHCl_3$) 3600, 3350, 1495, 1365, 1230, 1150, 1020, 865 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.80 (3 H, s), 1.00 (6 H, s), 1.53 (3 H, s), 2.47 (2 H, d, J = 8 Hz), 3.20 (1 H, dd, J = 12, 5 Hz), 4.77 (1 H, t, J = 7 Hz), 6.36 (1 H, br s), 7.33 (2 H, br s).

The diol mixture described above was dissolved in pyridine (80 mL) and acetic anhydride (50 mL) was added. After stirring for 14 h, volatile materials were evacuated under reduced pressure to give the crude material. Column chromatography on silica gel (200 g) using hexane and ethyl acetate as eluant afforded a diastereomeric mixture of diacetates **35** (10.11 g, 98% yield): IR ($CHCl_3$) 1720, 1370, 1250, 1115, 880 cm^{-1}; HRMS, m/z 402.2361 (M^+), calcd for $C_{24}H_{34}O_5$ 402.2406.

(±)-Baiyunol (1a). To a stirred and refluxing solution of lithium (5.23 g, 753 g atom) in liquid ammonia (400 mL) was added a solution of the diacetates **35** (10.11 g, 25.1 mmol) in THF (100 mL) over a period of 30 min, and the mixture was stirred for 30 min at −33 °C. To it was added ethanol (100 mL), and the mixture was stirred for 20 min. After removal of liquid ammonia under reduced pressure, water was added. Extraction with ether and concentration afforded the crude product. Column chromatography on silica gel (200 g) using hexane and ethyl acetate gave (±)-baiyunol (**1a**) (4.40 g, 58% yield) [mp 89–90 °C; IR, ^{1}H NMR, and ^{13}C NMR are indistinguishable with those of natural (+)-baiyunol. Anal. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.0. Found: C, 79.28; H, 10.03.] along with diols **34** (3.18 g, 42% yield).

Acknowledgment. We thank Professor O. Tanaka of Hiroshima University and Professor D. J. Faulkner of University of California, San Diego, for the identifications of natural products, and also Professor Tsuda of Kanazawa University for helpful discussions. Pure (*E,E*)-farnesol was kindly supplied from Dr. Y. Fujita of Kuraray Co. Ltd. This study is partly supported by the Grant-in-Aid of Scientific Research of the Ministry of Education, Science and Culture, Japanese Government.

Registry No. (±)-**1a**, 108944-65-6; **2**, 88641-99-0; **3a**, 76215-29-7; (±)-**3b**, 110418-48-9; **3c**, 108886-83-5; **3d**, 108886-82-4; **4**, 110418-49-0; **5**, 110418-50-3; **6**, 105631-19-4; (±)-**7** (isomer 1), 105663-33-0; (±)-**7** (isomer 2), 105663-32-9; (±)-**7** (isomer 3), 105663-34-1; (±)-**7** (isomer 4), 105631-20-7; **8**, 105631-21-8; (±)-**9a**, 96234-94-5; **10**, 23262-34-2; **11**, 110418-51-4; **12**, 110418-63-8; (±)-**13** (isomer 1), 110507-77-2; (±)-**13** (isomer 2), 110418-52-5; (±)-**16**, 105631-24-1; (±)-**17**, 105631-25-2; **18** (isomer 1), 105631-31-0; **18** (isomer 2), 105631-32-1; **18** (isomer 3), 105631-33-2; (±)-**19**, 105631-26-3; (±)-**20**, 105631-27-4; (±)-**21**, 110418-64-9; (±)-**22**, 110418-53-6; (±)-**23**, 110455-89-5; (±)-**24** (isomer 1), 105631-28-5; (±)-**24** (isomer 2), 105663-35-2; **25** (isomer 1), 110418-54-7; **25** (isomer 2), 110418-62-7; (±)-**26**, 105663-36-3; (±)-**27**, 105631-34-3; **28**, 110418-55-8; **29**, 110418-56-9; **30**, 110418-57-0; (±)-**32** (isomer 1), 108886-84-6; (±)-**32** (isomer 2), 108886-85-7; (±)-**33a**, 108886-86-8; (±)-**33b**, 110418-59-2; (±)-**34** (isomer 1), 110418-60-5; (±)-**34** (isomer 2), 110418-61-6; (±)-**35** (isomer 1), 108886-88-0; (±)-**35** (isomer 2), 108886-87-9; 3-furfuryl *p*-tolyl sulfone, 92631-12-4; 2-(3-furyl)-1,3-dithiane, 69301-58-2; (*E,E*)-farnesyl bromide, 28290-41-7.