2 (X = SO_2), 5687-92-3; 3 (X = S), 110-01-0; 3 (X = SO), 1600-44-8; 3 (X = SO_2), 126-33-0; 4 (X = S), 1613-51-0; 4 (X = SO_2), 4988-33-4; 5 (X = S), 75-18-3; 5 (X = SO), 67-68-5; 5 (X = SO_2), 67-71-0.

Supplementary Material Available: Table IV, giving the bond lengths and bond angles of compounds 2–5 from the geometries optimized with force-field MM2 calculations, and Table V, giving the calculated (ab initio STO-3G*) atomic charges on sulfur and α carbons, the overlap populations of S–O and C–S bonds, and the HOMO–LUMO energy differences for compounds 1–5 (2 pages). Ordering information is given on any current masthead page.

Synthesis of Cembrane Natural Products via [2,3] Wittig Ring Contraction of Propargylic Ethers

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A new route to the cembranoid carbon skeleton has been devised. Accordingly, the 17-membered ether **15** underwent facile [2,3] Wittig rearrangement to the 1*R**,2*R** 14-membered carbocycle **16** upon treatment with *n*-BuLi in THF–hexanes at −78 °C. In THF–HMPA the rearrangement of **15** gave mainly the isomeric 1*R**,2*S** carbocycle **17**. Directed hydroalanation of **16** followed by trapping with I_2 yielded the (*Z*)-vinyl iodide **21**. This was further elaborated via Pd-catalyzed carbonylation to the butenolide **28**, which was reduced to diol **29**. The monoacetate **30** underwent hydrogenolysis with Li/NH_3 to give epimukulol **18**. Hydromagnesiation of the alkynol **16** followed by carboxylation and reduction afforded (±)-desoxyasperdiol (**34**).

In recent years the cembrane diterpenes have emerged as a major class of natural products.[1] Of widespread occurrence in marine and terrestrial organisms this structurally diverse family of 14-membered carbocycles has increasingly attracted the attention of synthetic organic chemists. A major problem in cembrane synthesis centers about the efficient construction of the carbocyclic ring with control of sp^2 and sp^3 stereochemistry. Although carbocyclization has been successfully employed in several total syntheses, the efficiency and stereoselectivity of such processes are highly substrate dependent.[2]

As an alternative to direct carbocyclization we formulated a strategy based upon ring contraction of heteromacrocyclic intermediates as a possible route to the cembrane skeleton.[3] The [2,3] Wittig rearrangement (Figure 1) of allylic ethers seemed well suited to this end as previous studies on acyclic systems had established that a high degree of regio- and stereoselectivity was possible for such reactions.[4] The additional constraints engendered by the macrocyclic ring were expected to facilitate the rearrangement by holding the reacting centers in close proximity. The advantages of the approach would derive from the expectedly greater ease of heterocyclic over carbocyclic ring formation and the ensuing direct and stereocontrolled formation of the β-isopropenyl alcohol moiety on the ring-contracted product.

To test the proposed synthetic strategy we selected the 17-membered ether **15** for initial study. A propargylic rather than an allylic ether was chosen for two reasons. (1) Propargylic ethers are known to rearrange with high regio- and stereoselectivity in acyclic systems.[4] (2) The resulting propargylic alcohol offers the potential for conversion to a variety of cembranes through appropriate manipulation of the acetylenic grouping.

The synthesis of ether **15** was readily accomplished from the acetate **2** of *trans,trans*-farnesol (**1**).[5] Selective allylic oxidation of the *E*-isopropylidene methyl group was effected with SeO_2–TBHP[6] according to the procedure developed by Sharpless for the analogous oxidation of geranyl

(1) For a comprehensive review of cembranoid natural products isolated through 1977; see: Weinheimer, A. J.; Chang, C. W.; Matson, J. A. *Fortschr. Chem. Org. Naturst.* **1979**, *36*, 281. For a leading reference on tobacco cembranoids, see: Wahlberg, I.; Forsblom, I.; Vogt, C.; Eklund, A. M.; Nishida, T.; Enzell, C. R.; Berg, J. E. *J. Org. Chem.* **1985**, *50*, 4527.

(2) Cyclization methodology. (a) Ni-promoted allylic coupling: Dauben, W. G.; Beasley, G. H.; Broadhurst, M. D.; Muller, B.; Peppard, D. J.; Pesnelle, P.; Suter, C. *J. Am. Chem. Soc.* **1974**, *96*, 4723. Dauben, W. G.; Beasley, G. H.; Broadhurst, M. D.; Muller, B.; Peppard, D. J.; Pesnelle, P.; Suter, C. *J. Am. Chem. Soc.* **1975**, *97*, 4973. Crombie, L.; Kneen, G.; Pattenden, G. *J. Chem. Soc., Chem. Commun.* **1976**, 66. (b) Alkylation of sulfur-stabilized carbanions: Kodama, M.; Matsuki, Y.; Ito, S. *Tetrahedron Lett.* **1975**, 3065. Kodama, M.; Matsuki, Y.; Ito, S. *Tetrahedron Lett.* **1981**, *22*, 4275. Takayanagi, H.; Uyehara, T.; Kato, T. *J. Chem. Soc., Chem. Commun.* **1978**, 359. Dauben, W. G.; Saugier, R. K.; Fleishhauer, I. *J. Org. Chem.* **1985**, *50*, 3767. Marshall, J. A.; Cleary, D. G. *J. Org. Chem.* **1986**, *51*, 858. (c) Alkylation of protected cyanohydrins: Takahashi, T.; Nemoto, H.; Tsuji, J. *Tetrahedron Lett.* **1983**, *24*, 3485. (d) Friedel–Crafts acylation: Kato, T.; Kobayashi, T.; Kitahara, Y. *Tetrahedron Lett.* **1975**, 3299. Kato, T.; Suzuki, M.; Kobayashi, T.; Moore, B. P. *J. Org. Chem.* **1980**, *45*, 1126. Kitahara, Y.; Kato, T.; Kobayashi, T.; Moore, B. P. *Chem. Lett.* **1976**, 219. Kato, T.; Yen, C. C.; Kobayashi, T.; Kitahara, Y. *Chem. Lett.* **1976**, 1191. Kato, T.; Suzuki, M.; Takahashi, M.; Kitahara, Y. *Chem. Lett.* **1977**, 465. Kato, T.; Yen, C. C.; Uyehara, T.; Kitahara, Y. *Chem. Lett.* **1977**, 565. Kato, T.; Suzuki, M.; Nakazima, Y.; Shimizu, K.; Kitahara, Y. *Chem. Lett.* **1977**, 705. Aoki, M.; Tooyama, Y.; Uyehara, T.; Kato, T. *Tetrahedron Lett.* **1983**, *24*, 2267. (e) Homoaldol: Still, W. C.; Mobilio, D. *J. Org. Chem.* **1983**, *48*, 4785. Marshall, J. A.; DeHoff, B. S.; Crooks, S. L. *Tetrahedron Lett.* **1987**, *28*, 527. (f) Horner–Emmons–Wittig condensation: Tius, M. A.; Fauq, A. H. *J. Am. Chem. Soc.* **1986**, *108*, 1035. Marshall, J. A.; DeHoff, B. S. *Tetrahedron Lett.* **1986**, *27*, 4873.

(3) Preliminary communication: Marshall, J. A.; Jenson, T. M.; DeHoff, B. S. *J. Org. Chem.* **1986**, *51*, 4316. For applications to ten-membered rings, see: Takahashi, T.; Nemato, H.; Kanda, Y.; Tsuji, J.; Fujise, Y. *J. Org. Chem.* **1986**, *51*, 4315. Marshall, J. A.; Lebreton, J.; DeHoff, B. S.; Jenson, T. M. *Tetrahedron Lett.* **1987**, *28*, 732.

(4) For recent work on the [2,3] Wittig rearrangement, see: (a) Mikami, K.; Azuma, K.; Nakai, T. *Tetrahedron* **1984**, *40*, 2303 and references therein. (b) Marshall, J. A.; Jenson, T. M. *J. Org. Chem.* **1984**, *49*, 1707. (c) Midland, M. M.; Kwon, Y. C. *Tetrahedron Lett.* **1985**, *26*, 5017 and references therein.

(5) *trans,trans*-Farnesol was obtained from Aldrich Chemical Co., Milwaukee, WI.

(6) Abbreviations: DIBAH = diisobutylaluminum hydride; DMAP = 4-(*N,N*-dimethylamino)pyridine; HMPA = hexamethylphosphoric triamide; KHMDS = potassium bis(trimethylsilyl)amide; Red-Al = sodium bis(2-methoxyethoxy)aluminum hydride; TBHP = *tert*-butyl hydroperoxide; TBS = *tert*-butyldimethylsilyl; THF = tetrahydrofuran.

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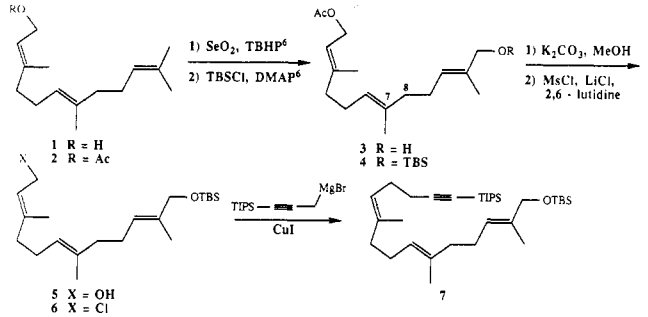
Table I. Cyclization of Halo Alcohols

12 Y = OH, Z = Cl
13 Y = Cl, Z = OH
14 Y = I, Z = OH

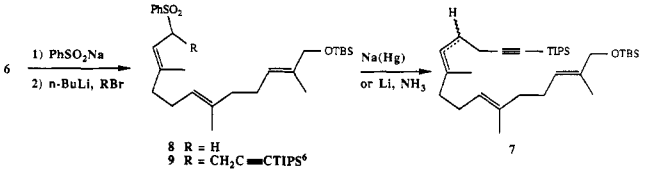
15

entry	halide	Z	Y	base	solv system	temp	yield, %
1	13	OH	Cl	NaH	PhH/18-crown-6	reflux	30
2	13	OH	Cl	KH	PhH/18-crown-6	reflux	<10
3	13	OH	Cl	KHMDS	PhH/18-crown-6	20–25 °C	<10
4	13	OH	Cl	KO-*t*-Bu	THF/HMPA	reflux	<10
5	13	OH	Cl	NaH	DME/HMPA	reflux	10
6	13	OH	Cl	NaH	PhH/HMPA	reflux	12
7	13	OH	Cl	NaOH	PhH/n-Bu_4NHSO_4	20–25 °C	34
8	14	OH	I	NaOH	PhH/n-Bu_4NHSO_4	20–25 °C	29
9	14	OH	I	NaH	THF/HMPA	reflux	45
10	14	OH	I	NaH	PhH/18-crown-6	reflux	55
11	14	OH	I	EtMgBr	THF/HMPA	reflux	28
12	12	Cl	OH	NaOH	PhH/n-Bu_4NHSO_4	20–25 °C	50
13	12	Cl	OH	EtMgBr	THF/HMPA	reflux	71

acetate.[7] As expected, this oxidation was less selective than that of its lower isopropenylogue owing to competing oxidation of the internal allylic centers leading to isomeric alcohols (OH at C8 and the C7 CH_3). With an excess of farnesyl acetate we were able to produce the desired allylic alcohol **3** in 25% yield (14% isolated with 56% recovery of **2**). Secondary and some primary alcohol impurities were removed by chromatography. Further purification was effected by selective silylation with TBSCl[6] and DMAP,[6] which gave the ether acetate **4** only slightly contaminated with material presumed to arise from oxidation of the internal methyl group.



The allylic chloride **6** was prepared via cleavage of the acetate **4** and treatment of the resulting alcohol with MsCl and LiCl according to the procedure of Collington and Meyers.[8] Homologation of this chloride to the acetylene **7** was effected via coupling with TIPS-protected[6] propargylmagnesium bromide–CuI in high yield with virtually no contamination by S_N2' or allenic byproducts.[9] Initially we examined an alternative coupling strategy involving the sulfone **8** derived from chloride **6**. Lithiation followed by



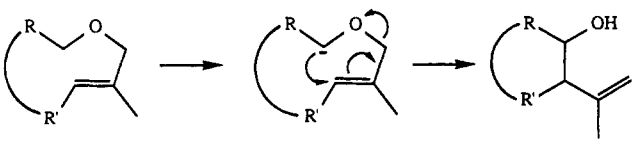
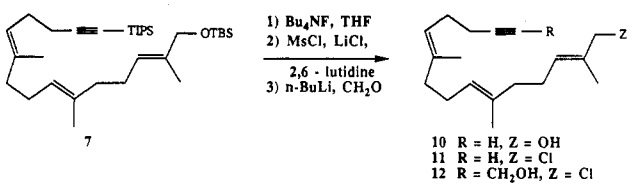


Figure 1. [2,3] Wittig ring contraction.

alkylation with TIPS-protected propargyl bromide afforded the allylic sulfone **9** in 70% yield, but reductive cleavage of the sulfone grouping resulted in a mixture of double bond isomers. The use of propargylmagnesium bromide itself as the coupling partner for chloride **6** was not examined because model studies with geranyl chloride showed appreciable formation of allenic byproducts.[10]

Cleavage of the silyl protecting groups from the coupled alkyne **7** led to the alcohol **10** in high yield. This product could be separated from isomeric allylic alcohol impurities by careful chromatography. Application of the Collington–Meyers procedure to alcohol **10** afforded chloride **11** in 88% yield.[8] Deprotonation with 1 equiv of n-BuLi followed by addition of paraformaldehyde gave the chloro alcohol **12**.



In our initial efforts to prepare the 17-membered ether **15** we examined cyclizations of the isomeric chloro alcohol **13** and the related iodo alcohol **14** (Table I).[11] These intermediates were prepared from acetylenic alcohol **10** via TBS protection, addition of formaldehyde, Collington–Meyers chloride[8] or Corey iodide formation,[12] and deprotection. Acceptable cyclization results were obtained with NaH as the base in benzene-18-crown-6 or THF–HMPA[6] as solvent. Potassium bases KH, KHMDS,[6] and KO-*t*-Bu caused immediate decomposition of the halo alcohols with the formation of deeply colored products. Cyclization of

(7) Umbriet, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 5526. Marshall, J. A.; Andrews, R. C. *J. Org. Chem.* **1985**, *50*, 1602.
(8) Collington, E. W.; Meyers, A. I. *J. Org. Chem.* **1971**, *36*, 3044.
(9) Corey, E. J.; Rücker, C. *Tetrahedron Lett.* **1982**, *23*, 719.
(10) Corey, E. J.; Kirst, H. A. *Tetrahedron Lett.* **1968**, 5041. Ireland, R. E.; Dawson, M. J.; Lipinski, C. A. *Tetrahedron Lett.* **1970**, 2247.
(11) For details, see: Jenson, T. M. Ph.D. Dissertation, University of South Carolina, 1986.
(12) Corey, E. J.; Pyne, S. G.; Su, W. *Tetrahedron Lett.* **1983**, *24*, 4883.

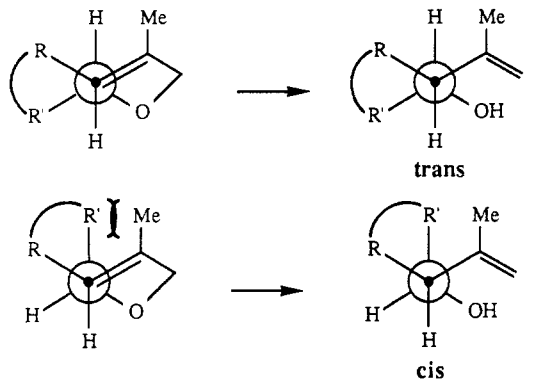
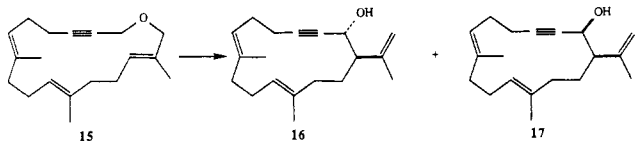


Figure 2. Diastereocontrol in [2,3] Wittig ring contractions.

Table II. [2,3] Wittig Ring Contraction of Cyclic Ether 15



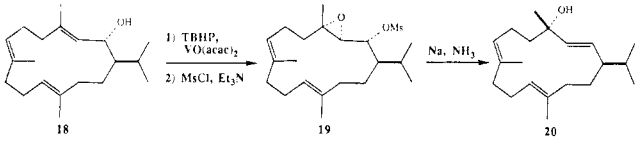
entry	solv system	temp, °C	16/17	yield, %
1	THF	−78	70:30	80
2	10% THF in hexanes	−78	71:29	73
3	10% THF in hexanes	−20	82:18	78
4	4% HMPA in THF	−78	25:75	76
5	8% HMPA in THF	−78	16:84	49
6	20% HMPA in THF	−78	12:88	45

iodo alcohol **14** proceeded in moderate yield with EtMgBr as the base in THF–HMPA.[6] Best results were obtained by using this base solvent combination on the chloro alcohol **12**, whereupon the ether **15** was secured in 71% yield.

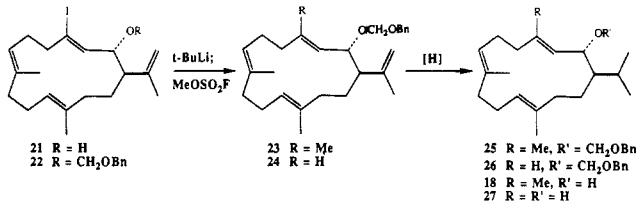
Treatment of cyclic ether **15** with *n*-BuLi in THF at −78 °C led to facile rearrangement, giving rise to a 70:30 mixture of trans and cis alcohols **16** and **17** in over 80% yield (Table II). The use of THF–hexane as solvent at somewhat higher temperature improved this ratio to 82:18. The rearrangement reactions were complete in 2 h or less at −78 °C compared to 8 h or more for comparable acyclic systems.[11,4] Stereochemical assignments were originally made on mechanistic grounds (Figure 2) and by comparison of the chemical shifts of the carbinyl protons with those of the related allylic alcohols mukulol (**31**) and epimukulol (**18**).[13] The validity of these assignments was established by subsequent transformations as described below.

We have previously observed enhanced *E*/*Z* stereoselectivity in [2,3] Wittig rearrangements of macrocyclic diallylic ethers employing THF–HMPA as the solvent.[4b] The use of these conditions with ether **15** led to an unexpected reversal of stereochemistry (Table II), giving the cis isomer **17** as the major product. This unprecedented result provided ready access to intermediates potentially convertible to natural cembranes with both cis and trans stereochemistry at the C1 and C2 positions.

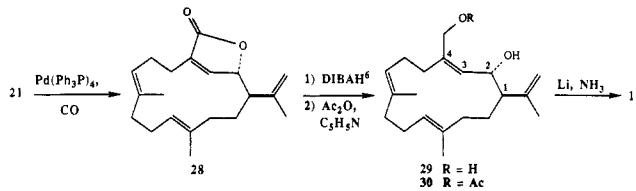
As our first effort in this direction we selected epimukulol **18**, a synthetic intermediate that has been transformed by Kato to the tobacco cembrane thunbergol (**20**).[14]



Directed hydroalanation of the trans propargylic alcohol **16** with Red-Al[6] followed by treatment with iodine afforded the vinyl iodide **21** in 87% yield.[15] This iodide proved surprisingly unreactive toward coupling with $LiMe_2Cu$.[16] It was recovered unchanged after several days' exposure to a large excess of the reagent at −78 to 0 °C. An alternative methylation procedure was therefore explored. Accordingly, alcohol **21** was protected as the (benzyloxy)methyl ether **22**. Lithiation with *t*-BuLi and subsequent addition of methyl fluorosulfonate afforded the methylated product **23** and the protonolysis product **24** as a 4:1 mixture in 76% overall yield. Unfortunately, this mixture could not be separated nor could the protonolysis be avoided despite our best efforts at excluding moisture. Consequently it was carried through the subsequent steps. Selective hydrogenation of the isopropenyl double bond was achieved with Wilkinson's catalyst, giving the isopropyl derivative **25** in 84% yield as an inseparable 4:1 mixture with **26**.[17] Hydrogenolysis of the (benzyloxy)methyl group with Na in NH_3 afforded epimukulol (**18**) contaminated with the desmethyl analogue **27**.



Unable to prevent the formation of the protonolysis byproduct **24**, we considered alternative approaches to epimukulol (**18**). Stille has shown that vinyl iodides are readily carbonylated with Pd(0) catalysts.[18] The reaction proceeds with retention of stereochemistry and is compatible with a free hydroxyl grouping. When applied to vinyl iodide **21** Stille's procedure led to the butenolide **28** in 56% yield. Reduction with DIBAH afforded the crystalline diol **29**, the 3*Z* isomer of desoxyasperdiol.[19] Selective acetylation of the primary alcohol of **29** with acetic anhydride–pyridine yielded the monoacetate **30**. Dissolving metal hydrogenolysis of this acetate with Li/NH_3 was accompanied by reduction of the isopropenyl double bond, affording epimukulol (**18**) directly in 72% yield. The identity of this material was established by spectral comparison with an authentic sample.[20] Reduction of the isopropenyl double bond in the hydrogenolysis reaction may be facilitated by proton donation from the proximate



(13) Kato, T.; Kobayashi, T.; Kugamai, T.; Kitahara, Y. *Synth. Commun.* **1976**, *6*, 365. Prasad, R. S.; Dev, S. *Tetrahedron* **1976**, *32*, 1437.

(14) Kato, T.; Suzuki, M.; Takahashi, M.; Kitahara, Y. *Chem. Lett.* **1977**, 465.

(15) Corey, E. J.; Posner, G. H. *J. Am. Chem. Soc.* **1968**, *90*, 5615. Denmark, S. E.; Jones, T. K. *J. Org. Chem.* **1982**, *47*, 4595.

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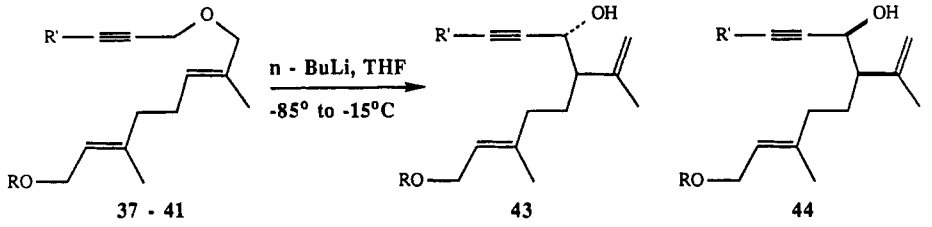
(17) Djerassi, C.; Gutzwiller, J. *J. Am. Chem. Soc.* **1966**, *88*, 4537.

(18) Cowell, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 4193. Baillargeon, V. P.; Stille, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 452.

(19) Marshall, J. A.; Cleary, D. G. *J. Org. Chem.* **1986**, *51*, 858. Aoki, M.; Tooyama, Y.; Uyehara, T.; Kato, T. *Tetrahedron Lett.* **1983**, *24*, 2267.

(20) We are indebted to Professors Kato and Dev (ref 13) for spectra and samples.

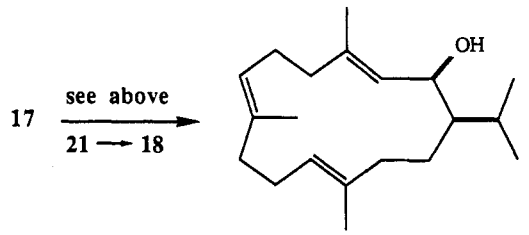
Table III. [2,3] Wittig Rearrangements of Acyclic Propargylic Ethers



entry	ether	R	R'	cosolv	yield, %	43/44	
1	**37**	H	H	TMEDA	45	87:13[a]	
2	**38**	MOM	H	none	28	67:33[a]	
3	**40**	MOM	CH_2OH	none	none	50	67:33[b]
4	**40**	MOM	CH_2OH	TMEDA	63	67:33[b]	
5	**40**	MOM	CH_2OH	HMPA	15	67:33[b]	
6	**41**	TBS	CH_2OH	none	none	35	67:33[b]
7	**41**	TBS	CH_2OH	TMEDA	57	55:45[b]	

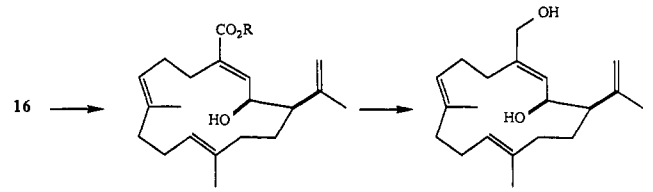
[a] Ratios derived from high-field ^1H NMR analysis of the acetate derivative. [b] Ratios derived from ^1H NMR analysis.

hydroxyl grouping. When applied to the isomeric cis propargylic alcohol **17** the foregoing sequence yielded racemic mukulol (**31**) identified through spectral comparison.



31

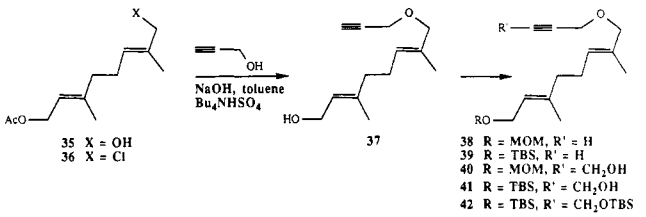
The hydroalanation–iodination–carbonylation sequence effects a net regioselective trans hydroformylation of the triple bond in the propargylic alcohols **16** and **17**. We were also interested in the equivalent cis addition process as a possible route to desoxyasperdiol (**34**). To that end, the titanocene-promoted hydromagnesiation reaction seemed ideally suited.[21] Indeed, addition of isobutylmagnesium bromide and titanocene dichloride to the trans alcohol **16** and subsequent introduction of gaseous carbon dioxide gave rise to the carboxylic acid **32**. The ester **33** was secured in 61% overall yield upon treatment with diazomethane. Reduction with DIBAH[6] afforded crystalline racemic desoxyasperdiol (**34**) in 84% yield.[22]



32 R = H
33 R = Me

34

Thus, [2,3] Wittig rearrangement of the 17-membered ether **15** proceeds readily and stereoselectively to the ring-contracted products **16** and **17**. To help assess the role of the macrocyclic ring in promoting this rearrangement, we examined the [2,3] Wittig rearrangement of ethers **37–41**, acyclic analogues of **15**. These ethers were prepared from alcohol **35**, the allylic oxidation product of geranyl acetate.[7] Coupling of the derived chloride **36**[8] with propargyl alcohol under phase-transfer conditions yielded ether **37**. This was protected as the MOM[6] or TBS[6] derivative **38** or **39**, which was then condensed with formaldehyde via the bromomagnesium acetylide to give the alcohol **40** or **41**.



35 X = OH
36 X = Cl

37

38 R = MOM, R' = H
39 R = TBS, R' = H
40 R = MOM, R' = CH_2OH
41 R = TBS, R' = CH_2OH
42 R = TBS, R' = CH_2OTBS

Treatment of the foregoing ethers with *n*-BuLi in THF at −85 °C followed by warming to −15 °C overnight afforded mixtures of the rearranged alcohols **43** and **44** (Table III). These reactions were considerably slower and less efficient than those of the cyclic ether **15**. Loss of the propargylic grouping leading to 8-hydroxygeraniol (from **37**) or its MOM (from **38** or **40**) or TBS derivative (from **41**) constituted the major side reaction. Attempted rearrangement of the bis(TBS ether) **42** gave none of the desired product. The use of TMEDA as a cosolvent generally improved the yield and altered the stereochemistry of the process but not dramatically (entries 3, 4 and 6, 7). HMPA adversely affected the yield without changing the stereoselectivity (entries 3 and 5).

The foregoing results indicate that the cyclic nature of ether **15** leads to major benefits for the [2,3] Wittig rearrangement. Presumably the effect stems from favorable juxtaposition of the two reacting centers. It is worth noting that the rearrangements summarized in Table III are generally less efficient than those reported for simpler prototype acyclic systems where yields in excess of 70% and stereoselectivities of over 9:1 are often observed.[4] The discrepancies may be related to the additional ether functions present in **37–42** which coordinate unproductively with the lithium counterion or possibly to the increased steric requirements of the allylic ether double bond substituents.

Experimental Section

(2*E*,6*E*,10*E*)-3,7,11-Trimethyl-12-[(*tert*-butyldimethylsilyl)oxy]-2,6,10-dodecatrien-1-ol (5). To a stirred mixture of 1.46 g (13.2 mmol) of SeO_2 and 5.7 g (57.0 mmol) of *t*-BuOOH in 90 mL of CH_2Cl_2 at 0 °C was added 13.81 g (52.2 mmol) of farnesyl acetate (**2**) in 15 mL of CH_2Cl_2 dropwise. After 1.5 h saturated brine was added, and the product was isolated by extraction with ether to afford 16.3 g of a light yellow oil. Chromatography on silica gel eluting with 15–20% EtOAc–hexanes afforded 7.67 g (56%) of recovered acetate **2**, 1.17 g (8%) of a

(21) Sato, F.; Ishikawa, H.; Watanabe, H.; Miyake, T.; Sato, M. *J. Chem. Soc., Chem. Commun.* **1981**, 718.
(22) We are indebted to Professor Kato for spectra and a sample of desoxyasperdiol.

mixture containing alcohol **3** and isomers, and 2.11 g (14%) of alcohol **3** slightly contaminated by isomeric alcohols according to TLC and ^{1}H NMR analysis. A solution of 3.88 g (13.8 mmol) of this alcohol prepared as described above, 2.5 g (16.6 mmol) of TBSCl,[6] 3.5 mL (25.0 mmol) of triethylamine, and a catalytic amount of DMAP[6] in 20 mL of CH_2Cl_2 at room temperature was stirred for 1 h. Water was added, and the mixture was extracted twice with ether. The combined organic layers were washed with saturated aqueous $CuSO_4$ and water and dried over anhydrous $MgSO_4$. Removal of solvent left an oil (**4**), which was dissolved in 20 mL of methanol and treated with a catalytic amount of anhydrous K_2CO_3 at 0 °C for 3 h. Water was added, and the solution was extracted three times with ether. The ether extracts were washed with water and dried over anhydrous $MgSO_4$. Removal of solvent left an oil, which was purified by column chromatography on silica gel (15% ethyl acetate–hexanes), affording 4.3 g (88%) of alcohol **5**: IR (film) ν 3310, 2925, 2850, 1470, 1390, 1260 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.03 (s, $Si(CH_3)_2$), 0.88 (s, $SiC(CH_3)_3$), 1.28 (br s, OH), 1.57, 1.58, 1.66 (s, vinyl CH_3s), 1.96–2.11 (m, allylic CH_2s), 3.98 (s, CH_2OTBS), 4.12 (br d, J = 4.3 Hz, CH_2OH), 5.10 (t, J = 6 Hz, vinyl H), 5.34 (t, J = 7 Hz, vinyl H), 5.39 (t, J = 6 Hz, vinyl H). Anal. Calcd for $C_{21}H_{40}O_2Si$: C, 71.53; H, 11.43. Found: C, 71.48; H, 11.50.

(2*E*,6*E*,10*E*)-2,6,10-Trimethyl-12-chloro-2,6,10-dodecatrienyl *tert*-Butyldimethylsilyl Ether (6). The procedure of Collington and Meyers was followed.[8] A solution of anhydrous LiCl (0.66 g, 15.7 mmol) in 10 mL of DMF was cooled to 0 °C, and a solution of 3.4 g (9.7 mmol) of allylic alcohol **5** in 2.3 mL (19.8 mmol) of 2,6-lutidine was added. After 20 min, 1.1 mL (14.2 mmol) of methanesulfonyl chloride was added, followed after 7 h by water and ether. The layers were separated, and the organic layer was washed with water. The combined aqueous layers were extracted with ether, and the extracts were washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to yield 3.67 g of chloride **6** as a yellow liquid: IR (film) ν 2930, 2840, 1660, 1460, 1260, 1070, 840, 780 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.04 (s, $Si(CH_3)_2$), 0.89 (s, $SiC(CH_3)_3$), 1.58 (br s, vinyl CH_3, 6 H), 1.67 (s, OH), 1.71 (s, vinyl CH_3), 1.96–2.14 (m, allylic CH_2s), 3.98 (s, CH_2OTBS), 4.08 (d, J = 8 Hz, CH_2Cl), 5.1 (m, vinyl H), 5.34 (t, J = 7 Hz, vinyl H), 5.42 (m, vinyl H). This material decomposed on standing; satisfactory analytical values could not be obtained.

(2*E*,6*E*,10*E*)-2,6,10-Trimethyl-2,6,10-pentadecatrien-14-yn-1-ol (10). To a slurry of 0.78 g (4.1 mmol) of CuI in 10 mL of THF at −78 °C was added 16.7 mL of 0.6 M 3-(triisopropylsilyl)-2-propynylmagnesium bromide[9] dropwise. The resulting slurry was stirred at −78 °C for 30 min, and the mixture was transferred to a −20 °C bath. After 15 min, 2.69 g (7.2 mmol) of chloride **6** in 4 mL of THF was added. The mixture was stirred for 3 h at −20 °C, then 10 mL of saturated aqueous NH_4Cl was added, the mixture was allowed to reach room temperature, and ether was added. The organic layer was washed with 3% NH_4OH until the washings were clear, the blue aqueous layers were extracted with ether, and the combined extracts were washed with water and dried over $MgSO_4$. Removal of solvent left an oil, which was dissolved in 10 mL of THF and treated with 22 mL of 1 M tetra-*n*-butylammonium fluoride. The dark solution was stirred overnight and then poured into 50 mL of water. The solution was extracted three times with ether, and the combined extracts were washed with water and dried over anhydrous $MgSO_4$. Removal of solvent left an oil, which was purified by column chromatography on silica gel (15% ether–hexanes), providing 1.16 g (62%) of acetylene **10**: IR (film) ν 3280, 2920, 2845, 1450, 1390, 1015 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (br s, OH), 1.58, 1.60, 1.64 (s, vinyl CH_3s), 1.92 (t, J = 2 Hz, acetylenic H), 1.96–2.24 (m, allylic CH_2s, propargylic CH_2), 3.96 (s, CH_2OH), 5.08–5.16 (m, vinyl H, 2 H), 5.36 (t, J = 5 Hz, vinyl H). Satisfactory analytical values could not be obtained owing to the presence of an inseparable UV-active impurity.

(2*E*,6*E*,10*E*)-2,6,10-Trimethyl-1-chloro-2,6,10-pentadecatrien-14-yne (11). Following the procedure described for the preparation of allylic chloride **6**, 0.10 g (2.4 mmol) of LiCl, 0.40 g (1.5 mmol) of the allylic alcohol **10**, and 0.35 mL (3.0 mmol) of 2,6-lutidine in 2 mL of DMF afforded 0.49 g of chloride **11** as a yellow liquid: IR (film) ν 3275, 2900, 1440, 1380, 1270, 1180 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 1.58, 1.60, 1.71 (s, vinyl CH_3s), 3.99 (s, CH_2Cl), 5.0–5.2 (m, vinyl H, 2 H), 5.48 (t, J = 6.5 Hz, vinyl H). The analytical sample was secured by chromatography on silica gel. Anal. Calcd for $C_{18}H_{27}Cl$: C, 77.53; H, 9.76. Found: C, 77.38; H, 9.82.

(6*E*,10*E*,14*E*)-7,11,15-Trimethyl-16-chloro-6,10,14-hexadecatrien-2-yn-1-ol (12). To a solution of 0.40 g (1.4 mmol) of acetylene **11** in 6 mL of THF at −78 °C was added 0.75 mL of 2.3 M *n*-BuLi. The resulting dark solution was stirred at −78 °C for 1 h, and then 0.10 g (3.3 mmol) of paraformaldehyde was added. The mixture was slowly warmed to room temperature and stirred for 0.5 h. The reaction was quenched with saturated aqueous NH_4Cl, then diluted with water, and extracted with ether. The extracts were dried over anhydrous $MgSO_4$, and the solvent was removed. The resulting oil was purified by column chromatography on silica gel (15% ethyl acetate–hexanes), affording 0.31 g (70%) of alcohol **12**: IR (film) ν 3320, 2910, 1440, 1390, 1270, 1115 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.52 (t, J = 6 Hz, OH), 1.58, 1.60, 1.71 (s, vinyl CH_3s), 1.99–2.15 (m, allylic CH_2s), 2.21 (br s, propargylic CH_2), 3.99 (s, CH_2Cl), 4.22 (d, J = 6 Hz, CH_2OH), 5.07–5.14 (m, vinyl H, 2 H), 5.49 (t, J = 6 Hz, vinyl H). Anal. Calcd for $C_{19}H_{29}ClO$: C, 73.88; H, 9.46. Found: C, 73.66; H, 9.51.

(7*E*,11*E*,15*E*)-8,12,16-Trimethyl-1-oxa-7,11,15-cycloheptatrien-3-yne (15). To a stirred, cooled (0 °C) solution of 0.90 g (2.9 mmol) of the propargylic alcohol **12** and 0.01 g of 1,10-phenanthroline in 1.9 mL (11.5 mmol) of HMPA[6] and 150 mL of THF was added dropwise 1.9 mL (2.9 mmol) of 1.5 M ethylmagnesium bromide in THF. After 5 min the cold bath was removed, and the reaction solution was heated to reflux. After 4 h the mixture was cooled to room temperature, saturated aqueous NH_4Cl was added, the layers were separated, and the aqueous layer was extracted with ether. The combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford 0.70 g (79%) of a yellow liquid. Purification by column chromatography on silica gel (2% ethyl acetate–hexane) gave 0.65 g (71%) of ether **15** as a colorless liquid: IR (film) ν 2900, 1420, 1350, 1120, 1060 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.55 (s, vinyl CH_3, 3 H), 1.61 (s, vinyl CH_3, 6 H), 2.0–2.4 (m, allylic CH_2, 12 H), 4.0 (m, carbinyl CH_2, 4 H), 5.16 (t, J = 6 Hz, vinyl H), 5.34 (t, J = 6 Hz, vinyl H), 5.51 (t, J = 6 Hz, vinyl H). Anal. Calcd for $C_{19}H_{28}O$: C, 83.68; H, 10.36. Found: C, 83.53; H, 10.29.

***rel*-(1*R*,2*R*)-(5*E*,9*E*)-2-Isopropenyl-5,9-dimethyl-5,9-cyclotetradecadien-13-yn-1-ol (16).** To a stirred, cooled (−78 °C) solution of 0.101 g (0.37 mmol) of the cyclic ether **15** in 3.6 mL of hexanes and 0.4 mL of THF was added 0.30 mL (0.69 mmol) of 2.3 M *n*-BuLi in hexane. After 2 h water was added, the reaction mixture was warmed to room temperature, and the layers were separated. The aqueous layer was extracted with ether, and the combined extracts were washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford 0.11 g of a yellow liquid. Purification by column chromatography on silica gel (5% ethyl acetate–hexane) gave 0.021 g (21%) of the cis propargylic alcohol **17**: IR (film) ν 3430, 2900, 1640, 1440, 1380, 1030, 890 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.56, 1.57, 1.77 (s, vinyl CH_3s), 4.46 (br s, carbinyl H), 4.83, 4.96 (s, vinyl H, 2 H), 5.1–5.2 (m, vinyl H, 2 H). Continued elution afforded 0.053 g (52%) of the trans propargylic alcohol **16**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.58 (s, vinyl CH_3, 6 H), 1.62 (s, vinyl CH_3), 4.06 (d, J = 9 Hz, carbinyl H), 4.82, 4.98 (s, vinyl H, 2 H), 5.15–5.25 (m, vinyl H, 2 H). Anal. Calcd for $C_{19}H_{28}O$: C, 83.68; H, 10.36. Found: C, 83.67; H, 10.39.

***rel*-(1*R*,2*S*)-(5*E*,9*E*)-2-Isopropenyl-5,9-dimethyl-5,9-cyclotetradecadien-13-yn-1-ol (17).** To a stirred, cooled (−78 °C) solution of 0.070 g (0.26 mmol) of the propargylic ether **15** and 0.10 mL (0.60 mmol) of HMPA[6] in 2.6 mL of THF was added 0.20 mL (0.46 mmol) of 2.3 M *n*-BuLi. After 35 min water was added, the reaction mixture was warmed to room temperature, and the layers were separated. The aqueous layer was extracted with ether, and the combined extracts were washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford 0.078 g of a yellow liquid. Purification by column chromatography on silica gel (5% ethyl acetate–hexane) gave 0.046 g (57%) of the cis propargylic alcohol **17**. Continued elution afforded 0.013 g (19%) of the trans alcohol **16**.

***rel*-(1*R*,2*R*)-(5*E*,9*E*,13*Z*)-2-Isopropenyl-5,9-dimethyl-13-iodo-5,9,13-cyclotetradecatrien-1-ol (21).** To a stirred solution of 0.072 g (0.26 mmol) of the trans propargylic alcohol **16** in 1.5 mL of THF was added 0.13 mL (0.44 mmol) of 3.4 M Red-Al.[6] After being stirred at room temperature for 13.5 h the reaction solution was cooled to −78 °C, and 0.20 g (0.79 mmol) of iodine in 1 mL of THF was added dropwise. After 3 min the cold bath was removed, and after an additional 7 min saturated aqueous Rochelle's salt was added followed by saturated aqueous $Na_2S_2O_3$. The layers were separated, and the organic layer was washed with saturated aqueous $Na_2S_2O_3$. The aqueous layers were combined and extracted with ether. The combined extracts were washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford 0.104 g (98%) of an opaque liquid. Column chromatography on silica gel (10% ethyl acetate–hexane) gave 0.092 g (87%) of iodide **21** as a clear, colorless liquid: IR (film) ν 3300, 3060, 2900, 1640, 1440, 890 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.57, 1.61, 1.72 (s, vinyl CH_3s), 2.71 (m, allylic CH_2), 4.15 (t, J = 9 Hz, carbinyl H), 4.85 (s, vinyl H), 4.9–5.0 (m, vinyl H, 2 H), 5.0 (s, vinyl H), 5.37 (d, J = 7 Hz, vinyl H). This material was contaminated by an inseparable protonolysis product, so satisfactory analytical values could not be obtained.

***rel*-(1*R*,2*R*)-(5*E*,9*E*,13*Z*)-2-Isopropenyl-5,9-dimethyl-13-iodo-5,9,13-cyclotetradecatrienyl (Benzyloxy)methyl Ether (22).** To a stirred, cooled (0 °C) solution of 0.21 g (0.53 mmol) of the vinyl iodide **21** in 0.3 mL of CH_2Cl_2 was added 0.10 mL (0.72 mmol) of benzyl chloromethyl ether and 0.12 mL (0.69 mmol) of ethyldiisopropylamine. After 2.5 h water and ether were added, the layers were separated, and the aqueous layer was extracted with ether. The combined extracts were washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated to afford 0.257 g of a yellow liquid. Purification by column chromatography on silica gel (2–5% ethyl acetate–hexanes) gave 0.177 g (65%) of the protected alcohol **22**: ^1H NMR (300 MHz, $CDCl_3$) δ 1.57, 1.61, 1.73 (s, vinyl CH_3s), 2.70 (m, allylic CH_2), 4.35 (m, CHOR), 4.79 (s, vinyl H), 4.88 (s, vinyl H), 4.93 (t, J = 6.3 Hz, vinyl H), 5.03 (m, vinyl H), 5.34 (d, J = 8.5 Hz, vinyl H), 7.26–7.33 (m, Ar Hs).

***rel*-(1*R*,2*S*)-(5*E*,9*E*,13*E*)-2-Isopropenyl-5,9,13-trimethyl-5,9,13-cyclotetradecatrienyl (Benzyloxy)methyl Ether (23).** To a stirred, cooled (−78 °C) solution of 0.035 g (0.07 mmol) of the vinyl iodide **22** in 0.5 mL of THF was added 0.15 mL (0.26 mmol) of 1.7 M *t*-BuLi in hexanes followed after 3 min by 28 μL (0.33 mmol) of methyl fluorosulfonate. After 1 h water was added, the layers were separated, and the aqueous layer was extracted with ether. The combined extracts were washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to yield 0.027 g of a yellow liquid. Purification by column chromatography on silica gel (5% ethyl acetate–hexanes) afforded 0.021 g (76%) of a 4:1 mixture of methylated and protonated material **23** and **24**: ^1H NMR (300 MHz, $CDCl_3$) δ 1.57, 1.59, 1.67, 1.74 (s, vinyl CH_3), 2.0–2.4 (m, allylic CH_2s), 4.32 (t, J = 9.9 Hz, CHOR), 4.78 (s, vinyl H), 4.89 (s, vinyl H), 4.9–5.0 (m, vinyl H, 3 H), 7.27–7.33 (m, Ar Hs).

***rel*-(1*R*,2*R*)-(5*E*,9*E*,13*E*)-2-Isopropyl-5,9,13-trimethyl-5,9,13-cyclotetradecatrienyl (Benzyloxy)methyl Ether (25).** A solution of $(Ph_3P)_3RhCl$ (0.051 g, 0.06 mmol) in 1.5 mL of EtOH and 1.5 mL of C_6H_6 was stirred under a hydrogen atmosphere for 20 min before 0.025 g (0.06 mmol) of the tetraene **23**/**24** in 1 mL of C_6H_6 was added. After 4 h the reaction mixture was concentrated under reduced pressure and purified by column chromatography on silica gel (3% ethyl acetate–hexanes) to afford 0.021 g (84%) of the triene **25**/**26** as a 4:1 mixture: ^1H NMR (300 MHz, $CDCl_3$) δ 0.92 (d, J = 7 Hz, isopropyl CH_3), 0.96 (d, J = 7 Hz, isopropyl CH_3), 1.54, 1.56, 1.64 (s, vinyl CH_3s), 2.03–2.24 (m, allylic CH_2), 4.30 (t, J = 9.5 Hz, CHOR), 5.04 (d, J = 9.5 Hz, vinyl H), 7.27–7.33 (m, Ar Hs).

***rel*-(1*R*,2*R*)-(5*E*,9*E*,13*E*)-2-Isopropyl-5,9,13-trimethyl-5,9,13-cyclotetradecatrien-1-ol (Epimukulol, 18). A. From Benzyl Ether 25.** To a stirred solution of 0.021 g (0.051 mmol) of benzyl ether **25** in approximately 6 mL of NH_3 and 0.3 mL of THF was added 0.01 g (0.43 mmol) of sodium metal. After 0.5 h solid NH_4Cl was carefully added followed by hexane. After the NH_3 had evaporated water was added, the layers were separated, and the aqueous layer was extracted with ether. The combined extracts were washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated to afford 0.019 g of a yellow oil. Purification by column chromatography gave 0.005 g (24%) of recovered starting material and 0.004 g (27%) of the desired alcohol **18** contaminated by the desmethyl product derived from **26**. **18**: ^1H NMR (300 MHz, $CDCl_3$) δ 0.92 (d, J = 7 Hz, isopropyl CH_3), 0.96 (d, J = 7 Hz, isopropyl CH_3), 1.54, 1.56, 1.64 (s, vinyl CH_3s), 1.85–2.21 (m, allylic CH_2), 4.15 (t, J = 9 Hz, C*H*OH), 4.87 (m, vinyl H, 1 H), 4.97 (m, vinyl H, 2 H), 5.2 (d, J = 9 Hz, vinyl H, 1 H).

B. From Acetate 30. To a stirred solution of 15 mg (0.04 mmol) of allylic acetate **30** in approximately 10 mL of NH_3 and 0.4 mL of THF was added 3 mg (0.4 mmol) of lithium metal. After 1.25 h, hexane was added followed by solid NH_4Cl. After the NH_3 had evaporated water was added, the layers were separated, and the aqueous layer was extracted with ether. The combined extracts were washed with water and brine and dried over $MgSO_4$. Removal of solvent left a colorless liquid, which was purified by column chromatography on silica gel (10% ethyl acetate–hexanes), affording 9 mg (72%) of epimukulol (**18**): ^1H NMR (300 MHz, $CDCl_3$) δ 0.92 (d, J = 7 Hz, isopropyl CH_3), 0.96 (d, J = 7 Hz, isopropyl CH_3), 1.04–1.43 (m, nonallylic Hs), 1.54, 1.56, 1.64 (s, vinyl Hs), 4.2 (t, J = 9 Hz, CHOH), 4.87 (m, vinyl H), 4.97 (m, vinyl H), 5.19 (d, J = 9 Hz, vinyl H).

***rel*-(3*R*,4*R*)-(1*Z*,7*E*,11*E*)-3-Hydroxy-4-isopropenyl-7,11-dimethyl-1,7,11-cyclotetradecatrienecarboxylic Acid Lactone (28).** To a solution of 47 mg (0.12 mmol) of vinyl iodide **21** in 3 mL of toluene and 5 mg (0.006 mmol) of $(Ph_3P)_4Pd$ under 1 atm of CO at 52 °C was added 52 mg (0.18 mmol) of tributyltin hydride in 10 mL of toluene (3.9 mL/h). The reaction solution was cooled to room temperature 0.5 h after the addition and diluted with water, and the resultant layers were separated. The organic layer was washed with 3% NH_4OH, water, and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford a black liquid. Purification by column chromatography on silica gel (5% ethyl acetate–hexanes) gave 20 mg (56%) of butenolide **28**: IR (film) ν 3050, 2900, 1750, 1640, 1440, 1130, 1060, 890 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.3 (m, nonallylic CH_2), 1.45, 1.55, 1.73 (s, vinyl CH_3s), 4.63 (s, vinyl H), 4.71 (d, J = 10.7 Hz, CHOH), 4.86 (s, vinyl H), 4.85–4.93 (m, vinyl H, 2 H), 7.15 (s, vinyl H). Anal. Calcd for $C_{20}H_{28}O_2$: C, 79.96; H, 9.39. Found: C, 79.84; H, 9.45.

***rel*-(1*R*,2*R*)-(5*E*,9*E*,13*Z*)-2-Isopropenyl-13-(hydroxymethyl)-5,9-dimethyl-5,9,13-cyclotetradecatrien-1-ol (29).** To a stirred solution of 20 mg (0.07 mmol) of butenolide **28** in 1 mL of hexanes at room temperature was added 1 mL (1 mmol) of 1 M DIBAH in hexanes. After 0.5 h, 1 mL of aqueous Rochelle's salt, 1 mL of 10% NaOH, and 3 mL of ether were added. The resultant mixture was stirred for 2 h, the layers were separated, and the aqueous layer was extracted with ether. The combined organic layers were washed with 10% NaOH, water, and brine, dried over anhydrous $MgSO_4$, and filtered. Removal of solvent gave 0.023 g of a beige solid. Column chromatography on silica gel (30% ethyl acetate–hexanes) afforded 0.012 g (59%) of diol **29** as a white solid: mp 96–97.5 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 1.4 (m, nonallylic CH_2), 1.55, 1.59, 1.69 (s, vinyl CH_3s), 4.13 (AB q, $\Delta\nu$ = 77.3 Hz, J_{AB} = 12 Hz, CH_2OH), 4.19 (dd, J = 9, 10 Hz, CHOH), 4.86 (s, vinyl H), 4.96–5.02 (m, vinyl H, 2 H), 5.02 (s, vinyl H), 5.16 (d, J = 9 Hz, vinyl H). Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.59. Found: C, 78.75; H, 10.64.

***rel*-(1*R*,2*R*)-(5*E*,9*E*,13*Z*)-2-Isopropenyl-13-(acetoxymethyl)-5,9-dimethyl-5,9,13-cyclotetradecatrien-1-ol (30).** To a stirred, cooled (−20 °C) solution of 19 mg (0.06 mmol) of diol **29** in 0.1 mL of pyridine and 0.3 mL of CH_2Cl_2 was added 7 μL (0.07 mmol) of Ac_2O. The mixture was then warmed to room temperature and stirred for 14 h. Water and ether were added, the layers were separated, and the organic layer was washed with saturated $CuSO_4$, water, and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by column chromatography on silica gel (5% ethyl acetate–hexanes) gave 3 mg of diacetate, 2 mg of the diol **29**, and 16 mg (74%) of the monoacetate **30**: ^1H NMR (300 MHz, $CDCl_3$) δ 1.32–1.44 (m, nonallylic CH_2), 1.56, 1.59, 1.69 (s, vinyl CH_3s), 2.05 (s, CO_2CH_3), 4.20 (t, J = 9.7 Hz, CHOH), 4.6 (AB q, $\Delta\nu$ = 57.3 Hz, J_{AB} = 12.1 Hz, CH_2OAc), 4.85 (s, vinyl H), 4.95–4.97 (m, vinyl H, 2 H), 5.0 (s, vinyl H), 5.22 (d, J = 9.3 Hz, vinyl H). Anal. Calcd

for $C_{22}H_{34}O_3$: C, 76.26; H, 9.89. Found: C, 76.18; H, 9.91.

***rel*-(1*R*,2*R*)-(5*E*,9*E*,13*E*)-2-Isopropenyl-13-carbomethoxy-5,9-dimethyl-5,9,13-cyclotetradecatrien-1-ol (33).** To a stirred solution of 1.8 mL (0.68 mmol) of 0.38 M *i*-BuMgBr in Et_2O was added 47 mg (0.17 mmol) of the trans propargylic alcohol **16** followed 20 min later by 8 mg (0.03 mmol) of titanocene dichloride. After 2 h, 1.5 mL of THF was added, and CO_2 was passed through a Dreirite–$CaCl_2$ drying tower and into the gray reaction mixture for 2 h. The light brown mixture was carefully diluted with 10% HCl and ether, the layers were separated, and the acidic aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and partially concentrated. The orange residue of acid **32** was treated with an ethereal solution of diazomethane. The solution was then stirred for several minutes with acetic acid, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford 0.078 g of an orange liquid. Purification by column chromatography on silica gel (10% ethyl acetate–hexanes) yielded 0.035 g (61%) of the unsaturated ester **33**: IR (film) ν 3450, 3050, 2800, 1710, 1640, 1440, 1200, 900 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.54, 1.58, 1.80 (s, vinyl CH_3), 1.9–2.4 (m, allylic CH_2s), 3.72 (s, CO_2CH_3), 4.36 (m, C*H*OH), 4.79 (s, vinyl H), 4.99–5.03 (m, vinyl Hs), 6.61 (d, J = 9 Hz, C*H*=CCO_2CH_3). Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.90; H, 9.78.

(±)-Desoxyasperdiol (34). To a cooled (0 °C), stirred solution of 13 mg (0.04 mmol) of the ester **33** in 0.7 mL of hexanes was added dropwise 0.2 mL (0.2 mmol) of 1 M DIBAH[6] in hexanes. After 25 min, 0.5 mL of saturated Rochelle's salt, 0.5 mL of 10% NaOH, and 3 mL of ether were added. After being stirred for 1 h the mixture was diluted with water and ether, and the layers were separated. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, concentrated under reduced pressure, and purified by column chromatography (40% ethyl acetate–hexanes) to afford 10 mg (84%) of a white solid: mp 97–98 °C (lit.[19] mp 97–98.5 °C); ^1H NMR (300 MHz, $CDCl_3$) δ 1.54, 1.61, 1.77 (s, vinyl CH_3), 1.9–2.4 (m, allylic CH_2s), 4.09 (AB q, J_{AB} = 13 Hz, $\Delta\nu$ = 22 Hz, C*H*$_2$OH), 4.35 (dd, J = 4, 9 Hz, C*H*RC=CH_2), 4.74, 4.95 (br s, C=CH_2), 5.0–5.05 (m, vinyl Hs), 5.52 (d, J = 9 Hz, vinyl H). The spectrum was identical with that of an authentic sample kindly provided by Professor Kato.

(2*E*,6*E*)-3,7-Dimethyl-8-chloro-2,6-octadienyl Acetate (36). The procedure of Myers and Collington was followed.[8] To a stirred, cooled (0 °C) mixture of 2.14 g (51 mmol) of lithium chloride in 51 mL of dimethylformamide were added oxidized geranyl acetate **35** (9.84 g, 46.4 mmol)[7] and 6.0 mL (52 mmol) of 2,6-dimethylpyridine followed after 15 min by 3.8 mL (49 mmol) of methanesulfonyl chloride. After 12 h water and ether were added, and the ether layer was washed with water, saturated aqueous $CuSO_4$, water, and brine. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated to afford 9.68 g (91%) of an unstable yellow liquid: ^1H NMR (300 MHz, $CDCl_3$) δ 1.7 and 1.75 (s, vinyl CH_3s), 2.0 (s, $COCH_3$), 2.1–2.3 (m, allylic CH_2s), 3.95 (s, CH_2Cl), 4.55 (d, J = 8 Hz, CH_2OAc), 5.2–5.6 (m, vinyl Hs).

(2*E*,6*E*)-2,6-Dimethyl-8-hydroxy-2,6-octadienyl Propargyl Ether (37). To a stirred mixture of 6.75 g (169 mmol) of NaOH and 0.71 g (2.1 mmol) of tetra-*n*-butylammonium hydrogen sulfate in 3.6 mL of water and 5.5 mL of toluene were added 6.0 mL (100 mmol) of propargyl alcohol and 9.68 g (42.1 mmol) of the allylic chloride **36**. After 1 h the black reaction mixture was diluted with water and ether, and the layers were separated. The organic layer was washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford 7.04 g (80%) of a brown liquid. Purification by column chromatography on silica gel (30% ethyl acetate–hexanes) yielded 5.72 g (65%) of ether **37**: IR (film) ν 3350, 3260, 2900, 2825, 2100, 1660, 1440, 1080, 1000 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.65 and 1.68 (s, vinyl CH_3s), 2.0–2.2 (m, allylic CH_2s), 2.4 (t, J = 2 Hz, HC≡C), 3.95 (s, CH_2O), 4.1 (d, J = 2 Hz, C≡CCH_2OR), 4.18 (d, J = 6 Hz, CH_2OTBS), 5.4 (m, vinyl Hs). Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.83; H, 9.72.

(2*E*,6*E*)-2,6-Dimethyl-8-[(*tert*-butyldimethylsilyl)oxy]-2,6-octadienyl Propargyl Ether (39). To a stirred solution of 0.60 g (2.9 mmol) of allylic alcohol **37** in 6 mL of CH_2Cl_2 were added 0.035 g (0.3 mmol) of DMAP,[6] 0.53 g (3.5 mmol) of TBSCl,[6] and 1.0 mL (7.2 mmol) of Et_3N. After 14 h the mixture was diluted with water and ether, the layers were separated, and the aqueous layer was extracted with ether. The combined extracts were washed with water, saturated aqueous $CuSO_4$, water, and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to yield 0.87 g (94%) of a yellow liquid. Purification by column chromatography on silica gel (5% ethyl acetate–hexanes) afforded 0.77 g (87%) of TBS ether **39**: IR (film) ν 3300, 2925, 2850, 1670, 1260, 1070, 840, 780 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.045 and 0.046 (s, $Si(CH_3)_2$), 0.88 (s, $SiC(CH_3)_3$), 1.60 and 1.63 (s, vinyl CH_3s), 2.0–2.18 (m, allylic CH_2s), 2.38 (t, J = 2 Hz, HC≡C), 3.91 (s, C=C$(CH_3)CH_2$OR), 4.05 (d, J = 2 Hz, C≡CCH_2OR), 4.16 (d, J = 6 Hz, CH_2OTBS), 5.29 (t, J = 5 Hz, vinyl H), 5.41 (t, J = 6 Hz, vinyl H). Anal. Calcd for $C_{19}H_{34}O_2Si$: C, 70.75; H, 10.62. Found: C, 70.63; H, 10.60.

4-Hydroxy-2-butynyl (2*E*,6*E*)-2,6-Dimethyl-8-[(*tert*-butyldimethylsilyl)oxy]-2,6-octadienyl Ether (41). To a cooled (−78 °C), stirred solution of 0.28 g (0.87 mmol) of alkyne **39** in THF was added 0.60 mL (0.96 mmol) of 1.6 M *n*-BuLi. After 1 h solid paraformaldehyde (0.057 g, 1.9 mmol) was added, and the cold bath was removed. After 2 h, water and ether were added, and the resultant layers were separated. The organic layer was washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford 0.29 g (95%) of a brown liquid. Purification by column chromatography on silica gel (20% ethyl acetate–hexanes) yielded 0.23 g (75%) of propargylic alcohol **41**: IR (film) ν 3400, 2925, 2825, 1670, 1260, 1080, 840, 780 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.046 (s, $Si(CH_3)_2$), 0.88 (s, $SiC(CH_3)_3$), 1.60 and 1.62 (s, vinyl CH_3s), 2.0–2.2 (m, allylic CH_2s), 3.89 (s, C=C$(CH_3)CH_2$OR), 4.08 (t, J = 2 Hz, C≡CC*H*$_2$OR), 4.17 (d, J = 6 Hz, CH_2OTBS), 4.28 (br s, $HOCH_2C$≡C), 5.28 (t, J = 5.8, vinyl H), 5.40 (t, J = 6.5 Hz, vinyl H). Anal. Calcd for $C_{20}H_{36}O_3Si$: C, 68.13; H, 10.29. Found: C, 68.19; H, 10.34.

Rearrangement of Ether 41. To a cooled (−85 °C), stirred solution of 0.19 g (0.54 mmol) of ether **41** in 5.4 mL of THF was added dropwise 1.3 mL (2.1 mmol) of 1.6 M *n*-BuLi. The cooling bath was allowed to warm to −15 °C overnight. The mixture was diluted with water and ether, and the layers were separated. The organic layer was washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford 0.23 g of a yellow liquid. Purification by column chromatography on silica gel (30% ethyl acetate–hexanes) yielded 0.066 g (35%) of alcohols **43**/**44** (R = TBS, R′ = CH_2OH): IR (film) ν 3275, 3050, 2900, 1640, 1460, 1380, 1260, 1120, 1080, 840, 780 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.05 ($(CH_3)_2Si$), 0.90 ($(CH_3)_3CSi$), 1.60, 1.75 (vinyl CH_3s), 4.16, 4.34 (2 d, ca. 2:1, J = 6 Hz, CH_2OTBS), 4.28 (m, CHOH, CH_2OH), 4.83, 4.86; 4.96, 4.98 (4 s, ca. 2:1, C=CH_2), 5.30 (t, J = 6 Hz, vinyl H).

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