hydroxy-3-cyclohexenecarboxylate (23) as an oil: IR (CCl_4) 3500, 3080, 3040, 2980, 1740, 1640 cm^{-1}; ^1H NMR (200 MHz) δ 1.26 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 1.99 (m, 1 H), 2.06 (m, 3 H), 2.32 (dd, J = 13.8, 7.9 Hz, 1 H, $CH_2CH{=}CH_2$), 2.44 (dd, J = 13.8, 7.3 Hz, 1 H, $CH_2CH{=}CH_2$), 3.05 (d, J = 8.6 Hz, 1 H, OH), 4.10 (d, J = 7.6 Hz, 1 H, CHOH), 4.19 (q, J = 7.2 Hz, 2 H, CH_2CH_3), 5.06 (d, J = 11.9 Hz, 1 H, CH=CH), 5.08 (dd, J = 11.9, 3.6 Hz, 1 H, CH=CH), 5.78 (m, 3 H, $CH{=}CH_2$); GCMS m/z 210 (M^+) 169 (M^+ - allyl, 13), 151 ($M^+ - H_2O$ - allyl, 22), 141 (75), 119 ($M^+ - H_2O$ - COOEt, 38), 113 (98), 95 (100), 79 (51).

Oxidation of the Alcohols 11 and 12. The mixture of alcohols 11 and 20 (30 mg, 0.1428 mmol) was oxidized by the Swern procedure with oxalyl chloride (59 μL, 0.65 mmol), DMSO (100 μL, 1.30 mmol), and triethylamine (0.42 mL, 3.0 mmol). A portion of the product mixture was separated by HPLC to give 13 (1.5 mg, 5%) and 14 (3.2 mg, 11%). These products were identical with those obtained by the oxidation of alcohols 9 and 10 as shown by the identity of IR and GCMS spectra.

Oxidation of Alcohol 12. Alcohol 12 (11.7 mg, 0.057 mmol) was oxidized with oxalyl chloride (11.2 μL, 0.12 mmol), DMSO (19 μL, 0.25 mmol), and triethylamine (80 μL, 0.56 mmol). The GCMS and IR data of the isolated ketone are identical with those of ketone 14.

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Supplementary Material Available: X-ray crystallography material for urethane 15 (10 pages). Ordering information is given on any current masthead page.

Total Synthesis of Dehydroambliol-A and Its Unnatural *Z* Isomer†

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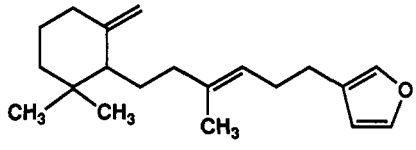
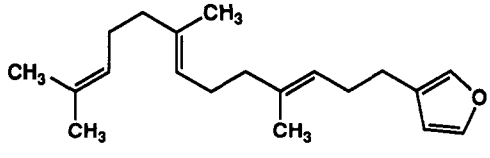
Convergent total syntheses of dehydroambliol-A (1a), its unnatural *Z* isomer 1b, and ambliofuran (2) are described. The syntheses utilized 2-(3′-furyl)-1,3-dithiane (6) as a common intermediate. Analysis of their proton and carbon magnetic resonance spectra confirm that in the natural product dehydroambliol-A and in synthetic dehydroambliol-A the Δ^7-bond possesses the *E* geometry, while in the unnatural isomer of dehydroambliol-A, the Δ^7-bond is of the *Z* configuration.

The isolation and structure elucidation of several metabolites from the class of marine sponge known as *Dysidea amblia* has been reported.[1] By use of a combination of spectroscopic and degradative chemical studies, a diterpenoid-based structure was suggested for dehydroambliol-A (1) and ambliofuran (2).



Dehydroambliol-A (1)

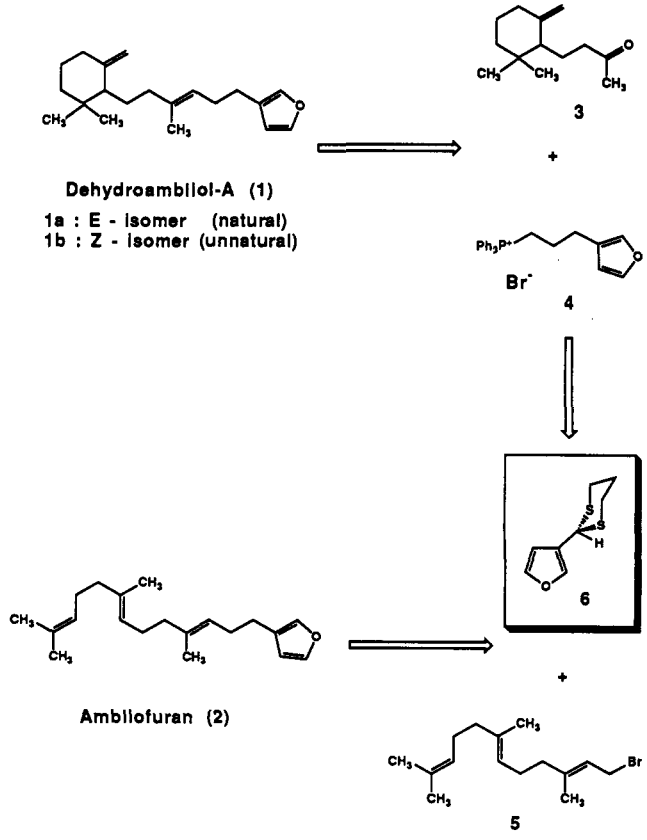
1a : E - isomer (natural)
1b : Z - isomer (unnatural)



Ambliofuran (2)

Although a synthesis of ambliofuran (2) has been reported recently,[2] the total synthesis of dehydroambliol-A (1) has not been described. We wish to report the synthesis of the natural product dehydroambliol-A (1a) and its unnatural Z isomer 1b. In addition, an alternative synthesis of ambliofuran (2) is described.

Scheme I. Retrosyntheses of Dehydroambliol-A (1) and Ambliofuran (2)



† This work was abstracted from the thesis research of C.V.M. presented to the Graduate School of Rutgers University in partial fulfillment of the requirements of the Ph.D. degree.

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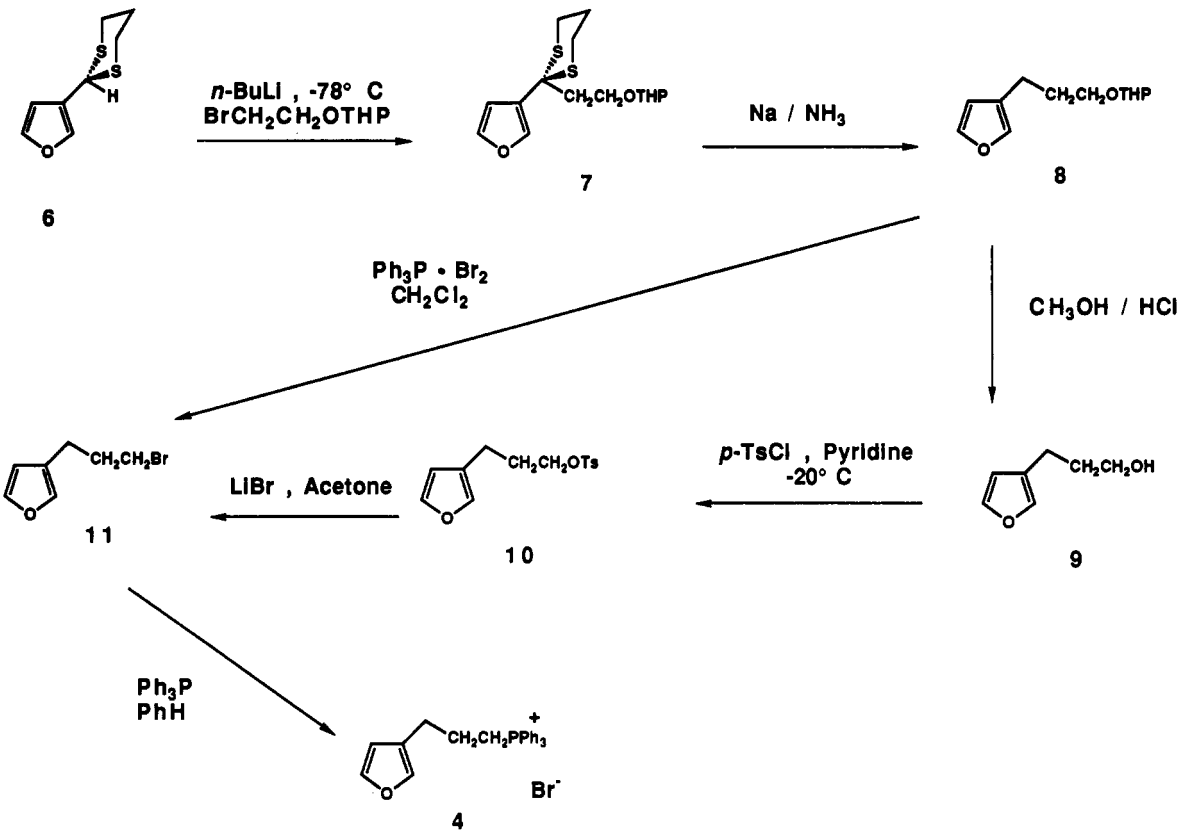
Scheme II. Synthesis of [3-(3′-Furyl)propyl]triphenylphosphonium Bromide (4)



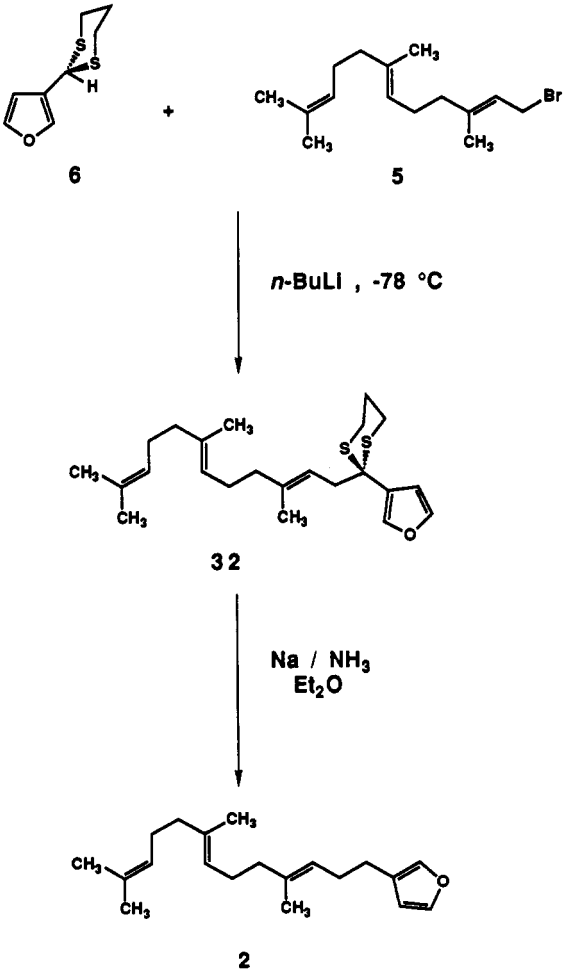
Results and Discussion

Retrosyntheses of **1** and **2** via a convergent route utilizing the dithiane **6**[3] as a common intermediate are described in Scheme I.

The synthesis of dehydroambliol-A (**1**) required the preparation of compounds **3** and **4**. Compound **4** was obtained with the intermediate dithiane **6**, Scheme II. Treatment of **6** with 1 equiv of *n*-butyllithium at −78 °C followed by the addition of the tetrahydropyranyl ether of 2-bromoethanol[4] gave the dithiane adduct **7** (84%). Removal of the dithiane group in **7** by use of sodium in liquid ammonia gave the tetrahydropyranyl ether **8** (88%). Deprotection of the tetrahydropyranyl ether was accomplished by treating **8** with methanolic hydrogen chloride to produce alcohol **9** (93%). Compound **9** was transformed into its corresponding tosylate **10** (66%) by use of 2 equiv of *p*-toluenesulfonyl chloride in pyridine at −20 °C. Heating an acetone solution of **10** under reflux, in the presence of a 5-fold excess of anhydrous lithium bromide, gave the corresponding bromo derivative **11** (80%). The overall yield of **11** from **8** using this reaction sequence was 50%.

An alternative, and more efficient method, to produce **11** involved the direct transformation of **8** to **11** (Scheme II). Treatment of the tetrahydropyranyl ether **8** with triphenylphosphine dibromide in methylene chloride at 0 °C gave the bromide **11** directly (84%). Heating a benzene solution containing **11** and triphenylphosphine

Scheme III. Synthesis of Dihydro-γ-ionone (3)



(1) Walker, R. P.; Faulkner, D. J. *J. Org. Chem.* **1981**, *46*, 1098.
(2) Nishizawa, M.; Yamada, H.; Hayashi, Y. *Tetrahedron Lett.* **1984**, *25*, 187.
(3) Hoppmann, A.; Weyerstahl, P. *Tetrahedron*, **1978**, *34*, 1723.
(4) 2-Bromo-1-tetrahydropyranylethanol was prepared from 2-bromoethanol and dihydropyran (1.1 equiv) in methylene chloride at 0 °C with use of a catalytic amount of *p*-toluenesulfonic acid.

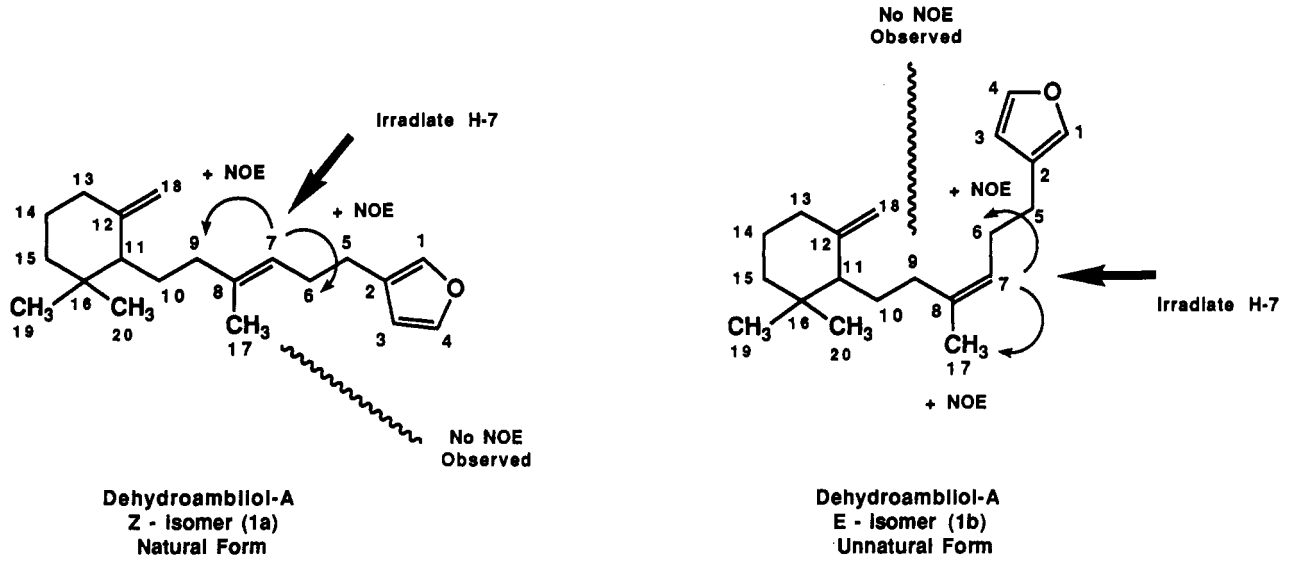


Figure 1. ^1H NOE difference studies for dehydroambliol-A and its *Z* isomer.

under reflux produced the desired phosphonium salt **4** (78%).

Dihydro-γ-ionone (**3**) has been identified as a chemical degradation product of ambrien.[5] Since its discovery, several syntheses of **3** have been reported.[6,7] Our synthesis of **3** is described in Scheme III. Treatment of **18** with 1 equiv of sodium hydride followed by the addition of excess allyl bromide gave a mixture of O- and C-allylated products, **19** and **20**, in a ratio of 2:3, respectively, as determined by ^1H NMR spectroscopy. The ^1H NMR spectrum of the mixture exhibited *three* distinct singlets for the *geminal* dimethyl groups. Resonances were observed at δ 0.80, 1.16, and 1.30, with the intensity of the resonance at δ 1.16 being approximately twice that of the other two resonances. Examination of Drieding molecular models of **19** and **20** suggested that the *geminal* dimethyl groups in the O-allylated product **19** might experience similar magnetic environments, while the geminal dimethyl groups in the asymmetric C-allylated product **20** might be magnetically nonequivalent. This proposal was consistent with the appearance and assignment of the C–CH_3 region in the ^1H NMR spectrum of the **19** and **20** mixture.

When the mixture described previously was heated at 150 °C, the O-allylated product **19** underwent a Claisen rearrangement to produce the C-allylated product **20** quantitatively. Decarboxylation of **20** using wet lithium iodide in collidine heated under reflux gave the substituted cyclohexanone **21** (56%). Ozonolysis of **21** and subsequent reduction of the ozonide with sodium borohydride gave the diol **22** (65%). The diol **22** was treated with 1 equiv of *p*-anisylchlorodiphenylmethane to give the protected secondary alcohol **23** (97%) exclusively. Using a modification of the Sarett oxidation procedure, **23** was oxidized to ketone **24** (81%). Treatment of **24** with triphenylmethylphosphonium ylide gave the exocyclic olefin **25** (43%). The substituted trityl protecting group in **25** was removed reductively using sodium in liquid ammonia to give the primary alcohol **26** (71%). The primary alcohol **26** was converted to its corresponding tosylate **27** using *p*-toluenesulfonyl chloride in pyridine at 0 °C (75%). Treatment of **27** with potassium cyanide in the presence of dibenzo-18-crown-6 gave the homologated cyano derivative **28** (90%).

Interestingly, treatment of **28** with methylmagnesium bromide gave the imine **29** as the major product. Further hydrolysis of **29** in the presence of hydrochloric acid (1 N) heated under reflux was accompanied with rearrangement of the exocyclic olefin, which produced the thermodynamically more stable endocyclic olefin **30** (68%).

Alternatively, basic hydrolysis of **28** gave the carboxylic acid **31** (85%). The ^1H NMR spectrum of **31** exhibited *two* one-proton resonances at δ 4.64 and 4.80, suggesting that the regiochemistry of the exocyclic olefin was not altered under the hydrolytic conditions. The carboxylic acid **31** was treated with 2 equiv of methyllithium to give **3** (77%).

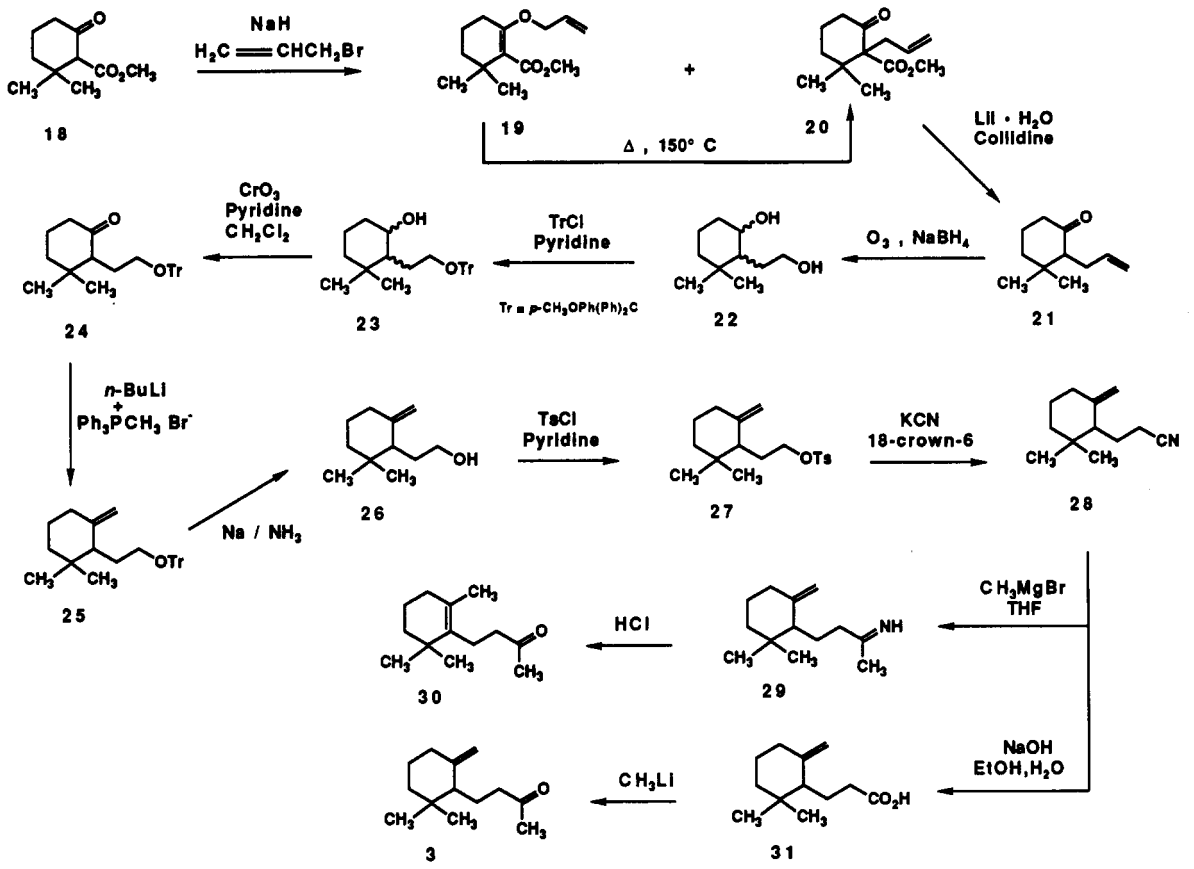
The final step in the synthesis of dehydroambliol-A (**1**) requires formation of a carbon-to-carbon double bond between **3** and **4** via a Wittig reaction (Scheme I). Treatment of **4** with *n*-butyllithium at −20 °C in benzene followed by the addition of **3** gave **1** (68%). The *E*/*Z* isomer ratio of the product obtained in the reaction was 3:2 in favor of the naturally occurring trans, *E* isomer **1a**. By use of reversed-phase high-pressure liquid chromatography (HPLC), dehydroambliol-A (**1a**) and its unnatural **Z** isomer **1b** were separated.

The ^1H and ^{13}C NMR chemial shifts for dehydroambliol-A (**1a**), its unnatural **Z** isomer **1b**, and those reported[1] from spectra of an authentic sample of dehydroambliol-A are presented in Table I (supplementary material). Assignment of the resonances in the spectra of **1a** and **1b** to their corresponding atoms was accomplished by analysis of the two-dimensional (2-D), ^1H–^1H (COSY) and ^1H–^{13}C heteronuclear (HETCOR) correlation spectra (supplementary material). Differences observed between the ^{13}C spectra of the *E* and *Z* isomers of **1** allowed their differentiation.

The most significant differences in chemical shift between the *E* and *Z* isomers of **1** are seen in the resonance signals corresponding to the C-7, C-9, and C-17 carbon atoms. These signals differ by approximately δ 1, 8, and 7, respectively. The C-17 resonance signal at δ 16.1 in the ^{13}C spectrum of the *E* isomer **1a** is characteristic of a methyl group attached to a trisubstituted olefin with trans geometry.[8] In addition, the ^{13}C chemical shift of the C-17 resonance signal in **1a** is virtually identical with the ^{13}C

(5) Ruzicka, L., Seidel, C. F.; Pfeiffer, M. *Helv. Chim. Acta* **1948**, *31*, 827.
(6) Stauffacher, D.; Schinz, H. *Helv. Chim. Acta* **1954**, *37*, 1223.
(7) Stoll, M. *Helv. Chim. Acta* **1955**, *38*, 1587.
(8) Couperus, P. A.; Claque, D. H.; van Dangen, J. *Org. Magn. Reson.* **1976**, *8*, 426.

Scheme IV. Synthesis of Ambliofuran (2)



chemical shift for the C-17 resonance signal in an authentic sample of the natural product, δ 16.1, while the ^{13}C chemical shift for the C-17 resonance signal in the *Z* isomer appears at δ 23.5.

Since the *E* and *Z* isomers of **1** were available in pure form, a ^1H NOE difference experiment was conducted on each isomer to establish further the geometric isomerism that exists about the Δ^7-bond (Figure 1). In the *E* isomer **1a**, a positive NOE was observed in the ^1H resonance signals corresponding to the C-6 and C-9 methylene protons when the C-7 vinyl proton was irradiated. No NOE effect was observed in the ^1H resonance signal corresponding to the C-17 methyl group. These observations are consistent with a trans geometry about the Δ^7-bond and establishes the *E* isomer **1a** as the synthetic equivalent of dehydroambliol-A.

In the *Z* isomer **1b**, a positive NOE was observed in the ^1H resonance signals corresponding to the C-6 methylene and C-17 methyl protons when the C-7 vinyl proton was irradiated. No NOE effect was observed in the ^1H resonance signal corresponding to the C-9 methylene group. These observations are consistent with a cis geometry about the Δ^7-bond and establish the *Z* isomer **1b** as the unnatural form of dehydroambliol-A.

An alternative synthesis of ambliofuran (**2**) utilizing the dithiane **6**[3] was also investigated (Scheme IV). Commercially available (*E,E*)-farnesyl alcohol was converted to (*E,E*)-farnesyl bromide (**5**) with carbon tetrabromide and triphenylphosphine in acetonitrile (94%). Treatment of **6** with 1.1 equiv of *n*-butyllithium at −78 °C followed by the addition of 1.1 equiv of **5** gave the dithiane adduct **32** (62%). Reductive removal of the dithiane moiety in **32** using sodium in liquid ammonia gave ambliofuran (**2**; 83%). The ^1H NMR spectrum of synthetic **2** was in complete agreement with the ^1H NMR spectrum of the natural product.[1]

In summary, the total synthesis of dehydroambliol-A (**1**) in its natural, *E* isomer **1a** and unnatural, *Z* isomer **1b** form has been accomplished. In addition, an alternate synthesis of ambliofuran (**2**) has been completed. The syntheses of **1** and **2** utilized the dithiane **6** as a common intermediate.

Experimental Section

General Procedures. ^1H and ^{13}C NMR spectra were obtained using Varian XL-200, RX-200, or XL-400 spectrometers. Melting points are uncorrected. Analytical HPLC was performed with use of a variable wavelength or absorption detector (wavelengths 254 and 229 nm). HPLC columns used were either Whatman 5 Partisil, Waters 10 Porasil, or reversed-phase C-18 Waters 10. Analytical thin-layer chromatography (TLC) was performed with either 20 × 20 cm or 10 × 20 cm 250-μm plates manufactured by Analtech. Column chromatography was performed with use of 60–200 mesh J. T. Baker silica gel.

2-(3′-Furyl)-2-[2-(tetrahydropyran-2-yloxy)ethyl]-1,3-dithiane (7). A solution of **6**[3] (1.0 g, 5.3 mmol) in dry tetrahydrofuran (THF, 10 mL) was cooled to −78 °C and 1.6 M *n*-butyllithium (3.3 mL, 5.3 mmol) was added dropwise. The temperature was maintained for 2 h at −78 °C while 2-(2-bromoethoxy)tetrahydropyran[9] (1.66 g, 8.0 mmol) dissolved in THF (2 mL) was added dropwise. The temperature was maintained for 2 h and then allowed to warm to room temperature, and the mixture was stirred for 18 h. The reaction was quenched with aqueous NH_4Cl. The aqueous layer was extracted with diethyl ether (25 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and evaporated under reduced pressure to yield 2.0 g of crude oil that was purified by column chromatography (silica gel, EtOAc/hexane (5:95) to yield 1.39 g (84%) of product: IR (neat) 2950, 1360, 1140, 1130, 1020, 880, 800 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40–2.10 (m, 8 H, CH_2), 2.35 (t, 2 H, CH_2, J = 7.2 Hz), 2.60–2.95 (m, 4 H, CH_2S), 3.45 (m, 2 H, CH_2O), 3.85 (m, 2 H, CH_2O), 4.55 (d of d, 1 H, CH, J = 3.6, 3.0), 6.49 (d, 1 H, Ar, J = 1.2 Hz), 7.41 (s, 1 H, Ar), 7.53 (d, 1 H, Ar,

(9) Parham, W. E.; Anderson, E. L. *J. Am. Chem. Soc.*, **1948**, *70*, 4087.

J = 0.8 Hz); ^{13}C NMR ($CDCl_3$) δ 143.5, 142.2, 128.8, 110.7, 98.9, 63.5, 62.2, 49.0, 43.2, 42.9, 30.7, 30.6, 27.5, 25.4, 25.1, 19.5. MS m/e (relative intensity) 314 (M^+, 12), 229 (8), 185 (13), 85 (100). Anal. Calcd for $C_{15}H_{22}O_3S_2$; C, 57.32; H, 7.00; S, 20.38. Found: C, 57.40; H, 7.14; S, 20.05.

3-[3-(Tetrahydropyran-2-yloxy)propyl]furan (8). Sodium metal (1.0 g, 40 mmol) was added in small pieces to a stirred solution of **7** (1.1 g, 3.5 mmol) in anhydrous diethyl ether (40 mL) and anhydrous NH_3 (100 mL) producing a blue solution. The reaction was stirred for 0.25 h, and then ethanol was added dropwise until all the blue color disappeared. The NH_3 was allowed to evaporate and the ethanol was removed under reduced pressure. The residue was dissolved in ether, washed with brine, dried ($MgSO_4$), and filtered. The ether was removed under reduced pressure and the residue purified by column chromatography (silica gel, EtOAc/hexane (3:1)) to yield 0.64 g (88%) of a colorless oil: IR (neat) 2874, 1500, 1350, 1200, 1030, 880, 780 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40–2.00 (m, 8 H, CH_2), 2.53 (t, 2 H, CH_2, J = 7.2 Hz), 2.50 (m, 2 H, OCH_2), 3.82 (m, 2 H, OCH_2), 4.61 (d of d, 1 H, CHO, J = 3.6, 3.0 Hz), 6.31 (s, 1 H, Ar), 7.26 (s, 1 H, Ar), 7.38 (d, 1 H, Ar, J = 2 Hz); ^{13}C NMR ($CDCl_3$) δ 142.7, 138.8, 124.6, 111.0, 98.9, 66.8, 62.4, 30.7, 30.0, 25.5, 21.5, 19.7; MS m/e (relative intensity) 210 (M^+, 1), 137 (2), 126 (22), 110 (22), 85 (100). Anal. Calcd for $C_{12}H_{18}O_3$; C, 68.57; H, 8.57. Found: C, 68.41; H, 8.30.

3-(3-Furyl)propan-1-ol (9).[10] A solution of **8** (0.50g, 2.4 mmol) and 10% methanolic HCl solution (10 mL) was stirred for 0.25 h at room temperature. The solution was partioned between ethyl acetate and water. The organic layer was washed with brine, dried ($MgSO_4$), filtered, and evaporated under reduced pressure to yield 0.30 g of crude product. The oil was passed through a filtration column (silica gel, EtOAc/hexane (5:95)) to yield 0.28 g (93%) of product: IR (neat) 3350, 2870, 1500, 1180, 1080, 1025, 880, 780 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40 (br s, 1 H, OH), 1.85 (m, 2 H, CH_2), 2.54 (t, $2CH_2O$, J = 7.2 Hz), 3.70 (t, 2 H, CH_2, J = 6.2 Hz), 6.30 (s, 1 H, Ar), 7.26 (s, 1 H, Ar), 7.37 (d, 1 H, Ar, J = 1.8 Hz); ^{13}C NMR ($CDCl_3$) δ 142.8, 138.9, 124.4, 110.9, 62.2, 32.0, 21.0; MS m/e (relative intensity) 126 (M^+, 25), 108 (4), 95 (19), 82 (100), 53 (39). Anal. Calcd for $C_7H_{10}O$; C, 66.67; H, 7.94. Found: C, 66.90; H, 8.04.

3-[3-[(4-Methylbenzenesulfonyl)oxy]propyl]furan (10). A solution of **9** (0.25 g, 2.0 mmol) and dry pyridine (5 mL) was cooled to 0 °C and treated with freshly recrystallized *p*-toluenesulfonyl chloride (0.76 g, 4.0 mmol). The solution was kept at −20 °C for 48 h. Pyridine hydrochloride precipitated as long white needles and was filtered. The solution was poured into ice and water and extracted with diethyl ether (2 × 10 mL). The combined ethereal solutions were washed with water, dried ($MgSO_4$), and filtered, and the solvent was removed under reduced pressure yield 0.37 g (66%) of a colorless oil. TLC indicated the product to be pure, and it was used directly without further purification: IR (neat) 2950, 1600, 1380, 1180, 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.92 (m, 2 H, CH_2), 2.48 (s + t, 5 H, CH_3 + CH_2), 4.06 (t, 2 H, CH_2, J = 6.2 Hz), 6.20 (s, 1 H, Ar), 7.12 (s, 1 H, Ar), 7.35 (s, 1 H, Ar), 7.39 (d, 2 H, Ar, J = 8 Hz), 7.80 (d, 2 H, Ar, J = 8 Hz); MS m/e (relative intensity) 280 (M^+, 7), 109 (18), 108 (100), 79 (93).

3-(3-Bromopropyl)furan (11). Method A. A mixture of **10** (0.30 g, 1.1 mmol), LiBr (0.56 g, 5.5 mmol), and dry acetone (10 mL) was stirred and heated under reflux for 20 h. The mixture was cooled and quenched with water. The aqueous layer was extracted with diethyl ether, and the organic layer was washed with water, dried ($MgSO_4$), filtered, and evaporated under reduced pressure to yield 0.17 g (80%) of product: IR (neat) 2940, 1440, 1200, 1122, 1030, 890, 760, 730, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.11 (m, 2 H, CH_2), 2.62 (m, 2 H, CH_2Ar, J = 7.4 Hz), 3.43 (t, 2 H, CH_2Br, J = 6.6 Hz), 6.29 (s, 1 H, Ar), 7.27 (s, 1 H, Ar), 7.38 (s, 1 H, Ar).

Method B. A solution of triphenylphosphine (0.56 g, 2.2 mmol) and dry CH_2Cl_2 (10 mL) was cooled to 0 °C, and Br_2 (0.35 g, 1 equiv) was added dropwise, causing a slight yellow solution to persist. The ice bath was removed and the solution allowed to warm to room temperature. A solution of CH_2Cl_2 (1 mL) and **8** (0.50 g, 2.0 mmol) was added in one portion and the reaction stirred for 0.5 h. The reaction was quenched with water and the layers separated. The organic layer was washed with water, dried ($MgSO_4$), and evaporated under reduced pressure to yield 0.50 g of crude product. The product was passed through 50 g of silica gel with ethyl acetate as the eluent, and the solvent was removed under reduced pressure to yield 0.24 g (63%) of product. The spectral data are identical with those obtained from the material prepared by Method A.

[3-(3-Furyl)propyl]triphenylphosphonium Bromide (4). A heterogeneous mixture of triphenylphosphine (3.0g, 1.1 mmol) and **11** (2.0g, 1.0 mmol) in dry benzene (25 mL) was stirred and heated under reflux for 48 h. The heterogeneous mixture was cooled to room temperature and the precipitate filtered. The benzene was removed under reduced pressure to give a solid that was washed with diethyl ether and dried under high vacuum to yield 3.5 g (78%) of crude product: IR (Nujol) 2950, 1601 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.90 (q, 2 H, CH_2, J = 6.8 Hz), 2.88 (t, 2 H, CH_2, J = 6.8 Hz), 3.90 (t, 2 H, CH_2, J = 6.8 Hz), 6.20 (s, 1 H, Ar), 7.95–7.25 (m, 17 H, Ar); MS m/e (relative intensity) 371 (M^+, 100). Anal. Calcd $C_{25}H_{24}BrOP$: C, 66.52; H, 5.32. Found: C, 66.73; H, 5.42.

Methyl 2-Allyl-3,3-dimethyl-1-oxocyclohexane-2-carboxylate (20) and Methyl 1-(Allyloxy)-3,3-dimethylcyclohex-1-ene-2-carboxylate (19). To a stirred suspension of dry THF (100 mL) and 50% sodium hydride mineral oil dispersion (4.8 g, 0.10 mol) was added dropwise **18** (18.4 g, 0.10 mol) dissolved in an equal volume of THF. The reaction was stirred at room temperature for 1 h, and then allyl bromide (13.31 g, 0.11 mol) dissolved in THF (10 mL) was added dropwise. After the addition, the reaction was stirred at 60 °C for 18 h. The reaction was cooled, and water (100 mL) was added dropwise. The reaction mixture was poured into diethyl ether (300 mL), and the organic layer was separated. The diethyl ether was washed with water and then brine, dried ($MgSO_4$), and filtered. The filtrate was evaporated under reduced pressure to yield 25 g of a crude oil that was distilled to give 19.5 (87%) of a mixture of O-alkylated and C-alkylated products: bp 75–95 °C (0.1 Torr); ^1H NMR ($CDCl_3$; O-alkylation) 1.16 (s, 6 H, 2 × CH_3); (C-alkylation) 0.80 (s, 3 H, CH_3), 1.20 (s, 3 H, CH_3).

Methyl 2-Allyl-3,3-dimethyl-1-oxocyclohexane-2-carboxylate (20). A mixture of **19** and **20** (20 g, 89 mmol) under a static nitrogen atmosphere was stirred vigorously while being heated at 150 °C for 1.5 h. The oil was distilled to yield 20 g (100%) of **20**: bp 95–96 °C (0.1 Torr); IR (neat) 1725, 1705, 1637 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.80 (s, 3 H, CH_3), 1.20 (s, 3 H, CH_3), 1.50–3.00 (m, 6 H, $CH_2CH_2CH_2$), 3.58 (s, 3 H, OCH_3), 4.91 (m, 3 H, CH_2CH=), 5.78 (m, 2 H, =CH_2); ^{13}C NMR ($CDCl_3$) δ 207.9, 171.4, 135.6, 117.0, 68.4, 51.2, 41.0, 39.9, 37.2, 33.9, 26.5, 23.5, 21.5; MS m/e (relative intensity) 224 (M^+, 5), 209 (6), 193 (10), 137 (22), 43 (100). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.64; H, 8.93. Found: C, 69.90; H, 9.17.

2-Allyl-3,3-dimethylcyclohexanone (21). A mixture of lithium iodide dihydrate (50.8 g, 0.30 mol) and 2,4,6-collidine (240 mL) was heated under reflux, and as soon as all the lithium iodide was dissolved, **20** (49 g, 0.22 mol) dissolved in 2,4,6-collidine (50 mL) was added dropwise. A pale yellow precipitate immediately formed. The reaction was then heated under reflux for 19 h. The reaction was cooled and poured into a mixture of 6 N HCl (450 mL), diethyl ether (450 mL), and ice (250 mL). The aqueous layer was separated and extracted with diethyl ether (2 × 50 mL). The combined ethereal extracts were washed with 6 N HCl (2 × 150 mL), 2 N Na_2CO_3 solution (2 × 50 mL), and saturated NaCl (150 mL), dried ($MgSO_4$), and filtered, and the solvent was removed under reduced pressure. The residue was distilled to yield 34.1 g (56%) of a colorless oil: bp 65–70 °C (0.65 Torr); IR (neat) 1710, 1640, 915 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.76 (s, 3 H, CH_3), 1.04 (s, 3 H, CH_3), 1.50–2.55 (m, 9 H, CH_2), 4.95 (d of d, 2 H, =CH_2), 5.75 (m, 1 H, =HC); MS m/e (relative intensity) 166 (M^+, 41), 151 (38), 123 (41), 109 (67), 94 (100). Anal. Calcd for $C_{11}H_{18}O$: C, 79.52, H 10.84. Found: C, 79.41: H, 10.64.

2-(3′,3′-Dimethyl-1′-hydroxycyclohexyl)ethanol (22). A solution of **21** (7.0 g, 42 mmol) in anhydrous methanol (1 L) was cooled to −50 °C, and ozone was bubbled through the solution for 0.25 h. Once a persistent blue color was observed, the addition of ozone was discontinued and nitrogen was bubbled through the

(10) Vig, O. P.; Chugh, O. P., Handa, V. K.; Vig, A. K. *J. Ind. Chem. Soc.* **1975**, *52*, 199.

solution for 0.25 h. The temperature was allowed to warm to -30 °C, and sodium borohydride (15.54 g, 0.42 mol) was added in small portions over 0.25 h. The -30 °C temperature was maintained and the solution stirred for 1 h. $NaBH_4$ (15.54 g, 0.42 mol) was added, and the reaction was allowed to warm to room temperature overnight. The methanol was concentrated under reduced pressure to one-third of its volume and the residue dissolved in ethyl acetate. The solution was stirred, and water (200 mL) was added dropwise. The organic layer was separated, washed with brine, and dried ($MgSO_4$) and the solvent removed under reduced pressure. The residual solvent was removed under high vacuum and the product crystallized. The solid was recrystallized from hexane to yield 5.4 g (75%) of product: mp 56–57 °C; IR (Nujol) 3250, 1460, 1385, 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (s, 3 H, CH_3) 0.96 (s, 3 H, CH_3), 1.04–2.08 (m, 9 H, $-CH_2-$), 3.12 (br s, 2 H, 2 × OH), 3.58 (m, 1 H, CH_aOH), 3.75 (m, 1 H, CH_bOH), 4.05 (m, 1 H, -CH-); MS m/e (relative intensity) 172 (M^+, 2), 154 (3), 136 (10), 111 (100). Anal. Calcd for $C_{10}H_{20}O_2 \cdot 1/2H_2O$: C, 66.30; H, 11.50. Found: C, 66.67; H, 11.08.

1-[2′-(*p*-Anisyldiphenylmethoxy)ethyl]-2-hydroxy-6,6-dimethylcyclohexane (23). A solution of **22** (5.4 g, 0.030 mol) in dry pyridine (50 mL) was stirred at room temperature, and *p*-anisylchlorodiphenylmethane (9.2 g, 0.030 mol) dissolved in pyridine (50 mL) was added dropwise. The reaction was stirred at room temperature for 18 h. The pyridine was removed under reduced pressure, and the residue was dissolved in ethyl acetate. The organic layer was washed with water, dried ($MgSO_4$), and filtered. The solvent was removed under reduced pressure to yield 13.0 g (97%) of a yellow oil. This was used directly without further purification: IR (neat) 3400, 1600, 1240, 1055, 1020, 820, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (s, 3 H, CH_3), 0.88 (s, 3 H, CH_3), 1.00–1.80 (m, 9 H, CH_2), 1.92 (br s, 1 H, OH), 3.08 (m, 1 H, CH_aO), 3.24 (m, 1 H, CH_bO), 3.77 (s, 4 H, OCH_3 + OH), 6.84 (d, 2 H, J = 6 Hz), 7.10–7.40 (m, 10 H, Ar), 7.46 (d, 2 H, J = 6 Hz); MS *m/e* (relative intensity) (FAB) 445 (M + 1), 345, 289, 273. Anal. Calcd for $C_{30}H_{36}O_3$: C, 81.08; H, 8.11. Found: C, 80.88; H, 8.00.

1-[2′-(*p*-Anisyldiphenylmethoxy)ethyl]-2-oxo-6,6-dimethylcyclohexane (24). A mixture of CH_2Cl_2 (665 mL), dry pyridine (435 mL), and CrO_3 (26.4 g, 0.26 mol) was stirred for 0.5 h under nitrogen, and then **23** (13.11 g, 0.029 mol) dissolved in CH_2Cl_2 (50 mL) was added dropwise.[11] After the addition was complete, the reaction was stirred at room temperature for 1.5 h. The reaction mixture was poured onto a short-path column containing Florisil (500 g) to remove any inorganic salts, and the filtrate was collected. The Florisil was washed several times with CH_2Cl_2 (200 mL). The filtrate and the column washings were combined and the solvent removed under reduced pressure to yield 12 g of a viscous oil. The oil was triturated with hexane to give a solid that was recrystallized from EtOAc/hexane to yield 10.50 g (81%) of a white solid: mp 118–119 °C; IR (Nujol) 1701, 1585, 1560, 1420, 1230, 1050, 1010, 810, 730, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.74 (s, 3 H, CH_3), 1.07 (s, 3 H, CH_3), 2.88 (m, 1 H, CH_aO), 3.20 (m, 1 H, CH_bO), 3.80 (s, 3 H, $-OCH_3$), 6.83 (d, 2 H, Ar, J = 8 Hz), 7.42 (d, 2 H, Ar, J = 8 Hz); ^{13}C NMR ($CDCl_3$) 212.6, 158.3, 144.9, 144.7, 136.1, 130.2, 128.3, 127.6, 112.9, 86.1, 62.6, 57.1, 55.1, 41.4, 39.7, 39.7, 29.6, 24.2, 23.1, 21.4; MS (FAB) *m/e* (relative intensity) 274 ($M - C_{10}H_{17}O_2$, 24), 273 (100), 165 (22), 153 (74). Anal. Calcd for $C_{30}H_{34}O_3$: C, 81.41; H, 7.74. Found: C, 81.29; H, 7.74.

1-[2′-(*p*-Anisyldiphenylmethoxy)ethyl]-2-methylene-6,6-dimethylcyclohexane (25). To a stirred solution of anhydrous diethyl ether (100 mL) and 1.6 M *n*-butyllithium in hexane solution (17.7 mL) at ambient temperature was added in small portions methyltriphenylphosphonium bromide (10.0 g, 0.028 mol). Once the addition was complete, the yellow mixture was stirred for 3 h. An addition funnel containing **24** (5.0 g, 11 mmol) dissolved in THF (15 mL) was attached and the contents added dropwise at room temperature. The reaction mixture was heated under reflux for 4 h and then stirred at room temperature overnight. The disappearance of the yellow color together with the absence of starting ketone, as determined by TLC, indicated the reaction was complete. The solid was filtered and washed several times with diethyl ether. The ethereal solution was washed with water and brine, dried ($MgSO_4$), and filtered. The ether was removed under reduced pressure to yield 5 g of a crude oil. The oil was column chromatographed (silica gel, EtOAc/hexane (1:9)), and the solvent was removed under reduced pressure to yield 2.0 g (43%) of product: IR (neat) 1640, 1610, 1510, 1465, 1260, 1185, 900, 820, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.84 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 2.84 (m, 1 H, CH_aO), 3.08 (m, 1 H, CH_bO), 3.80 (s, 3 H, CH_3), 4.38 (d, 1 H, =CH, J = 2.2 Hz), 4.84 (d, 1 H, =CH, J = 2.2 Hz), 6.78 (d, 2 H, Ar, J = 8 Hz), 7.22 (m, 10 H, Ar), 7.40 (d, 2 H, Ar, J = 8 Hz); MS (FAB) *m/e* (relative intensity) 274 ($M - C_{11}H_{19}O$, 24), 273 (100), 213 (17). Anal. Calcd for $C_{31}H_{36}O_2$: C, 84.54: H, 8.18. Found: C, 84.81; H, 8.36.

2-(2′-Methylene-6′,6′-dimethylcyclohexyl)ethanol (26).[12] Sodium metal (0.10 g, 45 mmol) was added to anhydrous liquid NH_3 (25 mL). The sodium dissolved immediately, and a deep blue color persisted. A solution of **25** (0.75 g, 17 mmol) dissolved in dry THF (5 mL) was added dropwise. A red color appeared immediately, and after the addition was complete, the reaction mixture was stirred for 0.5 h. The reaction was quenched by adding ethanol (10 mL) and the NH_3 allowed to evaporate. The ethanol was removed under reduced pressure, and the residue was taken up in diethyl ether, washed with water, dried ($MgSO_4$), and filtered. The ether was concentrated to yield 0.85 g of a thick oil. The oil was purified (silica gel, EtOAc/hexane (1:4)) to yield 0.20 g (71%) of product: IR (neat) 3300, 2950, 1640, 1440, 1050, 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83 (s, 3 H, CH_3), 0.92 (s, 3 h, CH_3), 3.62 (m, 2 H, CH_2O), 4.65 (d, 1 H, $=CH_a$, J = 2.2 Hz), 4.81 (d, 1 H, $=CH_b$, J = 2.2 Hz); MS *m/e* (relative intensity) 186 (M^+, 28), 150 (57), 122 (56), 107 (100). Anal. Calcd for $C_{11}H_{20}O$: C, 78.57; H, 11.90. Found: C, 78.50; H, 11.69.

1-[2′-(*p*-Toluenesulfonyl)ethyl]-2-methylene-6,6-dimethylcyclohexane (27). A solution of **26** (5.0 g, 29 mmol) and dry pyridine (50 mL) was cooled to 0 °C and treated with freshly recrystallized *p*-toluenesulfonyl chloride (11 g, 58 mmol). The solution was stored at -20 °C for 48 h. Pyridine hydrochloride precipitated as long white needles and was filtered. The solution was poured into ice and water and extracted with diethyl ether (2 × 50 mL). The combined ethereal extracts were washed with water, dried ($MgSO_4$), and filtered, and the solvent was removed under reduced pressure to yield a colorless oil. The oil was placed under high vacuum to remove residual solvent. The product solidified and was recrystallized from hexane to yield 5.0 g (75%) of a white solid: mp 43–44 °C; IR (Nujol) 1610, 1450, 1260, 1080, 900, 840, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.78 (s, 3 H, CH_3) 0.88 (s, 3 H, CH_3), 2.46 (s, 3 H, CH_3), 3.80–4.10 (m, 2 H, CH_2O), 4.20 (d, 1 H, $=CH_a$, J = 1 Hz), 4.79 (d, 1 H, =CH, J = 1 Hz), 7.35 (d, 2 H, Ar, J = 8 Hz), 7.80 (d, 2 H, Ar, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 147.6, 144.6, 133.3, 129.8, 109.9, 69.9, 49.6, 35.9, 34.5, 32.1, 28.0, 26.0, 25.7, 23.4, 21.6; MS *m/e* (relative intensity) 150 (57), 135 (81), 122 (46), 107 (100), 91 (83), 79 (83), 69 (92). Anal. Calcd for $C_{18}H_{26}O_3S$: C, 67.05; H, 8.13; S, 9.93. Found: C, 66.88; H, 8.12; S, 9.87.

1-(2′-Cyanoethyl)-2-methylene-6,6-dimethylcyclohexane (28). A stirred mixture of **27** (0.20 g, 0.6 mmol), potassium cyanide (0.21 g, 0.43 mmol), dry acetonitrile (5 mL) and dibenzo-18-crown-6 (10 mg) was stirred at room temperature for 1 h and then heated under reflux for 18 h. The solid was filtered and acetonitrile removed under reduced pressure. The residue was partitioned between ethyl acetate and water. The organic layer was separated, washed with water, dried ($MgSO_4$), filtered, and concentrated to yield an amber oil. Kugelrohr distillation gave 0.1 g (90%) of a colorless oil: IR (neat) 2245, 1640, 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 4.64 (d, 1 H, $=CH_a$, J = 1.8 Hz), 4.88 (d, 1 H, $=CH_b$); ^{13}C NMR ($CDCl_3$) δ 147.1, 120.1, 110.8, 52.7, 35.5, 34.7, 31.6, 28.0, 26.6, 23.3, 22.6, 15.7; MS *m/e* (relative intensity) 177 (M^+, 8), 162 (12), 134 (47), 121 (15), 109 (22), 93 (16), 79 (22), 40 (100). Anal. Calcd for $C_{12}H_{19}N$: C, 81.35; H, 10.73; N, 7.90. Found: C, 81.06; H, 10.70; N, 7.75.

3-(2-Methylene-6,6-dimethyl-1-cyclohexyl)propionic Acid (31). A solution of **28** (1.0 g, 60 mmol), ethanol (2 mL), and 25 N NaOH (1 mL) was heated under reflux for 18 h, at which point the evolution of NH_3 was no longer detected. The reaction mixture was poured into ice–water, and the pH was adjusted to 7 with

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(12) Julia, S.; Julia, M.; Linares, H.; Blondell, J. C. *Bull. Soc. Chim. Fr.* 1962, 1952.

concentrated HCl. The aqueous layer was extracted with diethyl ether (25 mL). The organic layer was washed with water, dried ($MgSO_4$), and filtered and the solvent removed under reduced pressure to yield a viscous oil that crystallized on standing. The solid was recrystallized from ethyl acetate/hexane to yield 1.0 g (85%) of product: mp 64–65 °C (lit.[7] mp 65–67 °C); IR (Nujol) 3600–3200, 1695, 1630, 895 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (s, 3 H, CH_3), 0.94 (s, 3 H, CH_3), 1.12 (m, 1 H, CH), 1.40–2.50 (m, 10 H, CH_2), 4.64 (d, 1 H, =CH, J = 2.2 Hz), 4.80 (t, 1 H, =CH, J = 1.2 Hz, J = 1.8 Hz), 11.00 (b s, 1 H, OH); ^{13}C NMR ($CDCl_3$) δ 180.8, 148.3, 109.9, 53.4, 35.8, 34.8, 32.7, 31.9, 28.7, 26.5, 23.5, 21.4; MS m/e (relative intensity) 196 (M^+, 35), 182 (24), 181 (97), 163 (34), 153 (50), 140 (86), 121 (76), 109 (94), 93 (74), 69 (100). Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.47; H, 10.18. Found: C, 73.44; H, 10.20.

4-(2-Methylene-6,6-dimethyl-1-cyclohexyl)butan-2-one (Dihydro-γ-ionone, 3). A stirred solution of **31** (0.40 g, 2.0 mol) in dry THF (15 mL) was cooled to 0 °C and treated rapidly with 1.5 M methyllithium in hexane (5.3 mL, 8.0 mmol). After the solution was stirred for 2 h at 0 °C, trimethylsilyl chloride (5.0 mL, 4.0 mmol) was added rapidly and the reaction allowed to warm to room temperature. The reaction mixture was poured into 1 M HCl (15 mL) while being stirred vigorously. The resulting two-phase mixture was stirred for 0.5 h then transferred to a separatory funnel and extracted twice with diethyl ether (25 mL). The combined ethereal extracts were washed with water (20 mL) and dried ($MgSO_4$) and the solvent removed under reduced pressure to give 0.37 g of crude methyl ketone. The product was purified by silica gel chromatography (hexane/EtOAc (9:1)) to yield 0.30 g (77%) of product: bp 64–66 °C (0.05 Torr) (lit.[7] mp 64–65 °C); IR (neat) 1720, 1635, 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.82 (s, 3 H, CH_3), 0.86 (s, 3 H, CH_3), 1.10–1.22 (m, 2 H, CH_2), 1.25–1.80 (m, 6 H, $(CH_2)_3$), 2.06 (s, 3 H, CH_3), 2.20–2.35 (m, 2 H, CH_2); ^{13}C NMR ($CDCl_3$) δ 209.4, 149.0, 109.5, 53.4, 42.3, 35.7, 34.8, 32.0, 30.1, 28.3, 26.5, 23.5, 20.3; MS m/e (relative intensity) 194 (M^+, 2), 180 (36), 79 (26), 161 (67), 137 (23), 136 (95), 121 (91), 95 (78), 43 (100). Anal. Calcd for $C_{13}H_{22}O$: C, 80.41; H, 11.44. Found: C, 80.78; H, 11.64.

Dehydroambliol-A (1). A suspension of 50% dispersion of sodium hydride (0.064 g, 1.3 mmol) and dry benzene (10 mL) was stirred for 0.12 h and decanted. Fresh benzene was added and the suspension stirred while **4** (0.59 g, 1.3 mmol) was added. The yellow heterogeneous mixture was stirred for 2 h, and then **3** (0.25 g, 1.3 mmol) dissolved in dry benzene (2 mL) was added dropwise. The solution was stirred for 3 h and the precipitate filtered. The filtrate was concentrated to one-third its volume, petroleum ether was added, and the solution was cooled in an ice bath. The residual triphenylphosphine oxide was removed by filtration and the filtrate concentrated to dryness to give 0.40 g of crude product. The oil was purified by silica gel chromatography (hexane) to yield 0.23 g (63%) of a 1:1 mixture of E and Z isomers.

Separation of *E* and *Z* Isomers. Separation of the isomers was accomplished by reversed-phase HPLC with use of a variable wavelength detector set at 220 nm. A Whatman C-18 (ODS-3) column was used, and the mobile phase was acetonitrile/water (3:1). The Z isomer had a retention time of 16.54 min, and the E isomer eluted at 17.60 min. Fractions (2 mL) were collected and analyzed. Fractions containing pure isomers were pooled and the solvent evaporated to give pure E and Z isomers.

Dehydroambliol-A (1a): IR ($CHCl_3$) 2925, 1618, 1420, 890 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.82 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 1.90–2.10 (m, 4 H, CH_2), 2.22 (d of d, 2 H, CH_2), 2.45 (q, 2 H, CH_2, J = 7 Hz), 4.50 (d, 1 H, =CH, J = 0.5 Hz), 4.75 (d, 1 H, =CH, J = 0.5 Hz), 5.15 (t, 1 H, =CH, J = 7 Hz), 6.28 (s, 1 H, Ar), 7.20 (s, 1 H, Ar), 7.33 (s, 1 H, Ar); ^{13}C NMR ($CDCl_3$) δ 149.4, 142.5, 138.8, 136.4, 125.0, 123.5, 111.1, 108.8, 53.5, 38.2, 36.3, 34.9, 32.5, 28.4, 28.4, 26.2, 25.1, 24.7, 23.8, 16.1; MS m/e (relative intensity) 286 (M^+, 7), 271 (26), 205 (14), 177 (40). Anal. Calcd for $C_{20}H_{30}O$: C, 83.91; H, 10.49. Found: C, 83.58; H, 10.55.

***Z* Isomer (1b):** IR ($CHCl_3$) 2925, 1620, 1420, 870 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.80 (s, 3 H, CH_3), 0.91 (s, 3 H, CH_3), 1.70–2.10 (m, 6 H, CH_2), 2.20 (q, 2 H, CH_2), 2.42 (t, 2 H, CH_2), 4.55 (d, 1 H, =CH, J = 0.5 Hz), 4.78 (d, 1 H, =CH, J = 0.5 Hz), 5.15 (t, 1 H, =CH, J = 7 Hz), 6.25 (s, 1 H, Ar), 7.20 (s, 1 H, Ar), 7.35 (s, 1 H, Ar); ^{13}C NMR ($CDCl_3$) δ 149.4, 142.5, 138.8, 136.7, 125.0, 124.1, 111.1, 108.8, 53.9, 36.6, 35.0, 32.8, 30.6, 28.5, 28.4, 26.0, 25.3, 24.7, 23.8, 23.5; MS m/e (relative intensity) 286 (M^+, 15), 271 (23), 205 (25), 177 (50). Anal. Calcd for $C_{20}H_{30}O$; C, 83.91: H, 10.49. Found: C, 83.79; H, 10.29.

2-(3-Furyl-2-(3,7,11-trimethyldodeca-2,6,10-trienyl)-1,3-dithiane (32). A solution of dithiane **6**[3] (9.0 g, 48 mmol) and dry THF (150 mL, dried over calcium hydride) under nitrogen was cooled to −60 °C and 1.6 M n-butyllithium (30 mL) in hexane was added dropwise. The temperature was kept at −60 °C for 8 h after the addition was complete. Freshly prepared (*E,E*)-farnesyl bromide (**5**; 14.12 g, 0.049 mol) dissolved in an equal volume of THF was added dropwise while the temperature was maintained at 60 °C. The reaction was kept at −60 °C for 2 h and then was allowed to warm to room temperature and stirred for an additional 10 h. The reaction was quenched with water and extracted with $CHCl_3$. The organic extracts were combined and washed with Na_2CO_3 solution followed by a brine wash. The $CHCl_3$ was dried ($MgSO_4$) and filtered and the solvent removed under reduced pressure to yield a dark oil. The oil was purified by HPLC with 3:1 hexane/ethyl acetate as eluent (R_f = 0.2) to yield 11.54 g (62%) of product: IR (neat) 2900, 1655, 1430, 1165, 865 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.53 (s, 3 H, CH_3), 1.60 (s, 3 H, CH_3), 1.61 (s, 3 H, CH_3), 1.68 (s, 3 H, CH_3), 1.72–2.22 (m, 10 H, CH_2), 2.56–2.75 (m, 2 H, CH_2), 2.75–2.95 (m, 2 H, CH_2), 5.14 (m, 3 H, =CH), 6.49 (d, 1 H, Ar), 7.39 (t, 1 H, Ar), 7.50 (m, 1 H, Ar); ^{13}C NMR ($CDCl_3$) δ 16.0, 16.5, 17.7, 25.4, 25.7, 26.4, 26.7, 27.5, 31.5, 39.7, 39.8, 42.3, 51.7, 111.2, 117.5, 124.1, 128.8, 131.1, 134.9, 139.1, 142.5, 143.2. MS m/e (relative intensity) 390 (M^+, 4), 253 (6), 187 (53), 186 (58), 185 (100), 111 (69), 69 (42). Anal. Calcd for $C_{23}H_{34}OS_2$: C, 70.76; H, 8.72; S, 16.41. Found: C, 70.52; H, 8.95; S, 16.30.

(*E,E*)-1-(3-Furyl)-4,8,12-trimethyl-3,7,11-tridecatriene (Ambliofuran, 2). Sodium metal (0.25 g, 10 mmol) in small pieces was added to a solution of **32** (0.33 g, 0.84 mmol) dissolved in anhydrous diethyl ether (10 mL) and anhydrous NH_3 (25 mL). The reaction was stirred for 0.25 h, and then ethanol was added dropwise until all the blue color disappeared. The NH_3 was allowed to evaporate, and the ethanol was removed under reduced pressure. The residue was dissolved in diethyl ether, washed with brine, dried ($MgSO_4$), and filtered. The ether was removed under reduced pressure and the residue purified by column chromatography (silica gel, EtOAc/hexane (3:1); R_f = 0.5) to yield 0.20 g (83%) of a colorless oil: IR (neat) 2920, 1665, 1440, 1028, 875 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.57 (s, 9 H, CH_3), 1.67 (s, 3 H, CH_3), 2.04 (m, 8 H, CH_2), 2.22 (q, 2 H, CH_2, J = 7 Hz), 2.40 (q, 2 H, CH_2, J = 7 Hz), 5.11 (m, 3 H, =CH), 6.26 (br s, 1 H, Ar), 7.20 (br s, 1 H, Ar), 7.32 (br s, 1 H, Ar); ^{13}C NMR ($CDCl_3$) δ 142.5, 138.9, 135.7, 134.9, 131.2, 124.9, 124.4, 124.1, 123.7, 111.1, 39.7, 28.5, 26.7, 26.5, 25.7, 25.1, 17.7, 16.0, 16.0; high-resolution mass spectrum (FAB) calcd for $C_{20}H_{31}O$ (M + 1) 287.2375, obsd, 287.2386.

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Supplementary Material Available: Table I, which compares the ^1H and ^{13}C chemical shift assignments for dehydroambliol-A (**1a**), its unnatural Z isomer **1b**, and an authentic sample of the natural product; ^1H, ^{13}C, two-dimensional (2-D), ^1H–^1H (COSY), and ^1H–^1H NOE spectra of dehydroambliol-A (E isomer) **1a** and its unnatural (Z isomer) **1b**; and ^1H–^{13}C HETCOR spectra of dehydroambliol-A (Z isomer) **1b** (11 pages). Ordering information is given on any current masthead page.