Base-Induced Rearrangement of Perhydronaphthalene-1,4-diol Monosulfonate Esters to 11-Oxatricyclo[5.3.1.$0^{2,6}$]undecanes. Total Synthesis of Furanether B

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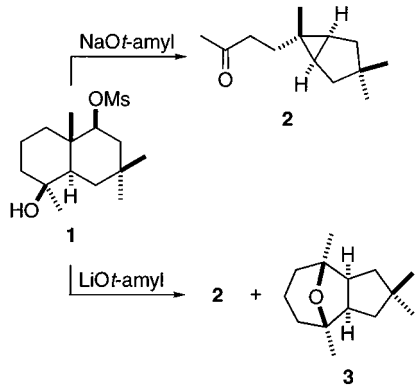
Received August 19, 1997[⊗]

It is observed that mesylate **1** on exposure to Li(O*t*-Bu)$_3$AlH in refluxing toluene rearranges selectively to the 11-oxatricyclo[5.3.1.$0^{2,6}$]undecane derivative **3**. A similar rearrangement, leading to a bridged tricyclic ether (**14** → **5**), has been used as the key to the total synthesis of furanether B (**4**), a naturally occurring lactarane sesquiterpene, with the readily available ketone **8** as the starting material. Completion of the synthesis of the natural product is accomplished by an annulation method based on a Pummerer-induced cyclization reaction.

Introduction

From our previous work on the chemical consequences of long-range orbital interactions in stereochemically rigid 1,4-diol monosulfonate esters, it is known that elimination, rearrangement, and homofragmentation are the preferred pathways by which these compounds react upon treatment with a strong base.[1] The synthetic utility of the elimination and rearrangement reaction has been demonstrated in the total syntheses of guaiane[2] and alloaromadendrane[3] sesquiterpenes, whereas the homofragmentation reaction has been used as the key step in the synthesis of α-santalanes.[4] We have demonstrated[1a,b] that the reaction outcome not only depends on the specific structural features of the 1,4-diol monosulfonate esters, but also on the nature of the base used as is illustrated in Scheme 1. While the reaction of mesylate **1** with sodium *tert*-amylate in refluxing benzene produces selectively the homofragmentation product **2**, the corresponding reaction with lithium *tert*-amylate as base results in a ca. 2:1 mixture of **2** and the rearranged tricyclic ether **3**, respectively.[1b] The co-occurrence of homofragmentation and rearrangement in the reaction of **1** with lithium *tert*-amylate has been explained by a decrease of the electron-donating ability of the alkoxide group with Li^+ as counterion.[5] It is further important to note that the rearranged product **3** formed in this reaction strongly resembles the oxatricyclo[5.3.1.0]-undecane ring system present in furanether B (**4**), a lactarane sesquiterpene isolated from the mushroom *Lactarius scrobiculatus*.[6] This strong resemblance and the expectation that a further decrease of the electron-donating ability of the alkoxide function would result in selective formation of the oxatricyclo[5.3.1.0]undecane ring system motivated us to study the synthesis of furanether B itself.

Scheme 1



To date, three total syntheses of furanether B have been reported: two complementary syntheses in which the key involves the Pauson−Khand cycloaddition reaction[7] and one based on a [3 + 4] annulation strategy.[8] The asymmetric synthesis of an intermediate in the Pauson−Khand cycloaddition approach has been reported recently.[9] Our synthetic approach toward furanether B starts with the readily available Robinson annulation product **7**[10] and presents as the key feature the base-induced rearrangement reaction (**6** → **5**) to establish

[⊗] Abstract published in *Advance ACS Abstracts*, December 15, 1997.

(1) (a) Orrū, R. V. A.; Wijnberg, J. B. P. A.; Jenniskens, L. H. D.; de Groot, A. *J. Org. Chem.* **1993**, *58*, 1199. (b) Orrū, R. V. A.; Wijnberg, J. B. P. A.; Bouwman, C. T.; de Groot, A. *J. Org. Chem.* **1994**, *59*, 374. (c) Bastiaansen, P. M. F. M.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **1995**, *60*, 4240.

(2) (a) Wijnberg, J. B. P. A.; Jenniskens, L. H. D.; Brunekreef, G. A.; de Groot, A. *J. Org. Chem.* **1990**, *55*, 941. (b) Koike, T.; Yamazaki, K.; Fukumoto, N.; Yashiro, K.; Takeuchi, N.; Tobinaga, S. *Chem. Pharm. Bull.* **1996**, *44*, 646. (c) Piet, D. P.; Orrū, R. V. A.; Jenniskens, L. H. D.; van de Haar, C.; van Beek, T. A.; Franssen, M. C. R.; Wijnberg, J. B. P. A.; de Groot, A. *Chem. Pharm. Bull.* **1996**, *44*, 1400.

(3) Jenniskens, L. H. D.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **1991**, *56*, 6585.

(4) Bastiaansen, P. M. F. M.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **1996**, *61*, 4955.

(5) The Li^+−O bond has a more covalent character than the Na^+−O bond: Paquette, L. A.; Gilday, J. P. *J. Org. Chem.* **1988**, *53*, 4972. As a result, the electron-donating ability of the alkoxide function with Li^+ as the counterion will be diminished. Also, see ref 1b.

(6) (a) Battaglia, R.; De Bernardi, M.; Fronza, G.; Mellerio, G.; Vidari, G.; Vita-Finzi, P. *J. Nat. Prod.* **1980**, *43*, 319. For an extensive review of lactarane sesquiterpenes, see: (b) Vidari, G.; Vita-Finzi, P. In *Studies in Natural Products Chemistry*; Atta-ur-Rahman, Ed.; Elsevier: Amsterdam, 1995; Vol. 17, pp 153−206.

(7) (a) Price, M. E.; Schore, N. E. *J. Org. Chem.* **1989**, *54*, 5662. (b) Price, M. E.; Schore, N. E. *Tetrahedron Lett.* **1989**, *30*, 5865.

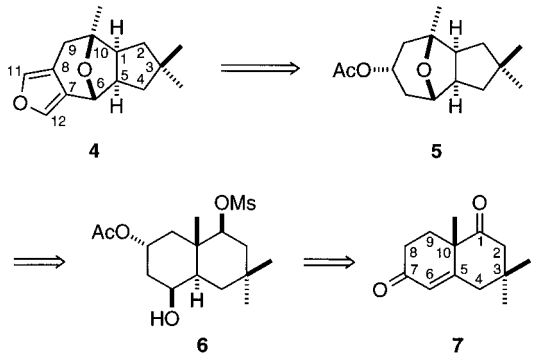
(8) Molander, G. A.; Carey, J. S. *J. Org. Chem.* **1995**, *60*, 4845.

(9) Davies, H. M. L.; Ahmed, G.; Rowen Churchill, M. *J. Am. Chem. Soc.* **1996**, *118*, 10774.

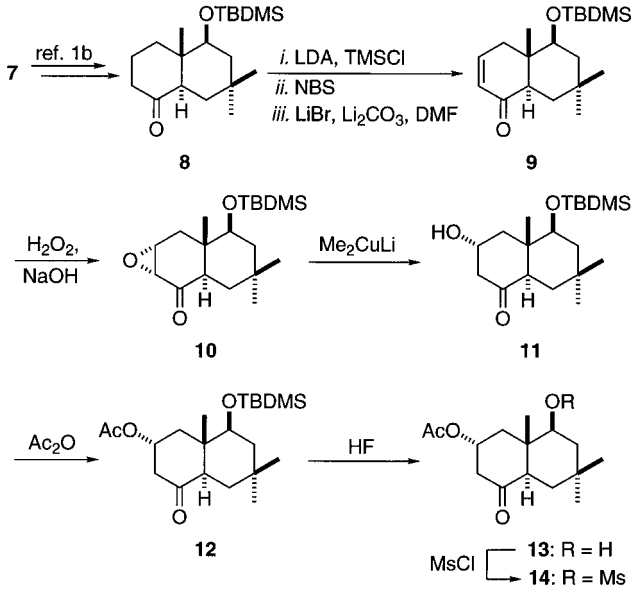
(10) Heathcock, C. H.; Gray, D. *Tetrahedron* **1971**, *27*, 1239.

S0022-3263(97)01545-4 CCC: $15.00
Published on Web 01/09/1998

Scheme 2



Scheme 3



the bridged ether core of **4** (Scheme 2). Further elaboration to furanether B (**5** → **4**) was planned via the regioselective synthesis of the corresponding butenolides (vide infra).

Results and Discussion

The first series of experiments was directed toward finding reaction conditions that allow selective formation of tricyclic ether **5** from mesylate **6**. For that purpose, the structurally comparable mesylate **1** was used as a model system.[11] After considerable experimentation with a wide range of bases, we found that treatment of **1** with 1 equiv of lithium tri-*tert*-butoxyaluminohydride (Li(O-*t*-Bu)$_3$AlH) in refluxing toluene resulted in a high yield (93%) of the cyclic ether **3**, and none of the homofragmentation product **2** was formed.[12] Apparently, the electron-donating ability of the alkoxide group with Li(O-*t*-Bu)$_3$Al$^+$ as counterion, produced after reaction of **1** with Li(O*t*-Bu)$_3$AlH, is not strong enough for induction of homofragmentation, and consequently, only rearrangement to tricyclic ether **3** takes place.

Having thus established that homofragmentation could be suppressed completely, the synthetic route toward furanether B was investigated. A previously described procedure[1b] was used to prepare ketone **8** from the known diketone **7**[10] (Scheme 3). It should be noted that attempts to obtain **7** in optically active form by following procedures developed for the asymmetric synthesis of the Wieland−Miescher ketone were unsuccessful.[13] The introduction of a hydroxyl function at the C(8) position of **8** was planned via cleavage of the C(7)−O bond in epoxyketone **10**. This compound was obtained in ca. 70% overall yield via bromination of the silyl enol ether of **8**, dehydrobromination, and epoxidation of the resulting enone **9** with H_2O_2 in the presence of NaOH. When the epoxide ring opening in **10** was tried with palladium metal catalysts in the presence of HCOOH and Et_3N[14] or of ammonium formate,[15] no reaction at all was observed. Also the use of NaI, NaOAc, and AcOH in acetone[16] was not successful. A more promising result was achieved when **10** was treated with Li in NH_3 at −78 °C.[17] The desired product **11** was formed in reasonable yield (44%), but the reaction could not be driven to completion. We eventually found that reductive cleavage of **10** could be accomplished with 3 equiv of Me_2CuLi[18] to afford **11** as the sole product in good yield. The broad one-proton signal ($W_{1/2} \approx 22$ Hz) at δ 4.11 in the ^{1}H NMR spectrum of **11** shows that the hydroxyl group at C(8) possesses the equatorial α orientation. With standard procedures, **11** was then converted to the mesylate **14** (**11** → **12** → **13** → **14**; see the Experimental Section).

In our initial synthetic route toward furanether B, the reduction of mesylate **14** and rearrangement of the resulting secondary alcohol **6** to tricyclic ether **5** were planned as two separate steps. Having demonstrated that selective rearrangement could be achieved with the reducing agent Li(O*t*-Bu)$_3$AlH,[19] we anticipated that direct conversion of **14** to **5** would be possible via a one-pot reduction/rearrangement process[20] (Scheme 4). A first attempt in which 1 equiv of Li(O*t*-Bu)$_3$AlH was employed indeed afforded the desired tricyclic ether **5**, but starting material **14** was also recovered. Further experimentation revealed that the use of 2.5 equiv of Li(O*t*-Bu)$_3$AlH was required to complete the reaction. In this way, an easily separable 10:1 mixture of **5** and **17**, respectively, was obtained in ca. 60% yield.[21] The formation of **5** can easily be explained by intramolecular trapping of the positive charge by the alkoxide substituent in the rearranged intermediate **16**. Because of the presence of a protected hydroxyl group at C(8) in **16**, the possible interference of a Grob fragmentation is blocked.[1b] The formation of a small amount of the exocyclic olefin **17** must proceed via an intramolecular elimination

(11) From a previous study,[1b] a relatively large quantity of **1** was available.

(12) Rearrangement is also the preferred pathway with $MgCl^+$ as counterion; see ref 4.

(13) For example, see: Harada, N.; Sugioka, T.; Uda, H.; Kuriki, T. *Synthesis* **1990**, 53 and references therein.

(14) Torii, S.; Okumoto, H.; Nakayasu, S.; Kotani, T. *Chem. Lett.* **1989**, 1975.

(15) Dragovich, P. S.; Prins, T. J.; Zhou, R. *J. Org. Chem.* **1995**, *60*, 4922.

(16) (a) Paulsen, H.; Eberstein, K.; Koebernick, W. *Tetrahedron Lett.* **1974**, 4377. (b) Rennecke, R.-W.; Eberstein, K.; Köll, P. *Chem. Ber.* **1975**, *108*, 3652.

(17) McChesney, J. D.; Wycpalek, A. F. *J. Chem. Soc., Chem. Commun.* **1971**, 542.

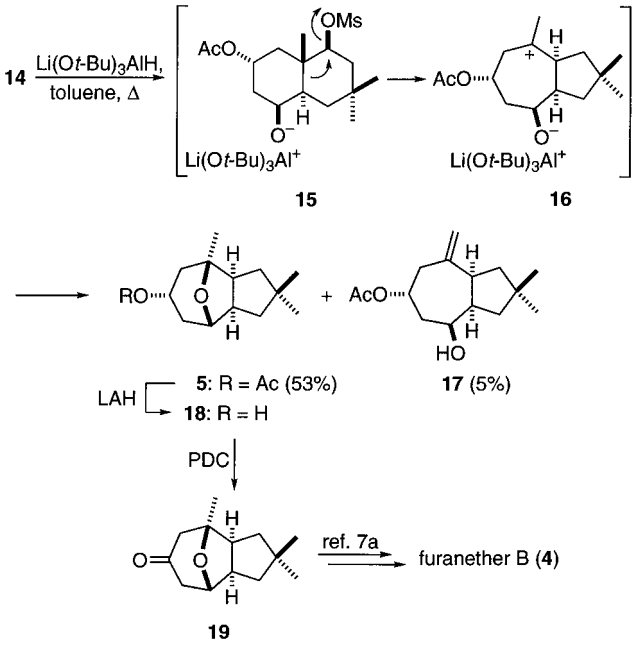
(18) (a) Bull, J. R.; Lachmann, H. H. *Tetrahedron Lett.* **1973**, 3055. (b) Szajewski, R. P. *J. Org. Chem.* **1978**, *43*, 1819.

(19) Li(O*t*-Bu)$_3$AlH is known to reduce ketones selectively in the presence of ester functions, see: Levine, S. G.; Eudy, N. H. *J. Org. Chem.* **1970**, *35*, 549.

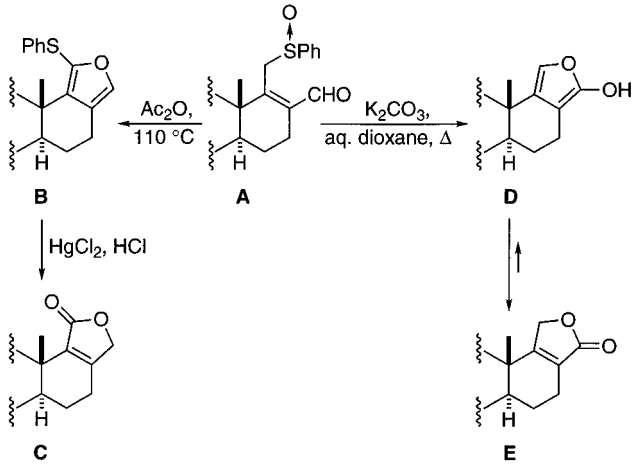
(20) It was assumed that reduction of the ketone function in **14** with Li(O*t*-Bu)$_3$AlH would proceed from the less sterically hindered α side.

(21) As a minor side reaction, some elimination of the acetate group had taken place.

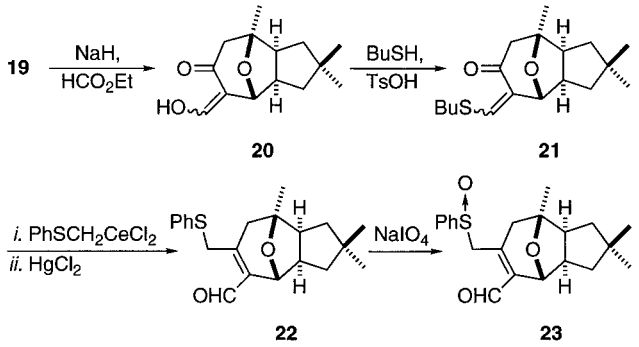
Scheme 4



Scheme 5



Scheme 6



reaction. Remarkably, this latter elimination process is the chief pathway by which other trans-fused perhydronaphthalene 1,4-diol monosulfonate esters with a β-hydroxyl group at C(4) react upon treatment with strong base, while cyclic ether formation is only a minor reaction pathway.[2,3] The stereochemistry of **5** was established by its transformation to the known ketone **19**, thereby completing a formal total synthesis of furanether B. Upon treatment of **5** with LAH and subsequent oxidation of the resulting alcohol **18**[22] with PDC, ketone **19** was obtained in 75% overall yield. The spectroscopic characteristics for **19** were identical with those reported in the literature.[7a,8]

Earlier research from this laboratory on the total synthesis of drimane sesquiterpenes has shown that γ-(phenylsulfinyl)-α,β-unsaturated aldehydes of type **A** could be converted regioselectively either to butenolide **C** or to butenolide **E**, depending on the reaction conditions used (Scheme 5).[23] To test whether these Pummerer-induced cyclization reactions[24] could be employed also as a common method for the synthesis of the lactaranolides **31** and **32**, sulfoxide **23** had to be prepared. For that purpose, the reaction sequence outlined in Scheme 6 was followed. With a slightly modified formylation procedure (**19** → **20**),[25] the known thiomethylene derivative **21** was prepared in 84% overall yield.[26] The introduction of the carbon atom that ends up as C(11) in the final product was initially planned via addition of lithiated thioanisole[27] to the C(8) carbonyl group in **21**, immediately followed by $HgCl_2$-assisted hydrolysis of the adduct in dilute HCl.[28] Unfortunately, addition of lithiated thioanisole to **21** refused to give any workable result; mainly conjugate addition was observed. In sharp contrast, its cerium analogue reacted very cleanly with **21**, affording the product of 1,2-addition almost exclusively.[29] After $HgCl_2$-assisted hydrolysis of the 1,2-adduct,[30] sulfide **22** was obtained in very good yield (84%). To ensure reproducible high yields in this reaction, sonication of a suspension of anhydrous $CeCl_3$ in dry THF turned out to be essential.[31] After oxidation of sulfide **22** with $NaIO_4$,[32] the desired sulfoxide **23** was obtained in quantitative yield.

With **23** in hand, we could now investigate the Pummerer-induced cyclization reactions toward the lactaranolides **31** and **32**. In contrast to the corresponding reactions in the drimane series (see Scheme 5), exposure of **23** to both Ac_2O at 110 °C[23a] and K_2CO_3 in aqueous dioxane at reflux temperature[23b] only led to complex product mixtures in which none of the expected products could be detected. It may be that, at the relatively high temperatures (>100 °C) used in these reactions, cleavage of the bridged ether function is responsible for these poor results. Therefore, trifluoroacetic anhydride (TFAA) at room temperature[33] was tried, but also in that case the outcome was disappointing. A more promising result was

(22) The alcohol **18** was also produced by treatment of **14** with LAH in refluxing toluene, but the yield of this reaction only amounted to 30%.

(23) (a) de Groot, A.; Jansen, B. J. M. *J. Org. Chem.* **1984**, *49*, 2034. (b) Jansen, B. J. M.; Bouwman, C. T.; de Groot, A. *Tetrahedron Lett.* **1994**, *35*, 2977.

(24) For a review of the Pummerer reaction, see: DeLucchi, O; Miotti, U.; Modena, G. *Org. React.* **1991**, *40*, 157.

(25) The formylation procedure described in ref 7a gave **20** in only 42% yield.

(26) It should be noted that, in our hands, the reported conversion[7a] of **21** to furanether B could not be achieved in acceptable yield.

(27) (a) Corey, E. J.; Seebach, D. *J. Org. Chem.* **1966**, *31*, 4097. (b) Ager, D. J. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1131.

(28) A similar protocol has proven to be successful in the synthesis of annulated drimane sesquiterpenes; see ref 23.

(29) For a relevant report on organocerium reagents, see: Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4392.

(30) In contrast to corresponding reactions described in ref 23, the $HgCl_2$-assisted hydrolysis to **22** proceeded smoothly without using acid.

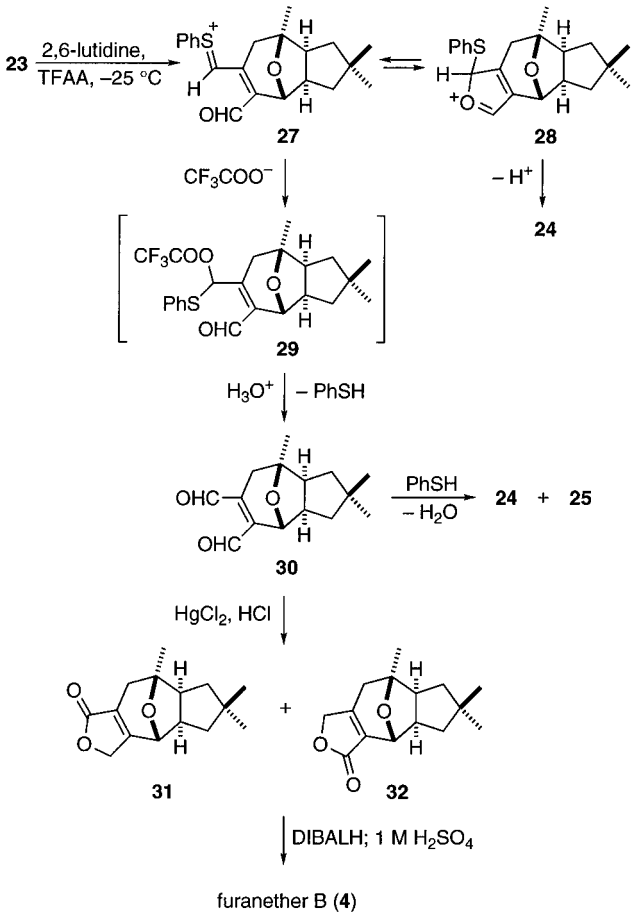
(31) Greeves, N.; Lyford, L. *Tetrahedron Lett.* **1992**, *33*, 4759.

(32) Leonard, N. J.; Johnson, C. R. *J. Org. Chem.* **1962**, *27*, 282.

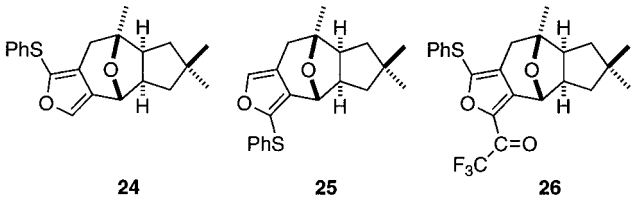
(33) Sharma, A. K.; Swern, D. *Tetrahedron Lett.* **1974**, 1503.

obtained by using an excess of TFAA in combination with 2,6-lutidine.[34] In this way, an inseparable 5:1:4 mixture of the expected (phenylthio)furan **24**, its regioisomer **25**, and the trifluoroacetylated compound **26**, respectively, was produced in ca. 70% yield.[35] By using 1 equiv of both TFAA and 2,6-lutidine, the formation of **26** could be suppressed and almost pure **24** was produced in 43% yield, together with 35% of the starting material **23**. Eventually, it was found that completion of the reaction without the undesired formation of **26** could be achieved by exposure of **23** to an excess of both TFAA and 2,6-lutidine at −25 °C for about 1−2 days. After careful workup,[36] crude **24** was obtained, but ^{1}H NMR and GCMS analysis showed that the product contained considerable amounts of dialdehyde **30**[37] and thiophenol. An attempt to purify this crude **24** by silica gel chromatography led to an inseparable mixture of **24** (major) and **25** (minor) in modest yield, while **30** was not found anymore. These results suggest that, on the column, some of **30** reacts with thiophenol to give **25** (and probably also additional **24**) before it decomposes.[38] Because it was expected that acid-catalyzed cyclization of dialdehyde **30** would lead to butenolide formation,[39] the above mixture of **24**, **30**, and thiophenol was directly treated with a $HgCl_2$−aqueous HCl mixture at 35 °C,[40] thereby avoiding the yield-lowering chromatography. In this way, the lactaranolides **31** and **32** were obtained as a 4:1 mixture,[41] respectively, in 80% yield. These findings are fully compatible with the reaction sequence outlined in Scheme 7. The initially generated thionium ion **27** is either captured by the adjacent aldehyde group to give oxonium ion **28**, which subsequently deprotonates to afford the phenylthiofuran derivative **24**, or it reacts with the trifluoroacetate anion to produce the *O,S*-ketal **29**. Although we were not able to detect **29**,[42] its formation is highly probable because of finding both dialdehyde **30** and thiophenol in the crude product mixture after

Scheme 7



workup. A silica gel-catalyzed reaction of **30** with thiophenol explains the formation of **24** and **25** on the column.



The synthesis of furanether B was completed by reduction of the above 4:1 mixture of **31** and **32** with DIBALH at −78 °C followed by aromatization of the resulting mixture of lactols with 1 M aqueous H_2SO_4.[8] The spectroscopic data for **4** were identical with those reported in the literature.[6a,7a,8] Although **23** refused to react regioselectively to give lactaranolide **32**, its regioisomer **31** could be produced as a single product by $HgCl_2$-induced hydrolysis of **24**,[43] albeit in modest overall yield (43% from **23**).

Summarizing these results, we may state that our synthetic route toward furanether B represents another example of the applicability of the intramolecular base-induced rearrangement of 1,4-diol monosulfonate esters in natural product synthesis. The problems encountered in the regioselective annulation of the lactaranolides studied here contrast sharply the ease by which the corresponding compounds in the drimane series are formed, and these problems are probably brought on by the presence of the bridged ether function. Nevertheless,

(34) Jommi, G.; Pagliarin, R.; Sisti, M.; Tavecchia, P. *Synth. Commun.* **1989**, *19*, 2467.

(35) By ^{1}H NMR and GCMS analysis of the 5:1:4 mixture, the following data for **25** were obtained: ^{1}H NMR (main peaks) δ 0.82 (s, 3H), 1.05 (s, 3H), 1.39 (s, 3H), 4.77 (s, 1H); MS *m/z* (relative intensity) 340 (M^+, 100), 325 (1), 297 (36), 269 (5), 231 (70), 203 (33), 115 (34), 91 (39), 77 (37), 43 (81); HRMS calcd for $C_{21}H_{24}O_2S$ (M^+) 340.1497, found 340.1503. For **26** these data were obtained: ^{1}H NMR (main peaks) δ 1.11 (s, 3H), 1.37 (s, 3H), 1.54 (s, 3H), 5.18 (s, 1H); MS *m/z* (relative intensity) 436 (M^+, 68), 421 (6), 393 (11), 367 (14), 325 (20), 285 (9), 187 (13), 109 (36), 91 (31), 77 (32), 43 (100); HRMS calcd for $C_{23}H_{23}F_3O_3S$ (M^+) 436.1320, found 436.1321.

(36) After being dried, the solution was concentrated under reduced pressure at −15 °C. If the solution was concentrated at room temperature, considerable amounts of **25** were detected in the remaining product mixture.

(37) By ^{1}H NMR and GCMS analysis of the crude product mixture, the following data for **30** were obtained: ^{1}H NMR (main peaks) δ 0.84 (s, 3H), 1.06 (s, 3H), 1.37 (s, 3H), 4.75 (s, 1H), 10.64 (s, 1H), 10.68 (s, 1H); MS *m/z* (relative intensity) 248 (M^+, 9), 219 (23), 205 (35), 187 (22), 152 (43), 123 (39), 107 (40), 95 (51), 77 (50), 43 (100).

(38) Lactarane dialdehydes are supposed to be highly reactive compounds, see: Sterner, O., Ph.D. Thesis, University of Lund, 1985.

(39) Jansen, B. J. M., Ph.D. Thesis, Wageningen Agricultural University, 1993.

(40) At room temperature, the reaction took more than 2 weeks to achieve completion.

(41) The chromatographic separation of **31** and **32** appeared to be problematic.

(42) Stable *O,S*-ketals formed in Pummerer rearrangements have been reported. For example, see: (a) Hatch, R. P.; Shringarpure, J.; Weinreb, S. M. *J. Org. Chem.* **1978**, *43*, 4172. (b) Padwa, A.; Kappe, C. O.; Cochran, J. E.; Snyder, J. P. *J. Org. Chem.* **1997**, *62*, 2786.

(43) The reaction was performed with **24** obtained from the incomplete reaction of **23** with 1 equiv of TFAA and 2,6-lutidine.

the successful completion of the total synthesis of furanether B demonstrates that our annulation approach based on the Pummerer-induced cyclization reaction is a useful alternative to other furan and butenolide annulation methods.

Experimental Section[44]

Materials. All reagents were purchased from Aldrich or Acros and were used without further purification, unless otherwise stated. The ketone **8** was prepared from the known Robinson annulation product **7**[10] as previously described.[1b] The compounds **3**,[1b] **4**,[7a,8] **18**,[7a] **19**,[7a,8] **20**,[7a] and **31**[8] were characterized before.

(3aα,4*β*,8*β*,8aα)-(±)-Decahydro-2,2,4,8-tetramethyl-4,8-epoxyazulene (3). To a degassed solution of 0.152 g (0.50 mmol) of **1**[1b] in 10 mL of dry toluene was added 0.127 g (0.50 mmol) of Li(O*t*-Bu)$_3$AlH. The reaction mixture was refluxed for 2 h under argon, cooled to 0 °C, and then quenched with 0.5 mL of saturated aqueous Na_2SO_4. After being stirred at 0 °C for 20 min, the reaction mixture was diluted with 25 mL of EtOAc, dried, and evaporated. The remaining residue was flash chromatographed [10:1 petroleum ether (bp 40−60 °C)/EtOAc] to give 0.097 g (93%) of **3** as a colorless oil. The NMR and mass spectral data for **3** were identical with those reported in the literature.[1b]

(4aα,5α,8a*β*)-(±)-4a,5,6,7,8,8a-Hexahydro-4a,7,7-trimethyl-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1(4*H*)-naphthalenone (9). To a stirred solution of 56 mL of LDA (2.0 M in THF/heptane) in 100 mL of THF, cooled to −78 °C, was added dropwise a solution of 30.46 g (94.0 mmol) of **8** in 75 mL of THF over 1 h. The reaction mixture was stirred at −78 °C for 1.75 h, after which time 19 mL (0.15 mol) of TMSCl was added dropwise. The reaction mixture was allowed to come to rt, diluted with 100 mL of ether, and filtered through a short pad of basic Al_2O_3. The filter cake was washed with ether, and the filtrate was concentrated under reduced pressure. The remaining residue was taken up in 100 mL of THF, and added dropwise to an ice cold solution of 19.0 g (0.107 mol) of NBS in 150 mL of THF over 40 min. After being stirred at 0 °C for 1 h, the reaction mixture was allowed to come to rt and concentrated under reduced pressure to half its volume. After addition of 200 mL of H_2O, the two-phase mixture was separated, and the aqueous phase was extracted four times with CH_2Cl_2. The combined organic layers were washed with brine, dried, and evaporated. The remaining residue was dissolved in 250 mL of DMF, and 17.4 g (0.235 mol) of Li_2CO_3 and 16.3 g (0.188 mol) of LiBr were added. The reaction mixture was heated at 140 °C for 2.5 h, allowed to come to rt, and filtered through a short pad of Hyflo. The filter cake was washed with 75 mL of DMF, and the filtrate was concentrated under reduced pressure to half its volume. After addition of 300 mL of H_2O, the aqueous layer was extracted four times with petroleum ether (bp 40−60 °C). The combined organic layers were washed with brine, dried, and evaporated. The remaining residue was flash chromatographed [20:1 petroleum ether (bp 40−60 °C)/EtOAc] to give 28.62 g (94%) of **9** as a yellow oil: ^{1}H NMR δ 0.04 (s, 3H), 0.05 (s, 3H), 0.80 (s, 3H), 0.87 (s, 9H), 0.92 (s, 3H), 0.97 (s, 3H), 1.18−1.41 (m, 3H), 1.61 (dd, J = 3.7, 12.9 Hz, 1H), 2.16 (ddd, J = 2.3, 2.5, 18.9 Hz, 1H), 2.40 (dd, J = 3.7, 12.5 Hz, 1H), 2.50 (dd, J = 5.9, 18.9 Hz, 1H), 3.66 (dd, J = 6.0, 10.2 Hz, 1H), 5.98 (dd, J = 2.5, 10.1 Hz, 1H), 6.81 (ddd, J = 2.3, 5.9, 10.1 Hz, 1H); ^{13}C NMR δ −4.79 (q), −3.96 (q), 10.20 (q), 18.00 (s), 25.76 (3q), 25.84 (q), 30.51 (s), 32.75 (t), 33.09 (q), 39.95 (t), 42.74 (s), 43.30 (t), 49.76 (d), 75.78 (d), 129.07 (d), 146.77 (d), 200.86 (s); MS m/z (relative intensity) 322 (M^+, 2), 265 (100), 221 (5), 173 (8), 131 (8), 105 (9), 75 (50), 73 (13); HRMS calcd for $C_{19}H_{34}O_2Si$ (M^+) 322.2328, found 322.2327.

(44) For a general description of the experimental procedures employed in this research, see: Kesselmans, R. P. W.; Wijnberg, J. B. P. A.; Minnaard, A. J.; Walinga, R. E.; de Groot, A. *J. Org. Chem.* **1991**, *56*, 7237. NMR spectra were recorded at 200 MHz (^{1}H) and at 50 MHz (^{13}C) in $CDCl_3$.

(2α,3α,4a*β*,5*β*,8aα)-(±)-3,4,4a,5,6,7,8,8a-Octahydro-4a,7,7-trimethyl-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-naphth[2,3]oxiren-1(2*H*)-one (10). To a stirred solution of 28.62 g (88.7 mmol) of **9** in 400 mL of MeOH were added 31 mL of 35% H_2O_2 and 45 mL of 1 M aqueous NaOH. After being stirred for 16 h, the reaction mixture was diluted with 400 mL of H_2O and 200 mL of brine and extracted four times with ether. The combined organic layers were washed with brine, dried, and evaporated. The remaining residue was flash chromatographed [20:1 petroleum ether (bp 40−60 °C)/EtOAc] to afford 21.41 g (71%) of **10** as a light yellow solid: mp 83−85 °C (from petroleum ether (bp 40−60 °C)); ^{1}H NMR δ 0.03 (s, 3H), 0.06 (s, 3H), 0.73 (s, 3H), 0.87 (s, 12H), 0.94 (s, 3H), 1.10−1.40 (m, 4H), 1.91 (d, J = 15.4 Hz, 1H), 2.13 (dd, J = 4.9, 15.4 Hz, 1H), 2.82 (dd, J = 3.9, 12.4 Hz, 1H), 3.24 (d, J = 3.7 Hz, 1H), 3.52−3.65 (m, 2H); ^{13}C NMR δ −4.80 (q), −3.94 (q), 12.81 (q), 17.98 (s), 25.60 (q), 25.76 (3q), 30.31 (s), 32.34 (t), 33.03 (q), 37.33 (t), 43.19 (t), 44.55 (d), 46.61 (s), 55.26 (d), 57.29 (d), 75.61 (d), 208.50 (s); MS m/z (relative intensity) 338 (M^+, 2), 281 (100), 161 (7), 123 (8), 119 (7), 105 (12), 75 (43), 73 (13); HRMS calcd for $C_{19}H_{34}O_3Si$ (M^+) 338.2277, found 338.2279. Anal. Calcd for $C_{19}H_{34}O_3Si$: C, 67.42; H, 10.13. Found: C, 67.10; H, 10.19.

(3α,4a*β*,5*β*,8aα)-(±)-3,4,4a,5,6,7,8,8a-Octahydro-3-hydroxy-4a,7,7-trimethyl-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1(2*H*)-naphthalenone (11). To a stirred suspension of 19.24 g (101 mmol) of dry CuI in 150 mL of ether, cooled to −25 °C, was added dropwise 105 mL of MeLi (1.6 M in ether) over 12 min. To the resulting bright yellow solution was added dropwise a solution of 11.41 g (33.7 mmol) of **10** in 100 mL of ether over 20 min. After being stirred at −25 °C for 1.5 h, the reaction mixture was quenched with 7.5 mL of saturated aqueous Na_2SO_4. The reaction mixture was allowed to come to rt and filtered through a short pad of Hyflo. The filtrate was dried and concentrated under reduced pressure, and the remaining residue was flash chromatographed [5:1 petroleum ether (bp 40−60 °C)/EtOAc] to yield 7.37 g (64%) of **11** as a colorless oil: ^{1}H NMR δ 0.03 (s, 3H), 0.05 (s, 3H), 0.65 (s, 3H), 0.86 (s, 9H), 0.89 (s, 3H), 0.95 (s, 3H), 1.25−1.45 (m, 5H), 1.76 (br s, OH), 2.20−2.45 (m, 3H), 2.74 (ddd, J = 2.0, 5.5, 13.0 Hz, 1H), 3.60 (dd, J = 6.1, 9.9 Hz, 1H), 4.11 (m, $W_{1/2} \approx$ 22 Hz, 1H); ^{13}C NMR δ −4.70 (q), −3.95 (q), 11.83 (q), 18.04 (s), 25.85 (3q), 26.12 (q), 30.42 (s), 32.78 (t), 33.03 (q), 41.46 (s), 43.11 (t), 46.27 (t), 50.89 (t), 51.81 (d), 67.34 (d), 75.61 (d), 209.36 (s); MS m/z (relative intensity) 340 (M^+, 4), 283 (46), 265 (59), 191 (53), 173 (35), 163 (52), 149 (43), 121 (31), 107 (31), 95 (34), 83 (40), 75 (100); HRMS calcd for $C_{19}H_{36}O_3Si$ (M^+) 340.2434, found 340.2431. Anal. Calcd for $C_{19}H_{36}O_3Si$: C, 67.02; H, 10.66. Found: C, 66.54; H, 10.78.

(3α,4a*β*,5*β*,8aα)-(±)-3-(Acetyloxy)-3,4,4a,5,6,7,8,8a-octahydro-4a,7,7-trimethyl-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1(2*H*)-naphthalenone (12). To a stirred solution of 11.20 g (33.0 mmol) of **11** in 100 mL of pyridine were added 10 mL of Ac_2O and a catalytic amount of DMAP. The reaction mixture was stirred at rt for 16 h, poured into 375 mL of ice cold 4 M aqueous HCl, and extracted four times with EtOAc. The combined organic layers were washed with brine, dried, and evaporated. The remaining residue was flash chromatographed [10:1 petroleum ether (bp 40−60 °C)/EtOAc] to yield 11.87 g (94%) of **12** as a white solid: mp 66−68 °C (from hexane); ^{1}H NMR δ 0.02 (s, 3H), 0.03 (s, 3H), 0.70 (s, 3H), 0.85 (s, 9H), 0.88 (s, 3H), 0.95 (s, 3H), 1.15−1.50 (m, 5H), 2.03 (s, 3H), 2.20−2.45 (m, 3H), 2.81 (ddd, J = 1.9, 5.8, 13.4 Hz, 1H), 3.59 (dd, J = 6.1, 9.9 Hz, 1H), 5.12 (m, $W_{1/2} \approx$ 23.5 Hz, 1H); ^{13}C NMR δ −4.72 (q), −4.00 (q), 11.64 (q), 18.02 (s), 21.24 (q), 25.81 (3q), 26.05 (q), 30.38 (s), 32.72 (t), 33.00 (q), 41.35 (s), 42.21 (t), 43.09 (t), 46.97 (t), 52.09 (d), 69.16 (d), 75.49 (d), 169.95 (s), 207.88 (s); MS m/z (relative intensity) 325 (M^+ − 57, 17), 265 (69), 191 (27), 173 (15), 163 (14), 117 (100), 83 (19), 75 (47), 73 (19); HRMS calcd for $C_{17}H_{29}O_4Si$ (M^+ − 57) 325.1835, found 325.1828. Anal. Calcd for $C_{21}H_{38}O_4Si$: C, 65.93; H, 10.01. Found: C, 65.66; H, 10.08.

(3α,4a*β*,5*β*,8aα)-(±)-3-(Acetyloxy)-3,4,4a,5,6,7,8,8a-octahydro-5-hydroxy-4a,7,7-trimethyl-1(2*H*)-naphthalenone (13). To a stirred solution of 12.99 g (34.0 mmol) of **12**

in 200 mL of MeCN was added 15 mL of 40% aqueous HF. The reaction mixture was stirred at rt for 17 h, poured into 300 mL of saturated aqueous $NaHCO_3$, and extracted four times with EtOAc. The combined organic layers were washed with brine, dried, and evaporated to give 8.73 g (95%) of **13** as a white solid: mp 164−166 °C (from hexane/EtOAc); ^{1}H NMR δ 0.75 (s, 3H), 0.92 (s, 3H), 0.99 (s, 3H), 1.30−1.62 (m, 5H), 2.03 (s, 3H), 2.28−2.46 (m, 3H), 2.52 (ddd, J = 1.9, 5.0, 12.6 Hz, 1H), 2.81 (ddd, J = 1.9, 5.8, 13.4 Hz, 1H), 3.66 (ddd, J = 5.4, 5.4, 10.8 Hz, 1H), 5.16 (m, $W_{1/2} \approx$ 24.0 Hz, 1H); ^{13}C NMR δ 11.29 (q), 21.15 (q), 26.02 (q), 30.52 (s), 32.74 (t), 32.85 (q), 40.83 (s), 41.76 (t), 42.67 (t), 46.89 (t), 52.01 (d), 68.94 (d), 74.94 (d), 170.00 (s), 207.65 (s); MS *m/z* (relative intensity) 226 (M^+ − 42, 1), 208 (100), 193 (35), 190 (42), 175 (77), 167 (48), 139 (36), 123 (81), 122 (75), 109 (43), 96 (37), 43 (40); HRMS calcd for $C_{13}H_{22}O_3$ (M^+ − 42) 226.1569, found 226.1565. Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.13; H, 9.02. Found: C, 66.68; H, 9.05.

(3α,4a*β*,5*β*,8aα)-(±)-3-(Acetyloxy)-3,4,4a,5,6,7,8,8a-octahydro-4a,7,7-trimethyl-5-[(methylsulfonyl)oxy]-1(2*H*)-naphthalenone (14). To a stirred solution of 8.73 g (32.5 mmol) of **13** in 100 mL of pyridine was added 3.8 mL (49.1 mmol) of MsCl. After being stirred at rt for 2 h, the reaction mixture was diluted with 450 mL of EtOAc and washed successively with 4 M aqueous HCl (three times), saturated aqueous $NaHCO_3$ (twice), and brine. The organic layer was dried and evaporated, and the remaining residue was crystallized from EtOAc to afford 6.86 g (61%) of **14** as a light yellow solid. The mother liquor was concentrated under reduced pressure and flash chromatographed [1:1 petroleum ether (bp 40−60 °C)/EtOAc] to give 4.31 g (38%) of another portion of **14**: mp 128−129 °C; ^{1}H NMR δ 0.82 (s, 3H), 0.96 (s, 3H), 1.02 (s, 3H), 1.25−1.45 (m, 2H), 1.55−1.80 (m, 3H), 2.03 (s, 3H), 2.30−2.50 (m, 3H), 2.83 (ddd, J = 1.9, 5.8, 13.6 Hz, 1H), 3.02 (s, 3H), 4.70 (dd, J = 5.5, 11.4 Hz, 1H), 5.14 (m, $W_{1/2} \approx$ 21.5 Hz, 1H); ^{13}C NMR δ 12.32 (q), 21.19 (q), 25.72 (q), 31.08 (s), 32.46 (t), 32.62 (q), 39.07 (q), 40.12 (s), 40.22 (t), 41.52 (t), 46.80 (t), 51.89 (d), 68.10 (d), 84.75 (d), 169.99 (s), 206.09 (s); MS *m/z* (relative intensity) 286 (M^+ − 60, 9), 245 (19), 190 (100), 175 (43), 163 (45), 147 (18), 121 (30), 107 (19), 95 (21), 43 (53); HRMS calcd for $C_{14}H_{22}O_4S$ (M^+ − 60) 286.1239, found 286.1239. Anal. Calcd for $C_{16}H_{26}O_6S$: C, 55.47; H, 7.57. Found; C, 55.17; H, 7.53.

(3aα,4*β*,6α,8*β*,8aα)-(±)-Decahydro-2,2,4-trimethyl-4,8-epoxyazulen-6-ol Acetate (5). The mesylate **14** (0.650 g, 1.88 mmol) was treated with Li(O*t*-Bu)$_3$AlH (2.5 equiv) for 45 min as described for **1**. Workup and flash chromatography [5:1 petroleum ether (bp 40−60 °C)/EtOAc] gave 0.248 g (53%) of **5** as a colorless oil: ^{1}H NMR δ 0.87 (s, 3H), 1.02 (s, 3H), 1.09 (m, 1H), 1.16 (s, 3H), 1.25−1.35 (m, 2H), 1.60−2.00 (m, 5H), 2.03 (s, 3H), 2.76 (q, J = 8.5 Hz, 1H), 2.97 (q, J = 8.6 Hz, 1H), 3.88 (br d, J = 3.6 Hz, 1H), 5.04 (br t, J = 5.0 Hz, 1H); ^{13}C NMR δ 21.55 (q), 22.76 (q), 25.86 (q), 28.16 (q), 34.45 (t), 41.40 (s), 42.24 (t), 42.78 (t), 47.35 (t), 48.51 (d), 50.21 (d), 68.13 (d), 79.01 (d), 79.52 (s), 170.33 (s); MS *m/z* (relative intensity) 252 (M^+, 14), 193 (86), 192 (100), 177 (41), 149 (95), 134 (24), 107 (25), 95 (32), 93 (22), 43 (33); HRMS calcd for $C_{15}H_{24}O_3$ (M^+) 252.1725, found 252.1729.

Further elution afforded 0.022 g (5%) of **17**: ^{1}H NMR δ 0.96 (s, 3H), 1.09 (s, 3H), 1.47−1.75 (m, 6H), 2.02 (s, 3H), 2.17 (dd, J = 9.9, 12.3 Hz, 1H), 2.30 (m, 1H), 2.53 (m, 1H), 2.68 (dd, J = 3.4, 12.2 Hz, 1H), 2.94 (br q, J = 9.7 Hz, 1H), 3.85 (br t, J = 6.3 Hz, 1H), 4.89−5.02 (m, 3H); ^{13}C NMR δ 21.36 (q), 27.00 (q), 29.16 (q), 37.58 (s), 40.46 (t), 41.75 (t), 43.81 (t), 45.03 (d), 45.76 (d), 45.83 (t), 70.90 (d), 71.02 (d), 113.68 (t), 147.00 (s), 170.22 (s); MS *m/z* (relative intensity) 192 (M^+ − 60, 78), 177 (57), 174 (37), 159 (68), 149 (29), 123 (42), 107 (39), 95 (44), 43 (100); HRMS calcd for $C_{13}H_{20}O$ (M^+ − 60) 192.1514, found 192.1510.

(3aα,4*β*,6α,8*β*,8aα)-(±)-Decahydro-2,2,4-trimethyl-4,8-epoxyazulen-6-ol (18). To a stirred suspension of 0.60 g of LAH (15.8 mmol) in 100 mL of ether was added dropwise a solution of 3.62 g (14.4 mmol) of **5** in 50 mL of ether. The reaction mixture was stirred at rt for 1 h, cooled to 0 °C, and then carefully quenched with 2 mL of saturated aqueous Na_2SO_4. After addition of 150 mL of EtOAc, the solution was dried and evaporated. The remaining residue was flash chromatographed [3:1 petroleum ether (bp 40−60)/EtOAc] to afford 2.43 g (81%) of **18** as a white solid: mp 72−73 °C; ^{13}C NMR δ 22.98 (q), 25.96 (q), 28.31 (q), 37.54 (t), 41.34 (s), 42.86 (t), 45.52 (t), 47.65 (t), 48.59 (d), 50.37 (d), 65.19 (d), 79.49 (d), 79.70 (s). The ^{1}H NMR and mass spectral data for **18** were identical with those reported in the literature.[7a]

(3aα,4*β*,8*β*,8aα)-(±)-Octahydro-2,2,4-trimethyl-4,8-epoxyazulen-6(1*H*)-one (19). To a stirred solution of 2.43 g (11.6 mmol) of **18** in 100 mL of CH_2Cl_2 was added 6.5 g (17.3 mmol) of PDC. After being stirred at rt for 15 h, the reaction mixture was filtered over a short pad of Hyflo. The filtrate was concentrated under reduced pressure and flash chromatographed [10:1 petroleum ether (bp 40−60 °C)/EtOAc] to give 2.25 g (93%) of **19** as a colorless oil. The NMR and mass spectral data for **19** were identical with those reported in the literature.[7a,8]

(3aα,4*β*,8*β*,8aα)-(±)-Octahydro-7-(hydroxymethylene)-2,2,4-trimethyl-4,8-epoxyazulen-6(1*H*)-one (20). To a stirred suspension of 0.78 g (26.0 mmol) of NaH (80% dispersion in mineral oil) in 75 mL of ether was added dropwise 0.5 mL (12.4 mmol) of MeOH at rt. After 5 min, a solution of 8.4 mL (0.10 mol) of ethyl formate and 2.25 g (10.8 mmol) of **19** in 50 mL of ether was added dropwise over 30 min. The reaction mixture was stirred at rt for 1 h, carefully quenched with 1 mL of EtOH, and then mixed with 60 mL of H_2O. The two-phase system was separated, and the aqueous layer was acidified with concentrated aqueous HCl to ca. pH 2 and extracted three times with ether. The combined organic layers were then extracted three times with 2 M aqueous KOH. The combined basic aqueous layers were cooled to 0 °C, acidified with concentrated aqueous HCl to ca. pH 2, and extracted three times with ether. The combined organic layers were dried and evaporated to afford 2.47 g (95%) of crude **20**,[45] which was used in the next reaction without further purification. The NMR and mass spectral data for **20** corresponded with those reported in the literature.[7a]

(3aα,4*β*,8*β*,8aα)-(±)-7-[(Butylthio)methylene]octahydro-2,2,4-trimethyl-4,8-epoxyazulen-6(1*H*)-one (21) was prepared from 0.205 g (0.867 mmol) of **20** and 0.11 mL (1.03 mmol) of butanethiol as previously described.[7a] Workup and flash chromatography [7:1 petroleum ether (bp 40−60 °C)/EtOAc] afforded 0.234 g (88%) of **21** as a ca. 3.5:1 mixture of the *E* and *Z* isomers: ^{1}H NMR (major peaks) δ 4.38, 4.63 (s, s, 1:3.5 ratio, 1H), 6.65, 7.34 (s, s, 1:3.5 ratio, 1H); HRMS calcd for $C_{18}H_{28}O_2S$ (M^+) 308.1810, found 308.1809.

(3aα,4*β*,8*β*,8aα)-(±)-1,2,3,3a,4,7,8,8a-Octahydro-2,2,8-trimethyl-6-[(phenylthio)methyl]-4,8-epoxyazulene-5-carboxaldehyde (22). To a stirred fine dispersion of anhydrous $CeCl_3$ in 5 mL of THF [prepared from 0.714 g (1.92 mmol) of $CeCl_3 \cdot 7H_2O$ by heating at 140 °C under reduced pressure (0.1 mmHg) and sonication[31]], cooled to −78 °C, was added 3.7 mL of lithiated thioanisole (0.49 M in ether)[46] over 10 min under argon. The mixture was stirred at −78 °C for 1.5 h, and then a solution of 0.286 g (0.930 mmol) of **21** in 3 mL of THF was added dropwise over 8 min. Stirring was continued at the same temperature for another 45 min, after which time 2 mL of saturated aqueous NH_4Cl was added. The reaction mixture was allowed to come to rt, diluted with 10 mL of THF, and filtered through a short pad of Hyflo. The filter cake was washed three times with THF, and the filtrate was concentrated under reduced pressure. The remaining residue was dissolved in 5 mL of EtOH containing 4% H_2O, and then 0.301 g (1.11 mmol) of $HgCl_2$ was added. The mixture was stirred at rt for 5 min, diluted with 75 mL of ether, and filtered through a short pad of Hyflo. The filtrate was washed three

(45) According to the ^{1}H NMR spectrum, **20** most likely consisted of a ca. 9:1 mixture of the intramolecularly hydrogen-bonded *Z*-isomer (one-proton singlet at δ 7.52) and the keto aldehyde form (one-proton singlet at δ 9.58), respectively. Also, see ref 7a.

(46) A solution of lithiated thioanisole (0.49 M in ether) was prepared by the following procedure. To a stirred solution of 0.9 mL (7.67 mmol) of thioanisole in 10 mL of ether was added 4.8 mL (7.68 mmol) of *n*-BuLi (1.6 M in hexane). The solution was heated at reflux temperature for 15 h and then cooled to rt.

times with brine, dried, and evaporated. The remaining residue was flash chromatographed [7:1 petroleum ether (bp 40−60 °C)/EtOAc] to give 0.267 g (84%) of **22** as a colorless oil: ^{1}H NMR δ 0.84 (s, 3H), 1.03 (s, 3H), 1.10−1.50 (m, 3H), 1.32 (s, 3H), 1.59 (m, 1H), 2.19−2.43 (m, 2H), 2.49, 2.55 (AB q, J_{AB} = 19.4 Hz, 2H), 3.33 (d, J = 13.2 Hz, 1H), 4.14 (d, J = 13.2 Hz, 1H), 4.49 (s, 1H), 7.20−7.45 (m, 5H), 9.32 (s, 1H); ^{13}C NMR δ 22.75 (q), 25.87 (q), 28.20 (q), 34.93 (t), 41.09 (s), 42.96 (t), 44.07 (t), 45.79 (t), 51.91 (d), 55.53 (d), 74.66 (d), 79.99 (s), 128.76 (d), 129.13 (2d), 132.88 (s), 134.18 (2d), 141.49 (s), 148.87 (s), 185.94 (d); MS *m*/*z* (relative intensity) 342 (M^+, 32), 250 (11), 248 (21), 233 (100), 215 (7), 206 (8), 191 (25), 161 (7), 125 (7), 95 (15); HRMS calcd for $C_{21}H_{26}O_2S$ (M^+) 342.1654, found 342.1654.

(3aα,4*β*,8*β*,8aα)-(±)-1,2,3,3a,4,7,8,8a-Octahydro-2,2,8-trimethyl-6-[(phenylsulfinyl)methyl]-4,8-epoxyazulene-5-carboxaldehyde (23). To a stirred solution of 0.171 g (0.50 mmol) of **22** in 10 mL of MeOH was added a solution of 0.167 g (0.78 mmol) of $NaIO_4$ in 1 mL of H_2O. After being stirred at rt for 3 d, the reaction mixture was diluted with 50 mL of MeOH and filtered through a short pad of Hyflo. The filtrate was concentrated under reduced pressure, and the remaining residue was taken up in 50 mL of ether. The solution was washed with H_2O (twice) and brine, dried, and evaporated to give 0.177 g (99%) of **23** as a ca. 2:1 mixture of two diastereomers: ^{1}H NMR (major peaks) δ 0.86 (s, 3H), 1.04 (s, 3H), 1.17, 1.20 (s, s, 2:1 ratio, 3H), 3.60, 3.79 (B parts of AB q, J = 13.0 Hz, 2:1 ratio, 1H), 3.98, 4.19 (A parts of AB q, J = 13.0 Hz, ratio 1:2, 1H), 4.56, 4.59 (s, s, 1:2 ratio, 1H), 7.48−7.64 (m, 5H), 9.38, 9.56 (s, s, 1:2 ratio, 1H); ^{13}C NMR δ 22.38, 22.47 (q), 25.88 (q), 28.16, 28.21 (q), 41.05, 41.09 (s), 43.04 (t), 45.99, 46.08 (t), 47.35, 47.45 (t), 52.26, 52.32 (d), 55.45, 55.69 (d), 56.36, 56.78 (t), 74.99, 75.10 (d), 79.64, 79.76 (s), 124.28 (2d), 129.36 (2d), 131.78, 131.82 (s), 140.37 (s), 141.44, 141.68 (s), 144.93, 145.35 (s), 186.42, 187.11 (d); MS *m*/*z* (relative intensity) 358 (M^+, 3), 343 (1), 342 (1), 341 (1), 233 (100), 205 (61), 191 (26), 81 (21), 69 (38), 43 (33); HRMS calcd for $C_{21}H_{26}O_3S$ (M^+) 358.1603, found 358.1600. Anal. Calcd for $C_{21}H_{26}O_3S$: C, 70.35; H, 7.31. Found: C, 70.20; H, 7.12.

(4α,4a*β*,7a*β*,8α)-(±)-4,4a,5,6,7,7a,8,9-Octahydro-6,6,8-trimethyl-1-(phenylthio)-4,8-epoxyazuleno[5,6-*c*]furan (24). To a stirred solution of 37.2 mg (0.11 mmol) of **23** in 1 mL of CH_2Cl_2 were added 12.5 μL (0.11 mmol) of 2,6-lutidine and 15.5 μL (0.11 mmol) of TFAA under argon. The reaction mixture was stirred at rt for 25 min, quenched with 5 mL of saturated aqueous $NaHCO_3$, and diluted with 10 mL of ether. The two-phase mixture was separated, and the organic layer was washed twice with 1 M aqueous HCl and four times with brine. The organic layer was dried and evaporated, and the remaining residue was flash chromatographed [10:1 petroleum ether (bp 40−60 °C)/EtOAc] to give 16.0 mg (43%) of **24** (GC purity >90%):[47] ^{1}H NMR δ 0.89 (s, 3H), 1.10 (s, 3H), 1.27−1.50 (m, 3H), 1.40 (s, 3H), 1.70 (m, 1H), 2.44−2.83 (m, 4H), 4.80 (s, 1H), 7.08−7.36 (m, 5H), 7.38 (s, 1H); ^{13}C NMR δ 23.51 (q), 26.03 (q), 28.31 (q), 36.00 (t), 41.47 (s), 42,87 (t), 45.95 (t), 51.02 (d), 55.88 (d), 75.18 (d), 80.12 (s), 126.02 (d), 126.51 (s), 126.94 (2 d), 128.68 (s), 129.04 (2 d), 136.17 (s), 136.69 (d), 137.50 (s); MS *m*/*z* (relative intensity) 340 (M^+, 100), 325 (11), 297 (9), 269 (22), 231 (31), 187 (44), 145 (29), 91 (52), 77 (37), 43 (75); HRMS calcd for $C_{21}H_{24}O_2S$ (M^+) 340.1497, found 340.1500. Further elution [1:1 petroleum ether (bp 40−60 °C)/EtOAc] afforded 12.9 mg (35%) of starting material **23**.

(4α,4a*β*,7a*β*,8α)-(±)-4,4a,5,6,7,7a,8,9-Octahydro-6,6,8-trimethyl-4,8-epoxyazuleno[5,6-*c*]furan-1(3*H*)-one (31) and Its Regioisomer 32. To a stirred solution of 19.6 mg (0.055 mmol) of **23** in 1 mL of CH_2Cl_2, cooled to −35 °C, were added 30 μL (0.3 mmol) of 2,6-lutidine and 40 μL (0.3 mmol) of TFAA under argon. The reaction mixture was kept at −25 °C for 22 h, after which time another 20 μL (0.2 mmol) of 2,6-lutidine and 25 μL (0.2 mmol) of TFAA were added. After standing at −25 °C for an additional 22 h, the reaction mixture was quenched with 5 mL of saturated aqueous $NaHCO_3$ and diluted with 25 mL of ether. The two-phase mixture was separated, and the organic layer was washed successively with 1 M aqueous HCl (twice), 1 M aqueous NaOH (twice), and brine (four times). The organic layer was dried and evaporated, and the remaining residue was dissolved in 3 mL of MeOH. After addition of 150 mg (0.55 mmol) of $HgCl_2$ and 1 mL of 4 M aqueous HCl, the solution was heated at 35 °C for 2.5 d. The reaction mixture was then diluted with 50 mL of ether, washed four times with brine, dried, and evaporated. The remaining residue was flash chromatographed [5:1 to 1:1 petroleum ether (bp 40−60 °C)/EtOAc] to give 10.9 mg (80%) of a white solid which, according to GC and NMR analysis, appeared to be a ca. 4:1 mixture of **31** and **32**, respectively.[48] This mixture was used in the next reaction without separation. The NMR and mass spectral data for **31** (major component) corresponded with those reported in the literature;[8] those for **32** (minor component) are shown below.

32: ^{1}H NMR (major peaks) δ 0.85 (s, 3H), 1.05 (s, 3H), 1.39 (s, 3H), 4.50 (br s, 1H), 4.66 (br s, 2H); MS *m*/*z* (relative intensity) 248 (M^+, 32), 233 (29), 215 (19), 206 (29), 191 (100), 145 (37), 105 (54), 95 (64), 77 (39), 43 (90); HRMS calcd for $C_{15}H_{20}O_3$ (M^+) 248.1412, found 248.1402.

Furanether B (4) was prepared from 8.3 mg (0.033 mmol) of the above 4:1 mixture of **31** and **32** in a fashion identical with that described for the conversion of **31** to **4**.[8] Workup and flash chromatography [5:1 petroleum ether (bp 40−60 °C]/EtOAc) afforded pure **4** as a white solid in 99% yield: mp 58 °C (lit.[8] mp 62−63 °C). The NMR and mass spectral data for **4** were identical with those reported in the literature.[6a,7a,8]

Acknowledgment. We thank A. van Veldhuizen for recording ^{1}H and ^{13}C spectra and H. Jongejan and C. J. Teunis for mass spectral data and elemental analyses.

Supporting Information Available: ^{1}H NMR spectra of **5**, **9**, **17**, **21**, **22**, and **24** (6 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO971545N

(47) GC analysis revealed the presence of small amounts (<5%) of **25** and **26**.

(48) Pure **31** could be obtained upon treatment of **24**[43] with $HgCl_2$ and 4 M aqueous HCl at 35 °C.