16%). Carboprephenate exhibited the following spectral characteristics: IR (neat) 3400, 1730, 1630, 1440, 1290, 1240, 1200, 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.11 (d, 1 H, J = 1.2 Hz), 5.94 (dd, 2 H, J = 10.5, 3.8 Hz), 5.87 (dd, 2 H, J = 10.5, 1.0 Hz), 4.29 (br s, 1 H), 3.64 (s, 6 H), 2.72 (s, 2 H); CIMS (isobutane), m/e (rel intensity) 253 (M + 1, 2), 203 (100).

Kinetics. The tubes used in the NMR kinetic studies were 7-in. No. 528PP 5-mm o.d. NMR tubes with approximately 3 in. of a 6-mm o.d. Pyrex tubing fused to the end. They were soaked in a concentrated ammonia solution for a minimum of 1 h and then oven dried (ca. 100 °C) for at least 12 h. Deuteriated solvents used were reagent grade quality with no further purification. Prior to each quantitative kinetic run on a new compound an approximate reaction half-life was determined as follows: a small amount (ca. 5 mg) of the compound was dissolved in the appropriate solvent (0.5 mL), degassed (vide infra), and sealed. It was then heated (75 °C unless otherwise noted) in an oil or water bath. ^1H NMR spectra were taken at various times and an approximate reaction half-life (and products) was noted.

All quantitative NMR studies were performed on a Bruker WM300 (300 MHz) Fourier transform spectrometer. For the quantitative studies, a solution of the compound was prepared and distributed among the appropriate number of NMR tubes. The tubes were degassed by 5 freeze-pump-thaw cycles, by using liquid nitrogen. When the solvent was aqueous methanol, a dry-ice/acetone bath, which caused the sample to become viscous but not to freeze, was used in place of liquid nitrogen. While in the dry-ice/acetone bath, the sample was exposed to a manifold that had been evacuated with a mercury diffusion pump. While the sample was being warmed, the manifold would be reevacuated. After degassing and sealing, the sample was heated in a Neslab Exacal EX-200 constant temperature bath (filled with watger or ethylene glycol), a Tamson Holland regulated temperature bath (silicone oil), or in the probe of the Bruker WM300. The temperature of the baths was noted on a NBS standardized total immersion thermometer by using the standard stem correction.[44] The NMR probe temperature was measured by using a Fluke 2190A digital thermometer (copper/constantan thermocouple). Samples were removed from the bath at the appropriate times and quenched (-78 °C or 0 °C bath), and an NMR spectrum was obtained. In some cases, the sample was then returned to the bath to obtain further data points. The proton relaxation times (τ) were measured by using an inverse-recovery delay program (Bruker software). Once τ was determined for all the protons in the reaction mixture, a value of 5 times the largest τ was used as the relaxation delay between pulses. The relative concentrations were determined by comparison of the integration values for the compound of interest against an internal standard or against the sum of starting material and product(s). The integrals of each resonance were plotted five times and measured with a ruler. An average value and standard deviation (σ) were then calculated. The weighted values ($1/\sigma^2$) were used to determine rate constants. Activation parameters were determined by nonlinear least-squares fit of the data to the Arrhenius or Eyring equations.

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(44) *CRC Handbook of Chemistry and Physics*, 59th ed., Weast, R. C. Ed.; CRC Press: Boca Raton, FL, p D-231.

Acyclic Stereocontrol in Catalyzed Intramolecular Diels-Alder Cyclizations Leading to Octahydronaphthalenecarboxaldehydes

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Abstract: Diels-Alder cyclizations of 2-methyl-2,8,10-undecatrienals (I) were effected at -23 to -13 °C in the presence of alkylaluminum chlorides to afford the endo products II and III in high yield. An OTBS grouping at C-7 exhibited high diastereocontrol in favor of the syn isomer III whereas a C-4 methyl substituent showed complete preference for the anti isomer (IV → V). On the other hand, C-7 methoxy, benzyloxy, or methoxymethyl substituents displayed no diastereomeric preference. Methyl substitution at C-6 in the trienal likewise played a negligible role in diastereocontrol. Both *syn*- and *anti*-4,6-dimethyl-2,8,10-undecatrienal cyclizations were controlled by the C-4 methyl substituent. The major stereochemical trends of this study were predicted from molecular modeling calculations performed on the boat-chair conformation of the product via Still's Model program. These findings are directly applicable to synthetic work on the hydronaphthalene subunit of the macrocyclic natural products chlorothricin and kijanimicin.

In the course of synthetic studies on the macrocyclic antitumor antibiotics chlorothricolide, kijanolide, and tetronolide (Figure 1)[1] we found that 7-alkoxy-2,8,10-undecatrienals such as I (Table I) undergo facile endo selective Lewis acid catalyzed Diels-Alder cyclization to give trans fused octahydronaphthalene aldehydes II and III related to chlorothricolide.[2,3] Interestingly, the TBS ether (I, R^2 = *tert*-butyldimethylsilyl) afforded mainly the syn[4]

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(2) (a) Marshall, J. A.; Audia, J. E.; Grote, J. *J. Org. Chem.* **1984**, *49*, 5279. (b) Marshall, J. A.; Audia, J. E.; Grote, J.; Shearer, B. G. *Tetrahedron* **1986**, *42*, 2893. (c) Marshall, J. A.; Audia, J. E.; Grote, J. *J. Org. Chem.* **1986**, *51*, 1155. (d) Marshall, J. A.; Audia, J. E.; Shearer, B. G. *J. Org. Chem.* **1986**, *51*, 1730.

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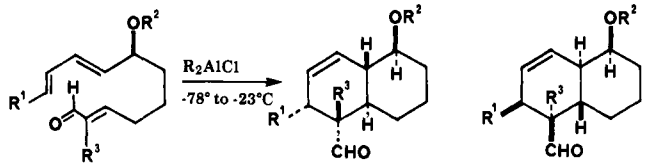
0002-7863/87/1509-1186$01.50/0

Table I. Diels–Alder Cyclication of 2,8,10-Undecatrienals



I II III

entry	R^1	R^2	R^3	conditions[b]	yield (%)	II/III[c]	ref
1	H	Me	H	A		50:50	5
2	H	Bn	H	A	91	50:50	5
3	H	TBS	H	A	77	5:95	2d
4	Me	TBS	Me	B	84	10:90	2a
5	$(CH_2)_4OBn$	MOM	Me	B	93	50:50	2b
6	$(CH_2)_4OBn$	TBS	Me	B	96	5:95	2b
7	$(CH_2)_5OBn$	TBS	Me	B	92	<5:95	2d

[a] Bn = CH_2Ph, TBS = *t*-$BuSiMe_2$, MOM = CH_2OMe. [b] A = Me_2AlCl, CH_2Cl_2, −78 to −23 °C, 10–14 h; B = Et_2AlCl, CH_2Cl_2, −78 to −23 °C, 12–14 h. [c] Ratios were estimated from ^1H NMR spectra.

Table II. Calculated Energies for Diastereomeric Cyclization Products II and III

				II[a]		III[a]	
entry	R^1	R^2	R^3	B–C[b]	B–TB[b]	B–C[b]	B–TB[b]
1	H	Me	H	18.89	28.82	18.76	28.85
2	H	Me	Me	24.12	34.05	24.10	34.10
3	Me	Me	Me	27.07	36.86	26.99	36.92
4	H	Bn[c]	H	22.66	32.50	22.71	33.06
5	H	*t*-Bu	H	24.32	34.02	25.73	35.27
6	H	*t*-Bu	Me	29.96	39.98	30.42	39.61
7	Me	*t*-Bu	Me	33.65	43.41	33.96	44.01

[a] Energy in kcal/mol. [b] B–C = boat–chair, B–TB = boat–twist boat; see Figure 2. [c] Bn = $PhCH_2$.

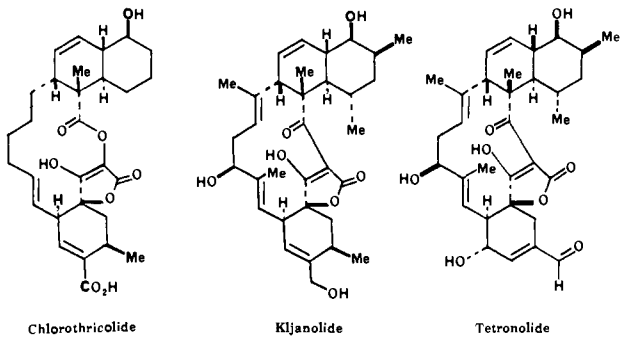


Figure 1. Macrocyclic tetronic acid natural product aglycones.

diastereoisomer III (entries 3, 4, 6, and 7) whereas the methyl, methoxymethyl, and benzyl ethers gave 1:1 mixtures of both II and III (entries 1, 2, and 5).[2,5] Alkoxy groups at the allylic position of the bridging chain thus exert little influence on the diastereoselectivity of the cyclization whereas a silyloxy group is strongly syn directing.[6] The result is surprising since it implies that the bulky OTBS grouping prefers an axial orientation in the cyclization transition state, assuming a chair-like conformation for the bridging ring.[7]

With the aim of extending this approach to hydronaphthalene precursors of kijanolide[1b] and tetronolide,[1c] we wished to examine the effect of C-4 and C-6 methyl substituents on the diastereoselectivity of the Diels–Alder cyclization (IV → V and/or VI)

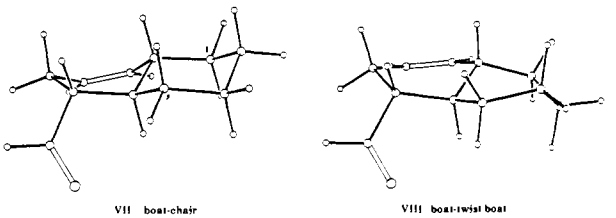


Figure 2. Prototype structures for Diels–Alder transition states.

(Table III). We were interested in using molecular modeling as a possible predictive tool for such an approach, but, owing to the complexity of the relevant structures, an application of rigorous ab initio techniques appeared unrealistic. However, considering Houk's recent calculations on the Diels–Alder transition state showing a high degree of sp^3 character for the terminal reacting centers of the diene and the dienophile,[8] it seemed reasonable to perform energy minimizations on structures resembling reaction products rather than trying to evaluate group interactions in some arbitrary parallel arrangement of diene and dienophile as is currently the custom. We felt that such a product-oriented approach could greatly simplify predictions of diastereoselectivity as it would allow calculations on fully developed structures by straightforward machine methods of general availability. As a starting point, we constructed simple unsubstituted prototypes of pertinent Diels–Alder products by using Still's Model program.[9] In keeping with the known stereoelectronic preferences of the Diels–Alder reaction, the A-ring was input as the endo boat conformer, the B-ring tether was placed in either a chair or a twist boat conformation, and the derived structures were allowed to minimize. This procedure led to a pair of structures VII and VIII

(4) The terms "anti" and "syn" are used here to denote the relationship between the adjacent hydrogens at C8 and C8a as is common for fused ring systems such as steroids and hydrophenanthrenes.

(5) Audia, J. E. Ph.D. Thesis, University of South Carolina, 1985, pp 45–51.

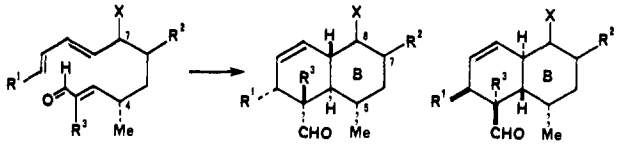
(6) Substituents at C-9 of 2,8,10-undecatrienoic esters have been found to strongly direct thermal Diels–Alder cyclizations to the endo, anti product. Boeckman, R. K.; Barta, T. E. *J. Org. Chem.* **1985**, *50*, 3423. Roush, W. R.; Kageyama, M. *Tetrahedron Lett.* **1985**, *26*, 4327.

(7) For other examples in which an OTBS grouping prefers an axial orientation in Lewis acid catalyzed cyclizations leading to hydronaphthalenes, see: Funk, R. L.; Zeller, W. E. *J. Org. Chem.* **1982**, *47*, 180. Hirama, M.; Uei, M. *J. Am. Chem. Soc.* **1982**, *104*, 4251.

(8) Brown, F. K.; Houk, K. N. *Tetrahedron Lett.* **1984**, *25*, 4609. Houk, K. N.; Paddon-Row, M. N.; Rondan, N. G.; Wu, Y.; Brown, F. K.; Spellmeyer, D. C.; Metz, J. T.; Li, Y.; Loncharich, R. J. *Science* (Washington, DC) **1986**, *231*, 1108.

(9) Cf. Still, W. C.; Galynker, I. *Tetrahedron* **1981**, *37*, 3996. Still, W. C.; Murata, S.; Revial, G.; Yoshihara, K. *J. Am. Chem. Soc.* **1983**, *105*, 625. We are indebted to Professor Still for a copy of his Model program and helpful advice on its operation.

Table III. Calculated Energies for Boat–Chair Conformers



IV V VI

entry	R^1	X	R^2	R^3	V[a]	VI[a]
1	H	H	H	H	18.22	22.98
2	H	H	H	Me	23.24	28.15
3	Me	H	H	Me	26.23	31.40
4	H	β-OMe	H	Me	26.98	28.62
5	H	α-OMe	H	Me	26.86	28.42
6	H	β-OMe	β-Me	Me	31.84	37.16
7	H	α-OMe	β-Me	Me	32.76	37.07
8	H	β-OMe	α-Me	Me	32.55	38.96
9	H	α-OMe	α-Me	Me	32.25	38.54

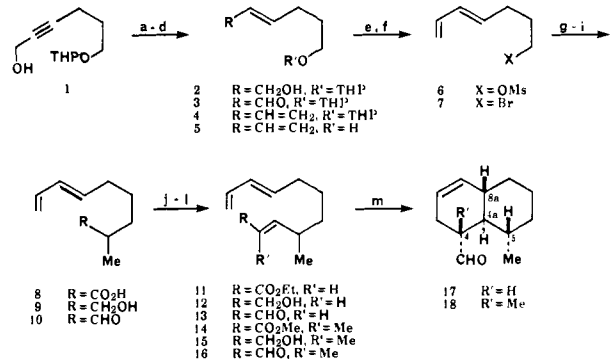
[a] Energy in kcal/mol.

(Figure 2) from which others could be built through replacement of hydrogens with alkoxy and methyl substituents, as required. Each derived structure was allowed to minimize without restraint. Duplicate runs showed good agreement. Although the resultant structures only approximated the Houk ab initio transition state in their geometry,[8] we felt that the major discrepancies might be systematic, and thus the calculated energies could still be used comparatively.

Our first calculations were performed on the alkoxy substituted Diels–Alder products II and III (Table I). Accordingly, each of the C-8 hydrogens in the two template structures VII and VIII (Figure 2) was replaced by the appropriate alkoxy substituent to give two diastereomeric pairs of conformers, a boat-chair–equatorial/boat-twist boat–pseudoaxial and a boat-chair–axial/boat-twist boat–pseudoequatorial.[10] These conformers were allowed to minimize without restraint giving the calculated energies summarized in Table II. In each case the boat–chair was appreciably lower in energy than the boat–twistboat conformer. Interestingly methoxy and benzyloxy substituents showed little orientational preference (entries 1–4) in agreement with previous experimental findings.[2] The *tert*-butoxy grouping (entries 5–7) favored the equatorial orientation to varying degrees depending upon the presence of substituents R^1 and R^3. Unfortunately, our version of Model did not contain parameters for silicon, so we were unable to calculate energies for the TBS ethers. However, since the *tert*-butoxy group shows a modest equatorial preference it seems unlikely that the experimentally observed axial preference of (*tert*-butyldimethylsilyl)oxy results solely from steric factors. Owing to the lability of the dienol precursors, we did not attempt to prepare *tert*-butyl ethers for cyclization studies.

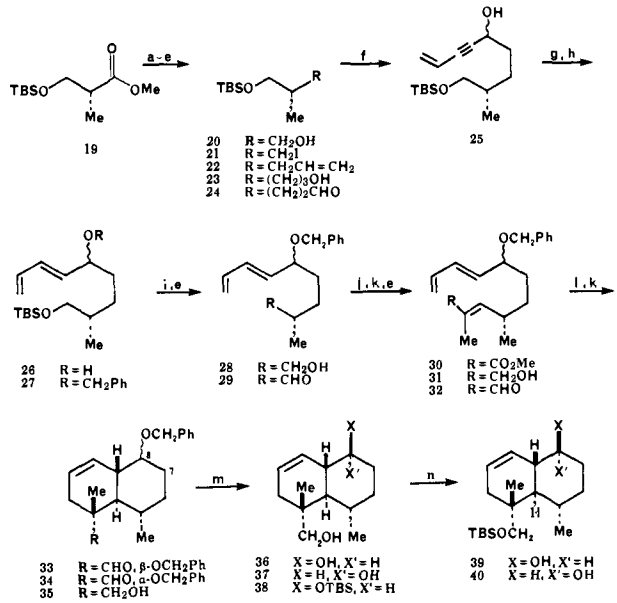
The next compounds of interest were the C-5 methylated hydronaphthalene diastereoisomers V and VI (Table III, R^2 = X = H). Here our calculations distinctly favored the diastereoisomer V (Table III, entries 1–3) corresponding to an equatorial C-5 methyl orientation in the boat–chair transition-state-like conformation of the product (Figure 2).[11] As a test of this prediction, the trienals **13** and **16** were prepared from the monoprotected propargylic diol **1** as outlined in Scheme I. Reduction of alcohol **1** with Red-Al[12] cleanly produced the trans allylic alcohol **2** whose oxidation and Wittig methylenation followed by hydrolysis led to the dienol **5**. The corresponding bromide, on treatment with dilithio propionate, gave the acid **8** quantitatively.[13] Reduction of this acid and oxidation of the resulting alcohol with PDC[14] in

Scheme I[a]



[a] (a) Red-Al, Et_2O; (b) PDC, DMF; (c) Ph_3P = CH_2, THF; (d) MeOH, Dowex H^+; (e) MsCl, Et_3N, CH_2Cl_2; (f) THF, LiBr; (g) CH_3CH = $C(OLi)_2$, THF, HMPA; (h) $LiAlH_4$, Et_2O; (i) PDC, CH_2Cl_2; (j) Ph_3P = $CHCO_2Et$ or Ph_3P = $C(Me)CO_2Me$; (k) DIBAH, Et_2O; (l) MnO_2, CH_2Cl_2; (m) $EtAlCl_2$, CH_2Cl_2, −78° to −23 °C; R′ = H, 1 h; R′ = Me, 12 h.

Scheme II[a]



[a] (a) $LiBH_4$, THF, 0° to 25 °C; (b) Ph_3P, imidazole, I_2, MeCN, 0° to 25 °C; (c) $(CH_2{=}CH)_2CuCNLi_2$, THF, −78° to −13 °C; (d) $(Siam)_2BH$, THF, −10° to 0 °C; H_2O_2, NaOH; (e) DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2; (f) $CH_2{=}CHC{\equiv}CH$, *n*-BuLi, THF, −28 °C; (g) Red-Al, Et_2O, 0° to 25 °C; (h) $PhCH_2Br$, HMPA, *n*-BuLi, THF, −78° to 25 °C; (i) $(n\text{-}Bu)_4NF$, THF, 25 °C; (j) Ph_3P = $C(Me)CO_2Me$, CH_2Cl_2, 0° to 25 °C; (k) DIBAH, Et_2O, −78 °C; (l) $EtAlCl_2$, CH_2Cl_2, ~0.1 *M*, −78° to −23 °C; (m) Na, NH_3, THF, −33 °C; NH_4Cl; (n) TBSCl, DMF, imidazole, 25 °C.

methylene chloride afforded aldehyde **10**. Condensation with ethyl α-(triphenylphosphoryliden)acetate led to the trans conjugated ester **11** and phosphorylidenepropionate yielded the methyl homologue **14** both with excellent stereoselectivity.[15] Reduction of each with DIBAH followed by MnO_2 oxidation gave the enals **13** and **16**, respectively.

Cyclization was effected with $EtAlCl_2$ at −78 to −23 °C with the unsubstituted trienal **13** requiring only 1 h compared to over 12 h for the methyl substituted homologue. Each gave a single cyclic product as judged by glass capillary GC and high field ^1H NMR analysis. Support for the assigned stereochemistry was secured through analysis of the methine proton coupling constants aided by a 2-D J-resolved experiment for **17**. The proton at C4a showed diaxial coupling with its neighbors at C4, C8a, and C5. Irradiation of the secondary methyl of each bicyclic aldehyde

(10) Calculations were thus performed on II and the mirror image of III (Figure 4) for convenience. The terms "axial, pseudoaxial, equatorial, and pseudoequatorial" refer to the alkoxy group orientation.

(11) The related boat–twist boat conformers were higher in energy by 2.7–7.0 kcal/mol. Reference 5, p 81.

(12) Denmark, S. E.; Jones, T. K. *J. Org. Chem.* **1982**, *47*, 4595.

(13) Pfeffer, P. E.; Silbert, L. S.; Chirinko, J. M. *J. Org. Chem.* **1972**, *37*, 451.

(14) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399.

(15) Cf. Nagoaka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873.

effected NOE enhancement of the formyl ^{1}H signal in keeping with the diequatorial syn-1,3 relationship of these two groupings. Thus in accord with prediction, a C-4 methyl substituent in undecantrienals such as IV exerts a strong directing effect on the Diels–Alder cyclization.[16]

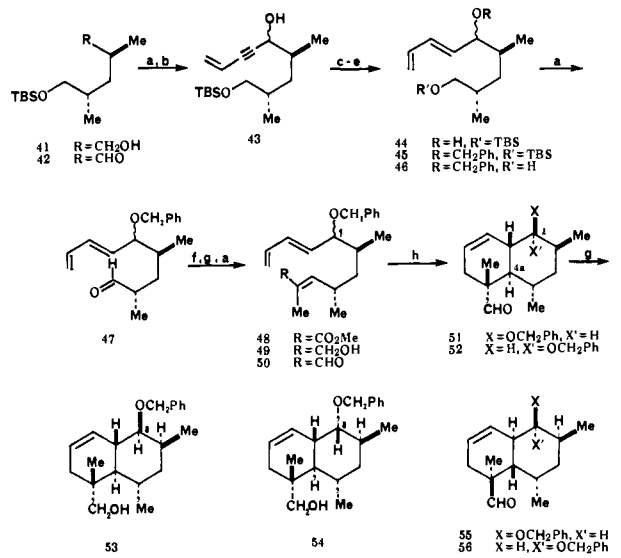
As a further test of the predictive capability of the modeling protocol we examined the 5-methyl-8-alkoxyhydronaphthalene system. The methoxy derivatives V and VI (Table III, $R^1 = R^2 = H$, X = β- or α-OMe, R^3 = Me) were selected as representative. In each case the diastereoisomer V possessed the lowest calculated energy, irrespective of the methoxy orientation (entries 4 and 5).

To test this prediction we prepared trienal **32**, a 1:1 mixture of C-7 epimers, as shown in Scheme II. The decision to use an epimeric mixture rather than the pure diastereoisomers was partly based on expedience. In addition we were considering routes to a kijanolide precursor wherein the C-7 methyl grouping (see **33**) would be introduced through alkylation of a bicyclic C-8 hydrazone derivative.[17] Accordingly the C-8 carbinyl center would eventually arise via stereoselective reduction of a bicyclic ketone. The stereochemical homogeneity of this center in the acyclic precursor was therefore not a matter of concern.

The synthesis of trienal **32** commenced with the TBS ether **19** of (*R*)-methyl 3-hydroxy-2-methylpropanoate.[18] Reduction with lithium borohydride gave alcohol **20** without significant racemization.[19] The derived iodide **21**, upon treatment with dilithiocyanodivinylcuprate[20] in THF, afforded olefin **22** which was converted to aldehyde **24** via successive hydroboration–oxidation and Swern oxidation.[21] Addition of lithiovinylacetylide to aldehyde **24** gave rise to a 1:1 mixture of the diastereomeric carbinols **25**. Reduction with Red-Al[12] smoothly afforded the trans dienol **26** which was protected as the benzyl ether **27**. Cleavage of the TBS ether followed by oxidation[21] yielded aldehyde **29**. Condensation with methyl α-(triphenylphosphorylidene)propionate led to the trans conjugated ester **30** exclusively. Sequential reduction and Swern oxidation[21] gave an optically active 1:1 mixture of diastereoisomeric trienals **32**.

Cyclization of **32** was cleanly effected with $EtAlCl_2$. High field ^{1}H NMR analysis of the product showed two resonances of equal intensity with the chemical shifts and coupling constants expected for the epimeric C-8 carbinyl protons of **33** and **34**. Separation could not be effected, so the mixture was reduced with DIBAH to a 1:1 mixture of alcohols **35**. This mixture likewise could not be separated, but upon hydrogenolysis of the benzyl protecting group a separable 1:1 mixture of diols **36** and **37** was obtained. Upon treatment with 1 equiv of *tert*-butyldimethylsilyl chloride in DMF-imidazole,[22] diol **36** afforded a 1:4 mixture of the mono TBS derivatives **38** and **39**. Diol **37**, on the other hand, with its more hindered axial C-8 alcohol gave only the primary TBS ether **40** under the same conditions. The monoprotected diols **38**, **39**, and **40** were converted to the MTPA Mosher esters[23] which showed enantiomeric excesses of 89, 88, and 82%, respectively, by integration of the signals arising from the diastereomeric methoxyl groups in the high field ^{1}H NMR spectra. Therefore, the route from ester **19** only slightly affects the chiral integrity of potentially labile intermediates. Aldehydes **33** and **34** and their transformation products were free of diastereoisomers as judged by inspection of the carbinyl and vinyl regions in their high field ^{1}H NMR spectra. Thus, in accord with prediction, the C-4 methyl substituent of trienal **32** exerts a strong directing effect regardless of the C-7 alkoxy orientation.[16]

Scheme III[a,b]



[a](a) $(COCl)_2$, DMSO, CH_2Cl_2, −60 °C; Et_3N, −25 °C; (b) CH_2=CHC≡CLi, THF, −78 °C; (c) Red-Al, Et_2O, 0° to 25 °C; (d) *n*-BuLi, THF, HMPA, $PhCH_2Br$, −78° to 25 °C; (e) Bu_4NF, THF, 25 °C; (f) Ph_3P = $C(Me)CO_2Me$, CH_2Cl_2, 0° to 25 °C; (g) *i*-Bu_2AlH, Et_2O, −78 °C; (h) $EtAlCl_2$, CH_2Cl_2, ~0.1 *M*, −78° to −13 °C.
[b]TBS = *tert*-$BuMe_2Si$.

The next question to be addressed concerned the effect of a methyl substituent at C-7 (e.g., Table III, V and VI, R^2 = Me) on the stereochemistry of the Diels–Alder cyclization. The two possible endo anti products V and VI (R^2 = β-Me, X = OR) each possess one equatorial and one axial methyl in addition to an equatorial or axial alkoxy grouping in ring B. Energy calculations were carried out as before by making appropriate substitutions on structures VII and VIII followed by minimization. The boat–twist boat conformers were again found to be appreciably higher in energy than their boat–chair counterparts. Of the four boat–chair diastereoisomers, the two related to V were calculated to be lower in energy by a decided margin (Table III, entries 6 and 7). The C-4 methyl grouping of trienal IV is thus predicted to retain its equatorial preference in the cyclization reaction despite the possible adverse influence of an axial methyl substituent in the developing B-ring.

As a test of this prediction, the benzyloxy trienal **50**, a 1:1 mixture of C-7 diastereoisomers, was prepared as shown in Scheme III. On the basis of our experience with trienal **32**, we felt that a satisfactory analysis of the cyclization outcome could be performed on such a mixture without the need for prior separation. Our long range synthetic goals might also be served by this strategy since reduction of a C-8 ketone in the bicyclic product (e.g., **51**; X, X' = O) would expectedly afford an alcohol with the requisite C-8 stereochemistry for conversion to kijanolide (Figure 1). The synthesis of **50** proceeded along the lines described for **32** starting from *anti*-2,4-dimethyl-1,5-hexanediol.[24] Oxidation of the mono

(16) For other examples in which substituents on the tether influence diastereoselectivity in Diels–Alder cyclizations, see: (a) Ciganek, E. *Org. React.* **1984**, *32*, 41–44. (b) Taber, D. F. *Intramolecular Diels–Alder and Alder-Ene Reactions*; Springer-Verlag: Berlin, 1984, pp 40–45. (c) Vig, O. P.; Trehan, I. R.; Kumar, R. *Ind. J. Chem.* **1977**, *15B*, 319. (d) Wilson, S. R.; Mao, D. T. *J. Am. Chem. Soc.* **1978**, *100*, 6289. (e) Näf, F.; Decorzant, R.; Thommen, W. *Helv. Chim. Acta* **1979**, *62*, 114. (f) Hirama, M.; Uei, M. *J. Am. Chem. Soc.* **1982**, *104*, 4251. (g) Taber, D. F.; Salek, S. A. *Tetrahedron Lett.* **1982**, *23*, 2361. (h) Burke, S. D.; Powner, T. H.; Kageyama, M. *Tetrahedron Lett.* **1983**, *24*, 4529. (i) Nicolaou, K. C.; Magolda, R. L. *J. Org. Chem.* **1981**, *46*, 1506. (j) Roush, W. R.; Myers, A. G. *J. Org. Chem.* **1981**, *46*, 1509. (k) Edwards, M. P.; Ley, S. V.; Lester, S. G. *Tetrahedron Lett.* **1981**, *22*, 361.

(17) Cf. Enders, D. *Current Trends in Organic Synthesis*; Nozaki, H., Ed.; Springer-Verlag: Vienna, 1982, pp 151–168.

(18) Both (*R*)- and (*S*)-methyl 3-hydroxy-2-methylpropanoate are available from Aldrich Chemical Company, Milwaukee, WI.

(19) Racemization would involve 1,5-silyl transfer. An enantiomeric excess of 90% was estimated by analysis of the ^{1}H NMR spectrum of the Mosher MTPA ester.[23]

(20) Lipschutz, B.; Kozlowski, J.; Wilhelm, R. S. *J. Am. Chem. Soc.* **1982**, *104*, 2305.

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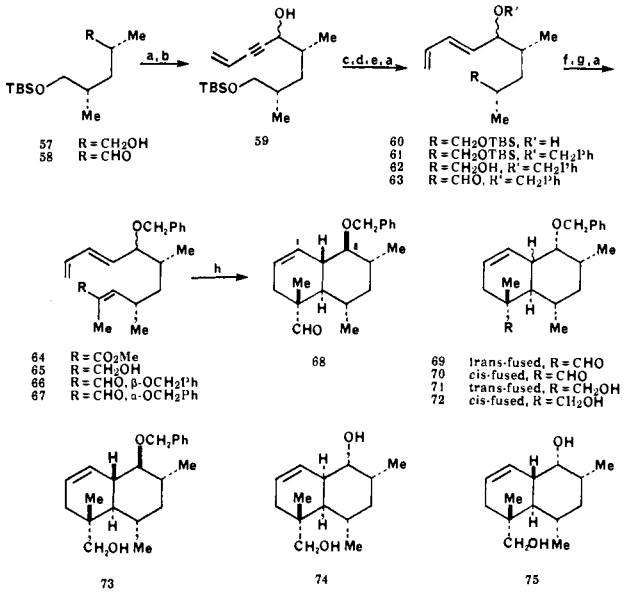
(23) Mosher, H. S.; Dale, J. A.; Dull, D. L. *J. Org. Chem.* **1969**, *34*, 2543.

(24) *trans*-2,4-Dimethylglutaric acid is separated from minor amounts of the cis isomer by fractional crystallization. Material of greater than 95% purity can thusly be obtained if required. Reduction of the dimethyl ester with lithium aluminum hydride affords the diol. Allinger, N. L. *J. Am. Chem. Soc.* **1959**, *81*, 232.

Scheme IV[a]



[a] (a) $(COCl)_2$, DMSO, CH_2Cl_2, −60 °C; Et_3N, −25 °C; (b) CH_2=CHC≡CLi, THF, −78 °C; (c) Red-Al, Et_2O, 0° to 25 °C; (d) *n*-BuLi, THF, HMPA, $PhCH_2Br$, −78° to 25 °C; (e) Bu_4NF, THF, 25 °C; (f) Ph_3P = C(Me)CO_2Me, CH_2Cl_2, 0° to 25 °C; (g) *i*-Bu_2AlH, Et_2O, −78 °C; (h) $EtAlCl_2$, CH_2Cl_2, ~0.1 M, −78° to −13 °C.

TBS derivative **41** to aldehyde **42** followed by addition of lithiovinylacetylide, reduction with Red-Al, benzylation, desilylation, Swern oxidation, and Wittig condensation, as before, led to the trans,trans triene ester **48**. The previously employed sequence of reduction and Swern oxidation then afforded the desired *anti*-4,6-dimethylundecatrienal **50** as a 1:1 mixture of C-7 epimers.

Cyclization was effected in 91% yield by treatment of the mixture with $EtAlCl_2$ at −78 to −13 °C in methylene chloride for 12 h. The product was judged to be a 1:1 mixture of the C-8 epimers **51** and **52** by integration of signals at 3.23 ppm (dd, J = 10.7 and 5.7 Hz) and 3.39 (br s) attributable to the axial and equatorial carbinyl protons. It should be noted that the appearance of the 3.23-ppm signal as a doublet of doublets with both axial–axial and axial–equatorial coupling serves to exclude the diastereoisomeric product **56** from consideration. The carbinyl proton of **56** would expectedly show axial–axial coupling to both adjacent protons.[25]

The aldehyde cyclization mixture could not be separated, but reduction with DIBAH led to a separable 1:1 mixture of alcohols **53** and **54** in 95% yield. Swern oxidation of each afforded pure samples of aldehydes **51** and **52**. Although our product analysis does not rule out the possible formation of small amounts of aldehydes **55** and **56** as byproducts, the predominant formation of the predicted isomers **51** and **52** is clearly established. These findings suggest a promising route to the hydronaphthalene subunit of kijanolide and tetronolide.[1b,c]

As a final test of the modeling approach we examined the *syn*-4,6-dimethyl-2,8,10-undecatrienal system (Table III, V and VI; R^2 = α-Me, X = OR). Here we expected the prediction to be clearcut owing to the unfavorable 1,3-diaxial dimethyl arrangement in the endo product VI (R^2 = α-Me, X = OR). This expectation was born out by calculations on the methoxy derivatives where both C-8 epimers exhibited a strong preference for diastereoisomer V (Table III, entries 8 and 9).

The synthesis of the *syn*-4,6-dimethyl-7-(benzyloxy)-2,8,10-undecatrienals **66** and **67** was carried out as shown in Scheme IV in exact analogy to the previous undecatrienals. As before, we chose to employ a 1:1 mixture of C-7 epimers as a matter of expedience. Cyclization was effected with $EtAlCl_2$ in methylene chloride at −78 to −13 °C for 12 h affording a mixture of bicyclic products in 85% yield. Separation by chromatography on silica gel gave three major fractions; 1, a 1:1 mixture of trans and cis bicyclic aldehydes **69** and **70** in ca. 25% yield; 2, a 1:3.7 mixture of **69** and its carbinyl epimer **68** in 30% yield; and 3, a 1:7 mixture of **68** and starting trienal in ca. 30% yield.[26] Aldehyde **68** was identified through its characteristic ^1H NMR spectrum, which showed a triplet at 2.80 ppm (J = 10.1 Hz) attributable to the axial C-8 carbinyl proton. In addition the C-1 vinyl proton appeared as a broad doublet at 6.0 ppm. We observed the similar deshielding of the C-1 proton in related trans fused hydro-

Table IV. ^1H NMR Data for Bicyclic Aldehydes

compd	shift (pattern, J)[a,b] H-1	H-2	H-8	CHO
17	5.45 (br d, 10.0)	5.60 (m)		9.53 (d, 4.7)
18	5.45 (br d, 10.4)	5.52 (m)		9.45
33	6.08 (br d, 10.1)	5.63 (m)	3.14 (dt, 10.3, 4.3)	9.50
34	5.46 (br d, 9.9)	5.63 (m)	3.72 (br s)	9.54
51	6.01 (br d, 10.2)	5.63 (ddd, 10.1, 3.0, 1.2)	3.23 (dd, 10.7, 5.7)	9.46
52	5.41 (br d, 10.0)	5.66 (ddd, 10.0, 5.0, 2.6)	3.39 (br s)	9.49
68	5.98 (br d, 10.1)	5.67 (ddd, 10.0, 4.9, 2.4)	2.80 (t, 10.1)	9.51
69	5.42 (br d, 10.0)	5.66 (m)	3.26 (dd, 2.0, 2.0)	9.53
70	5.64 (br s)	5.64 (br s)	3.61 (dd, 2.0, 2.0)	9.24

[a] Chemical shifts are given in ppm from internal tetramethylsilane at 400 MHz. [b] Coupling constants are measured in Hz: br = broad, s = singlet, d = doublet, t = triplet, m = multiplet.

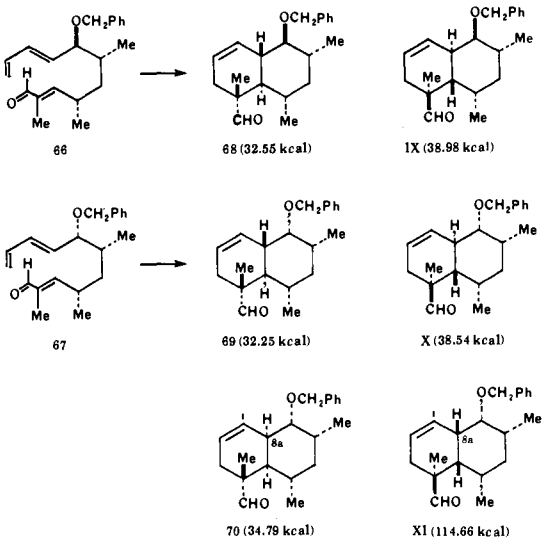


Figure 3. Cyclizations of epimeric trienals **66**/**67**. The calculated boat-chair energies are given in parentheses.

(25) A referee suggests that the ^1H NMR evidence for the Diels–Alder products **51** and **52** is inconclusive owing to the possibility of the alternative diastereomeric products **55** and **56** existing as cyclohex*ane* twist boat conformers to alleviate the expectedly large syn 1,3-dimethyl interaction between C4 and C5. Accordingly, **55** could show the H8 coupling pattern expected for **52**, and **56** could show the pattern expected for **51**. We feel that if **55** and **56** were indeed formed from **50**, the cyclohex*ene* ring of these products would more likely adopt expectedly lower energy twist boat conformations to relieve the C4/C5 interaction, thus leaving the relationship between H8a, H8, and H7 as stated. Additional evidence for the structure of **51** was secured from the 2D J resolved ^1H NMR spectrum of a homochiral sample of (+)-**51** which shows H4a as a triplet with J = 10.3 Hz. NOE enhancement between the C5 CH_3 and the aldehyde proton was also observed with (+)-**51**. Full details on the synthesis and structure elucidation of (+)-**51** will be disclosed in due course (work in progress with Stephen L. Crooks and Barry G. Shearer).

(26) Glass capillary gas chromatography was used to analyze these fractions.

naphthalene aldehydes with an 8β (equatorial) alkoxy substituent, including **33** and **51** (Table IV). The corresponding vinyl proton signal of analogous hydronaphthalene aldehydes with an 8α (axial) alkoxy substituent (e.g., **34**, **52**) is found at 5.4–5.5 ppm.

The ^{1}H NMR spectrum of the **69**/**70** mixture showed peaks at 5.42 (H-1) and 5.66 ppm (H-2) consistent with the α-benzyloxy orientation. In addition a singlet of twice the intensity of the 5.66-ppm peak appeared at 5.64 ppm. Roush has reported magnetic equivalence of the two vinyl protons in analogous cis fused bicyclic esters.[3b] Reduction of **69**/**70** with DIBAH led to an inseparable mixture of alcohols **71** and **72**. The derived diols **74** and **75**, however, were readily separated by chromatography. Table IV summarizes relevant ^{1}H NMR data for the bicyclic aldehyde Diels–Alder products.

Examination of the foregoing results indicates that the trienal isomer **66** affords the trans bicyclic aldehyde **68** in accord with the calculated prediction (Figure 3). The carbinyl epimer **67**, on the other hand, cyclizes to a nearly 1:1 mixture of the trans and cis fused bicyclic aldehyde **69** and **70**. The assignment of the cis fused product as **70**, rather than the other possible diastereoisomer XI (Figure 3), is based on ^{1}H NMR analysis. The C-1 vinyl proton of the derived alcohol **72** and diol **74** appear as broad doublets with J = 9.9 Hz as do the corresponding H-1 protons of the trans fused bicyclic aldehydes (Table IV). Thus H-1 and the adjacent ring-fusion proton H-8a show minimal vicinal coupling. In keeping with this observation, Dreiding models indicate the dihedral angle of these two protons to be near 90° in such compounds. The H-1/H-8a dihedral angle in XI, on the other hand, is near 30°, and rotation to 90° would impart considerable torsional strain.

Of the aldehydes examined in the current study, only **67** shows a significant tendency to cyclize via an exo transition state under Lewis acid catalysis.[27] The reasons for this departure are not clear. However, whatever the reasons, the transition-state geometry for exo cyclization undoubtedly differs from that for endo cyclization. Accordingly, deviations of our model from the actual transition state will likely differ for endo and exo pathways and systematic errors therefore will not cancel for the two. It should be noted that of the two a priori possible endo products (**68** and IX) from trienal **66** only **68** could be detected, in accord with prediction. Furthermore, in the cyclization of trienal **67**, the higher energy endo and exo products X and XI are absent or at best present in trace amounts, as expected from calculations.

In summary, we have developed an empirical approach for predicting the diastereoselectivity of Lewis acid catalyzed Diels–Alder cyclizations leading to ring-B-substituted hydronaphthalenes related to chlorothricolide and kijanolide.[1] The approach recognizes the stereoelectronic requirements of the Diels–Alder reaction (boat transition state) and utilizes productlike structures to evaluate relative transition-state energies, as suggested by recent ab initio calculations.[8] Deviations between such structures and the actual transition state appear to cancel for diastereoisomeric products as long as both are formed by the same (endo or exo) pathway. In the present study structure VII (Figure 2) was found to satisfactorily account for the diastereoselectivity of reactions leading to 8-alkoxy- and 4-methyl-substituted octahydronaphthalenes. Alkoxy substituents at C-8 showed little conformational preference both experimentally and by calculation (Figure 4), whereas a C-8 OTBS grouping gave mainly the "axial diastereoisomer" via III. A C-5 methyl substituent was found to exert a strong directing effect in favor of the "equatorial diastereoisomer" via V. Except for the OTBS effect, these trends are also in rough agreement with predictions arising from a subjective evaluation of nonbonded interactions in Dreiding models. The MM2 approach is preferred, however, especially for evaluating bond distortions and interannular steric interactions such as C-8/C-1 in II and III and C-4/C-5 in V and VI. Even though these calculations give only a rough approximation of the actual transition-state energies, the results can provide guidelines for synthetic planning at a higher confidence level than Dreiding models or the like.

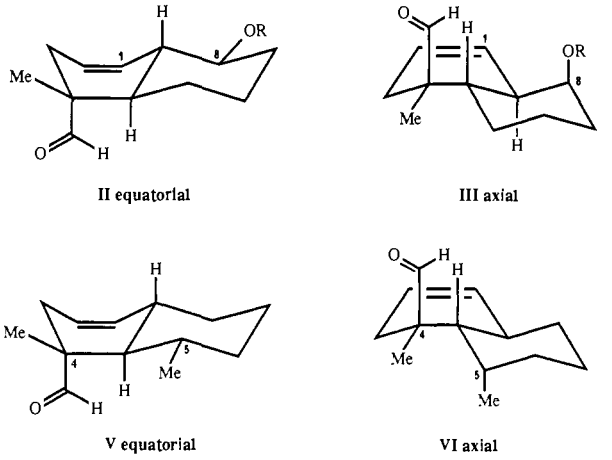


Figure 4. Diastereomeric transition state models.

Experimental Section

(*E*)-6-(Tetrahydropyranyloxy)-2-hexen-1-ol (2). To a stirred, cooled (0 °C) solution of 4.3 mL (30.7 mmol) of sodium bis(methoxyethoxy)-aluminum hydride (Red-Al) in 25 mL of Et_2O was added 1.95 g (9.6 mmol) of 6-tetrahydropyranyloxy-2-hexyn-1-ol (**1**) in 10 mL of Et_2O over 1 h.[12] The solution was warmed to 23 °C and stirred for 12 h. The reaction mixture was again cooled to 0 °C and cautiously quenched with H_2O. The aqueous layer was saturated with sodium chloride and was extracted with Et_2O. The combined organic layers were dried over anhydrous $MgSO_4$, solvent was removed, and the residue was purified by chromatography on silica gel eluting with 25% EtOAc in hexanes to afford 1.85 g (95%) of (E) allylic alcohol **2** as a colorless oil: IR (film) ν 3380, 2920, 2805, 1650, 1460, 1355 cm^{-1}; ^{1}H NMR ($CDCl_3$) (90 MHz) δ 1.70–1.30 (8 H, m, CH_2), 2.3–2.1 (2 H, m, allylic CH_2), 3.80–3.30 (4 H, m, CH_2O), 4.0 (2 H, br s, allylic CH_2O), 4.5 (1 H, br s, acetal H), 5.85–5.60 (2 H, m, vinyl H). Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07. Found 66.04; H, 10.09.

(*E*)-6-(Tetrahydropyranyloxy)-2-hexenal (3). To a stirred, cooled (−10 °C) solution of 180 g (0.478 mol) of pyridinium dichromate in 1.0 L of DMF was added 79.6 g (0.398 mol) of allylic alcohol **2** over 15 min.[14] The mixture was warmed to 0 °C, stirred for 2 h, poured into 1 L of H_2O, and extracted 4 times with Et_2O–pentane. The combined organic layers were washed with H_2O, saturated $CuSO_4$ solution, and brine and were dried over anhydrous $MgSO_4$. Distillation under reduced pressure afforded 67 g (85%) of aldehyde **3** as a colorless liquid: IR (film) ν 2920, 2850, 2710, 1690, 1640, 1440, 1360 cm^{-1}; ^{1}H NMR ($CDCl_3$) (90 MHz) δ 2.0–1.40 (8 H, m, CH_2), 2.6–2.3 (2 H, dt, J = 6 Hz, H4), 4.0–3.3 (4 H, m, CH_2O), 4.55 (1 H, br s, acetal H), 6.10 (1 H, dd, J = 8, 15 Hz, H2), 6.80 (1 H, dt, J = 15.6 Hz, H3), 9.50 (1 H, d, J = 8 Hz, H1). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.17. Found: C, 66.54; H, 9.19.

(*E*)-4,6-Heptadien-1-ol (5). To a stirred, cooled (−78 °C) suspension of 151 g (0.422 mol) of methyltriphenylphosphonium bromide in 600 mL of dry THF was added 150 mL (0.420 mol) of *n*-butyllithium (2.8 M in hexanes). The mixture was stirred at −78 °C for 30 min, and 66 g (333 mmol) of aldehyde **3** was added in 50 mL of dry THF. The mixture was stirred at −78 °C for 1 h, warmed to 23 °C, poured into 400 mL of H_2O, and extracted 3 times with Et_2O–pentane. The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated. The residue was suspended in pentane and filtered through 100 g of silica gel. The filtrate was concentrated and dissolved in 150 mL of methanol, and 1.0 g of activated Dowex AG 50W acidic ion exchange resin was added. The mixture was heated to 40 °C for 3 h, cooled to 23 °C, and filtered. Distillation (105 °C, 47 mmHg) afforded 24.7 g (66%) of heptadienol **5** as a colorless liquid: IR (film) ν 3320, 2930, 2860, 1650, 1610, 1440 cm^{-1}; ^{1}H NMR ($CDCl_3$) (400 MHz) δ 1.64–1.59 (2 H, m, H2), 2.11 (2 H, dt, J = 7.2 Hz, H3), 2.57 (1 H, br s, OH), 3.56 (2 H, *t*, J = 6.5 Hz, H1) 5.06–4.91 (2 H, 4 lines, H7), 5.69–5.60 (1 H, m, H4), 6.06–5.99 (1 H, m, H5), 6.30–6.20 (1 H, m, H6). Anal. Calcd for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 75.01; H, 10.73.

(*E*)-1-Bromo-4,6-heptadiene (7). To a stirred, cooled (0 °C) solution of 770 mg (6.86 mmol) of alcohol **5** in 15 mL of dry CH_2Cl_2 was added 2.35 mL (16.9 mmol) of Et_3N followed by 0.95 mL (12.3 mmol) of freshly distilled methanesulfonyl chloride. The turbid mixture was stirred at 0 °C for 1 h, poured into H_2O, and extracted 2 times with Et_2O. The

(27) We have previously noted small amounts of cis (exo) products in the cyclization of a TBS ether analogue of trienal I (R^1 = R^3 = Me, R^2 = TBS).[2b]

combined organic layers were dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure. The resulting crude mesylate was dissolved in 10 mL of dry THF containing 1.47 g (16.9 mmol) of anhydrous lithium bromide. The solution was heated to reflux for 18 h, cooled, poured into H_2O, and extracted with Et_2O. The organic layer was dried over anhydrous $MgSO_4$, and solvent was removed to afford 1.06 g (90%) of bromide **7**: IR (film) ν 3000, 2950, 1605, 1445, 1250, 1010 cm^{-1}; ^1H NMR ($CDCl_3$) (400 MHz) δ 1.90 (2 H, t, J = 7 Hz, H2), 2.25 (2 H, dt, J = 7 Hz, H3), 3.45 (2 H, t, J = 6.3 Hz, H1), 5.2–4.9 (2 H, m, H7), 5.7–5.6 (1 H, m, H4), 6.15–6.05 (1 H, m, H5), 6.35–6.25 (1 H, m, H6).

(*E*)-2-Methyl-6,8-nonadienoic Acid (8). To a stirred, cooled (0 °C) solution of 3.08 mL (22.0 mmol) of diisopropylamine in 15 mL of dry THF was added 8.5 mL (22.0 mmol) of 2.6 M *n*-butyllithium in hexanes. After 15 min, 0.85 mL (11.4 mmol) of propionic acid was added followed by 2.1 mL (12.0 mmol) of HMPA.[13] The mixture was heated to 50 °C for 1 h, cooled to 0 °C, and treated with 2.0 g (11.0 mmol) of bromide **7**. After warming to 23 °C and stirring 10 h, the solution was poured into 50 mL of ice–10% HCl and extracted thrice with CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated. The crude acid was purified by chromatography on silica gel eluting with 24:1:75 EtOAc/HOAc/hexanes to afford 1.9 g (100%) of acid **8** as a colorless oil: IR (film) ν 3050, 2950, 2890, 2600, 1690, 1605, 1450, 1400, 1235 cm^{-1}; ^1H NMR ($CDCl_3$) (90 MHz) δ 1.2 (3 H, d, J = 7.5 Hz, C-2 CH_3), 1.30–1.80 (4 H, m, H-3, H-4), 2.2–2.0 (2 H, m, H-5), 2.6–2.3 (1 H, m, H-2), 4.9 (1 H, br d, J = 11.5 Hz, H-9a), 5.1 (1 H, br d, J = 17 Hz, H-9b), 6.5–5.5 (3 H, m, H-6, H-7, H-8). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.52. Found: C, 71.39; H, 9.59.

(*E*)-2-Methyl-6,8-nonadien-1-ol (9). To a stirred, cooled (0 °C) suspension of 600 mg (15.0 mmol) of lithium aluminum hydride in 70 mL of dry Et_2O was added 1.89 g (11.0 mmol) of acid **8** in 30 mL of Et_2O over 5 min. The mixture was warmed to 23 °C over 2 h and cooled to 0 °C. The mixture was treated with 0.60 mL of H_2O, 0.60 mL of 15% NaOH solution, and 1.80 mL of H_2O and filtered. The salts were washed with 3 20-mL portions of Et_2O, and the organic layers were combined, dried over anhydrous $MgSO_4$, and concentrated. Column chromatography on silica gel eluting with 15% EtOAc in hexanes afforded 1.70 g (90%) of alcohol **9** as a colorless oil: IR (film) ν 3350, 2970, 2900, 2850, 1650, 1600, 1470 cm^{-1}; ^1H NMR ($CDCl_3$) (90 MHz) δ 0.85 (3 H, d, J = 7.0 Hz, C-2 CH_3), 1.8–1.2 (5 H, m, H-2, H-3, H-4), 2.2–1.9 (2 H, m, H-5), 3.5–3.4 (2 H, m, H-1), 4.9 (1 H, br d, J = 11.5 Hz, H-9a), 5.1 (1 H, br d, J = 17 Hz, H-9b), 6.5–5.5 (3 H, m, H-6, H-7, H-8). Anal. Calcd for $C_{10}H_{18}O$: C, 77.86; H, 11.68. Found: C, 77.87; H, 11.76.

(*E*)-2-Methyl-6,8-nonadienal (10). To a stirred, cooled (10 °C) solution of 1.02 g (6.6 mmol) of alcohol **9** in 20 mL of dry CH_2Cl_2 was added 10 g of dried 3Å sieves (10 μ powder) followed by 3.1 g (8.3 mmol) of pyridinium dichromate. After being warmed to 23 °C, the mixture was stirred for 3 h, diluted with 100 mL of Et_2O, and filtered through Celite. Solvent was removed under reduced pressure, and the crude aldehyde was purified by chromatography on silica gel eluting with 5% EtOAc in hexanes to afford 840 mg (84%) of **10** as a pale yellow oil: IR (film) ν 3070, 2960, 2925, 2850, 2700, 1725, 1650, 1610, 1470 cm^{-1}; ^1H NMR ($CDCl_3$) (90 MHz) δ 1.1 (3 H, d, J = 7.5 Hz, C-2 CH_3), 1.8–1.3 (4 H, m, H-3, H-4), 2.4–2.0 (3 H, m, H-2, H-5), 4.9 (1 H, br d, J = 11 Hz, H-9a), 5.1 (1 H, br d, J = 17 Hz, H-9b), 6.5–5.5 (3 H, m, H-6, H-7, H-8). Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.52. Found: C, 78.90; H, 10.59.

Ethyl (*E*,*E*)-4-Methyl-2,8,10-undecatrienoate (11). To a stirred, cooled (0 °C) solution of 500 mg (3.3 mmol) of aldehyde **10** in 15 mL of dry CH_2Cl_2 was added 1.74 g (5.0 mmol) of ethyl α-(triphenylphosphoryliden)acetate over 15 min.[15] The solution was warmed to 23 °C and stirred 14 h. Solvent was removed under reduced pressure, and the residue was chromatographed on silica gel eluting with 3% EtOAc in hexanes to afford 582 mg (79%) of ester **11** as a colorless oil: IR (film) ν 3070, 2955, 2920, 2850, 1720, 1650, 1605, 1460, 1375, 1275 cm^{-1}; ^1H NMR ($CDCl_3$) (90 MHz) δ 1.1 (3 H, d, J = 6 Hz, C-4 CH_3), 1.25 (3 H, t, J = 7 Hz, OCH_2CH_3), 2.1–1.9 (2 H, m, H-7), 2.4–2.2 (1 H, m, H-4), 4.15 (2 H, q, J = 7 Hz, OCH_2CH_3), 4.9 (1 H, br d, J = 11 Hz, H-11a), 5.1 (1 H, br d, J = 17 Hz, H-11b), 6.5–5.5 (4 H, m, H-2, H-8, H-9, H-10), 6.8 (1 H, dd, J = 7, 16 Hz, H-3).

(*E*,*E*)-4-Methyl-2,8,10-undecatrien-1-ol (12). To a stirred, cooled (−78 °C) solution of 100 mg (0.45 mmol) of ester **11** in 25 mL of dry Et_2O was added 1.0 mL (1.0 mmol) of DIBAH in hexanes. After 1 h, the reaction was quenched by slow addition of 15 mL of saturated sodium potassium tartrate solution. The mixture was extracted twice with Et_2O, and the combined organic layers were dried over anhydrous $MgSO_4$ and concentrated. The crude alcohol was purified by chromatography on silica gel eluting with 10% EtOAc in hexanes to afford 80 mg (99%) of alcohol **12** as a colorless oil: IR (film) ν 3350, 3070, 2950, 2900, 2850, 1650, 1605, 1460, 1380 cm^{-1}; ^1H NMR ($CDCl_3$) (90 MHz) δ 0.9 (3 H, d, J = 7 Hz, C-4 CH_3), 1.5–1.2 (4 H, m, H-5, H-6), 2.2–1.8 (3 H, m, H-4, H-7), 4.0 (2 H, br d, J = 3.5 Hz, H-1), 4.9 (1 H, br d, J = 11 Hz, H-11a), 5.1 (1 H, br d, J = 17 Hz, H-11b), 6.5–5.4 (5 H, m, H-2, H-3, H-8, H-9, H-10).

(*E*,*E*)-4-Methyl-2,8,10-undecatrienal (13). To a stirred solution of 1.2 g (6.7 mmol) of alcohol **12** in 45 mL of dry CH_2Cl_2 was added 6.0 g of active MnO_2. The mixture was stirred at 23 °C for 6 h and filtered through Celite. Removal of solvent under reduced pressure and chromatography on silica gel eluting with 3% EtOAc in hexanes afforded 1.02 g (85%) of aldehyde **13** as a colorless oil: IR (film) ν 3060, 2940, 2900, 2835, 2690, 1680, 1655, 1600, 1460, 1380, 1235 cm^{-1}; ^1H NMR ($CDCl_3$) (90 MHz) δ 1.1 (3 H, d, J = 6.5 Hz, C-4 CH_3), 1.7–1.2 (4 H, m, H-5, H-6), 2.3–2.0 (2 H, m, H-7), 2.6–2.3 (1 H, m, H-4), 4.9 (1 H, br d, J = 11 Hz, H-11a), 5.1 (1 H, br d, J = 17 Hz, H-11b), 6.6–5.5 (4 H, m, H-2, H-8, H-9, H-10), 6.75 (1 H, dd, J = 7.2 Hz, H-3), 9.55 (1 H, d, J = 7.5 Hz, H-1).

Methyl (*E*,*E*)-2,4-Dimethyl-2,8,10-undecatrienoate (14). To a stirred, cooled (0 °C) solution of 500 mg (3.3 mmol) of aldehyde **10** in 15 mL of dry CH_2Cl_2 was added 1.74 g (5.0 mmol) of methyl α-(triphenylphosphorylidene)propionate over 15 min. After having been warmed to 23 °C and stirred for 14 h, the solution was concentrated under reduced pressure, and the residue was chromatographed on silica gel eluting with 3% EtOAc in hexanes to afford 570 mg (78%) of ester **14** as a colorless oil: IR (film) ν 3050, 2900, 2830, 1720, 1640, 1600, 1435, 1245 cm^{-1}; ^1H NMR ($CDCl_3$) (90 MHz) δ 1.0 (3 H, d, J = 6.5 Hz, C-4 CH_3), 1.4–1.2 (4 H, m, H-5, H-6), 1.75 (3 H, br s, C-2 CH_3), 2.1–1.9 (2 H, m, H-7), 2.6–2.4 (1 H, m, H-4), 3.7 (3 H, s, CO_2CH_3), 4.9 (1 H, br d, J = 11 Hz, H-11a), 5.1 (1 H, br d, J = 17 Hz, H-11b), 6.7–5.5 (4 H, m, H-3, H-8, H-9, H-10) ppm.

(*E*,*E*)-2,4-Dimethyl-2,8,10-undecatrien-1-ol (15). Reduction of 100 mg (0.45 mmol) of ester **14** was performed as described for **11** to afford 85 mg (99%) of chromatographed alcohol **15** as a colorless oil: IR (film) ν 3350, 3090, 2900, 2850, 1650, 1605, 1460, 1440, 1380 cm^{-1}; ^1H NMR ($CDCl_3$) (90 MHz) δ 0.85 (3 H, d, J = 6.5 Hz, C-4, CH_3), 1.4–1.2 (4 H, m, H-5, H-6), 1.6 (3 H, br s, C-2 CH_3), 2.1–1.8 (2 H, m, H-7), 2.4–2.2 (1 H, m, H-4), 3.9 (2 H, br s, H-1), 5.1–4.9 (3 H, m, H-11, OH), 6.4–5.4 (4 H, H-3, H-8, H-9, H-10).

(*E*,*E*)-2,4-Dimethyl-2,8,10-undecatrienal (16). Oxidation of 650 mg (3.3 mmol) of alcohol **15** was performed as described for **12** affording 540 mg (84%) of aldehyde **16** as a colorless oil: IR (film) ν 3090, 2970, 2930, 2850, 2710, 1690, 1650, 1610, 1450, 1240 cm^{-1}; ^1H NMR ($CDCl_3$) (90 MHz) δ 1.05 (3 H, d, J = 6.5 Hz, C-4 CH_3), 1.6–1.4 (4 H, m, H-5, H-6), 1.75 (3 H, s, C-2 CH_3), 2.3–2.0 (2 H, m, H-7), 2.8–2.6 (1 H, m, H-4), 4.9 (1 H, br d, J = 11 Hz, H-11a), 5.1 (1 H, br d, J = 17 Hz, H-11b), 6.6–5.5 (4 H, m, H-3, H-8, H-9, H-10), 9.4 (1 H, s, CHO).

5α-Methyl-3,4,4aα,5,6,7,8,8aβ-octahydronaphthalene-4α-carboxaldehyde (17). To a stirred, cooled (−78 °C) solution of 340 mg (1.91 mmol) of enal diene **13** in 15 mL of dry CH_2Cl_2 was added 1.91 mL (1.91 mmol) of 1.0 M ethylaluminum dichloride in hexanes dropwise. The solution was warmed to −23 °C over 1 h and then treated with 25 mL of saturated $NaHCO_3$. The mixture was extracted with CH_2Cl_2, and the organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. Chromatography on silica gel eluting with 3% EtOAc in hexanes afforded 276 mg (81%) of cyclized product **17** as a colorless oil [IR (film) ν 3000, 2900, 2840, 2680, 1720, 1450, 1380 cm^{-1}; ^1H NMR ($CDCl_3$) (90 MHz) δ 0.85 (3 H, d, J = 6 Hz, C-5 CH_3), 2.40 (1 H, m, H-4), 5.45 (1 H, br d, J = 10.0 Hz, H-1), 5.60 (1 H, m, H-2), 9.53 (1 H, d, J = 4.7 Hz, CHO)]. Two-dimensional J-resolved ^1H NMR analysis established coupling constants of 10.4 Hz for H4a-H4, H4a-H8a, and H4a-H5 in accord with the assigned structure. In addition, the C-5 CH_3 and the formyl proton showed a strong NOE enhancement.

4β,5α-Dimethyl-3,4,4a,5,6,7,8,8aβ-octahydronaphthalene-4α-carboxaldehyde (18). Cyclization of 74 mg (0.38 mmol) of enal diene **16** was performed as described for **13**; except stirring was continued at −23 °C for 10 h. Chromatography on silica gel eluting with 3% EtOAc in hexanes afforded 60 mg (81%) of cyclized product **18** plus 4 mg of starting enal diene as colorless oils: IR (film) ν 3000, 2900, 2840, 2670, 1720, 1440, 1380 cm^{-1}; ^1H NMR ($CDCl_3$) (400 MHz) δ 0.80 (3 H, d, J = 6 Hz, C-5 CH_3), 1.6–1.1 (6 H, m), 1.9–1.6 (4 H, m), 2.2 (1 H, br d, J = 11 Hz), 5.45 (1 H, br d, J = 10.4 Hz, H-1), 5.55–5.50 (1 H, m, H-2), 9.45 (1 H, s, CHO).

***rel*-(2*R*,4*R*)-5-(*tert*-Butyldimethylsilyloxy)-2,4-dimethylpentan-1-ol (41).** A solution of 736 mg (5.57 mmol) of (±)-2,4-dimethyl-1,5-pentanediol[24] in 6 mL of DMF was treated with 728 mg (5.29 mmol) of *tert*-butyldimethylsilyl chloride and 493 mg (7.24 mmol) of imidazole at room temperature for 30 h. Purification by column chromatography on silica gel with 15% ether–hexane as eluent yielded 579 mg (42%) of silyl ether **41**: IR (film) ν 3320, 2950, 2850, 1465 cm^{-1}; ^1H NMR ($CDCl_3$) (400 MHz) δ 0.04 (6 H, s, $Si(CH_3)_2$), 0.85 (3 H, d, J = 6.6 Hz,

$CHCH_3$), 0.88 (3 H, d, J = 6.7 Hz, $CHCH_3$), 0.89 (9 H, s, $CH_3)_3Si$), 1.15 (2 H, 14 lines, CH_2), 1.53 (1 H, br s, OH), 1.73 (2 H, m, CH_3CH), 3.35–3.50 (4 H, m, CH_2); ^{13}C NMR ($CDCl_3$) (20 MHz) δ 69.0, 68.8, 36.8, 33.0, 32.9, 25.9, 16.6, 16.4, −5.4. Anal. Calcd for $C_{13}H_{30}O_2Si$: C, 63.35; H, 12.27. Found: C, 63.21; H, 12.31.

***rel*-(2*R*,4*R*)-5-(*tert*-Butyldimethylsilyloxy)-2,4-dimethylpentanal (42).** Silyl ether **41** (0.579 g, 2.35 mmol) was added to 0.33 mL (3.77 mmol) of oxalyl chloride, 0.53 mL (7.52 mmol) of Me_2SO, and 2.29 mL of triethylamine in a total of 24 mL of CH_2Cl_2.[21] Purification by column chromatography on silica gel, eluting with 5% ether–hexane provided 518 mg (90%) of aldehyde **42**: IR (film) ν 2900, 2825, 2775, 1720, 1460 cm^{-1}; ^1H NMR ($CDCl_3$) (400 MHz) δ 0.04 (6 H, s, $Si(CH_3)_2$), 0.88 (3 H, d, J = 6.7 Hz, $CHCH_3$), 0.89 (9 H, s, $(CH_3)_3Si$), 1.06 (2 H, d, J = 7.0 Hz), 1.44 (2 H, 14 lines CH_2), 1.70 (1 H, m), 2.42 (1 H, m), 3.42 (2 H, AB of ABX, J_{AX} = 5.8, J_{BX} = 6.0, J_{AB} = 9.8 Hz, CH_2OTBS), 9.17 (1 H, d, J = 2.0 Hz, CHO). Anal. Calcd for $C_{13}H_{28}O_2Si$: C, 63.88; H, 11.55. Found: C, 63.96; H, 11.57.

***rel*-(5*R*,6*S*,8*S*)- and *rel*-(5*R*,6*R*,8*R*)-9-(*tert*-Butyldimethylsilyloxy)-6,8-dimethylnon-1-en-3-yn-5-ol (43).** To a solution of 367 mg (3.53 mmol) of a 50% solution of 1-buten-3-yne in xylenes in 5 mL of THF at −78 °C was added 1.26 mL (3.29 mmol) of 2.6 M *n*-BuLi in hexanes and a solution of 518 mg (2.12 mmol) of aldehyde **42** in 5 mL of THF. The alcohols **43** were isolated in nearly quantitative yield as a roughly 1:1 mixture of diastereoisomers according to glass capillary GC and ^1H NMR analysis. An analytical sample was prepared by column chromatography on triethylamine-deactivated silica gel, eluting with 20% ether–hexane. IR (film) ν 3350, 2950, 2910, 2875, 2850, 1600, 1590, 1465 cm^{-1}; ^1H NMR ($CDCl_3$) (400 MHz) δ 0.03 (6 H, s, $Si(CH_3)_2$), 0.85 (3 H, d, J = 6.8 Hz, $CHCH_3$), 0.90 (9 H, s, $SiC(CH_3)_3$), 0.98 (3 H, d and d, J = 6.7 and 6.8 Hz, $CHCH_3$), 1.20 and 1.33 (2 H, m and m, CH_2), 1.71 and 1.86 (1 H, m and m), 2.01 (1 H, br s, OH), 3.42 (2 H, d and d, J = 4.1 and 4.2 Hz, CH_2OTBS), 4.37 (1 H, br t, $CHOH$), 5.67 (2 H, m, C=CH), 5.78–5.85 (1 H, m, C=CH). Anal. Calcd for $C_{17}H_{32}O_2Si$: C, 68.86; H, 10.88. Found: C, 68.92; H, 10.94.

(3*E*)-*rel*-(5*R*,6*S*,8*S*)- and (3*E*)-*rel*-(5*R*,6*R*,8*R*)-9-(*tert*-Butyldimethylsilyloxy)-6,8-dimethyl-1,3-nonadien-5-ol (44). A solution of 727 mg (2.12 mmol) of propargylic alcohol **43** in 7 mL of ether was treated with 2.18 mL (7.42 mmol) of 3.4 M Red-Al in toluene for 3 h.[12] The yield of alcohol **44** thus obtained was quantitative. Although this alcohol was normally used without further purification, an analytical sample could be prepared by column chromatography on triethylamine-deactivated silica gel, eluting with 20% ether–hexane: IR (film) ν 3350, 2950, 2910, 2875, 2850, 1600, 1465 cm^{-1}; ^1H NMR ($CDCl_3$) (400 MHz) δ 0.04 (6 H, s, $Si(CH_3)_2$), 0.84 (3 H, d and d, J = 6.6 and 6.8 Hz, $CHCH_3$), 0.88 and 0.90 (12 H, m, $SiC(CH_3)_3$ and $CHCH_3$), 1.15–1.25 (2 H, m, CH_2), 1.60 and 1.62 (1 H, br s and br s, OH), 1.63–1.76 (2 H, m, $CHCH_3$), 3.39 (2 H, m, CH_2OTBS), 3.99 (1 H, br m, $CHOH$), 5.08 (1 H, d, J = 10.2 Hz, cis H of $C=CH_2$), 5.20 (1 H, d and d, J = 16.8 and 16.5 Hz, trans H of $C=CH_2$), 5.71 (1 H, dd, J = 15.0, 6.7 Hz, C=CH), 6.19–6.25 (1 H, 10 lines, C=CH), 6.30–6.39 (1 H, td, J = 16.9, 10.1 Hz, C=CH). Anal. Calcd for $C_{24}H_{38}O_2Si$: C, 68.39; H, 11.48. Found: C, 68.47; H, 11.54.

(3*E*)-*rel*-(5*R*,6*S*,8*S*)- and (3*E*)-*rel*-(5*R*,6*R*,8*R*)-9-(*tert*-Butyldimethylsilyloxy)-6,8-dimethyl-5-(benzyloxy)-1,3-nonadiene (45). Alcohol **44** (733 mg, 2.12 mmol) was benzylated by using 0.82 mL (2.12 mmol) of 2.6 M *n*-BuLi in hexane, 0.35 mL (2.97 mmol) of benzyl bromide, and 0.74 mL (4.21 mmol) of HMPA in 2.5 mL of THF. Benzyl ethers **45** were obtained as a mixture with benzyl bromide after purification by chromatography on a 1.5 × 16 cm column of silica gel, eluting with 1.4% ether in hexane: IR (film) ν 2950, 2910, 2875, 2850, 1600, 1465 cm^{-1}; ^1H NMR ($CDCl_3$) (400 MHz) δ 0.03 and 0.04 (3 H, s and s, $Si(CH_3)_2$), 0.08–0.93 (15 H, m, $SiC(CH_3)_3$ and $CHCH_3$), 1.12–1.26 (2 H, m, CH_2), 1.60–1.86 2 H, m, $CHCH_3$), 3.39 (2 H, m, CH_2OTBS), 3.55 (1 H, m, $CHOBn$), 4.32 and 4.33 (1 H, d and d, J = 12.0 Hz, H of OCH_2Ph), 4.68 (1 H, d, J = 12.0 Hz, H of OCH_2Ph), 5.10 (1 H, d, J = 10.4 Hz, cis H of $C=CH_2$), 5.21 (1 H, m, trans H of $C=CH_2$), 5.58–5.65 (1 H, m, C=CH), 6.14–6.21 (1 H, m, C=CH), 6.34–6.43 (1 H, m, C=CH), 7.25–7.34 (5 H, m, aryl H). Anal. Calcd for $C_{24}H_{40}O_2Si$: C, 74.17; H, 10.37. Found: C, 74.08; H, 10.41.

(3*E*)-*rel*-(2*R*,4*R*,5*R*)- and (3*E*)-*rel*-(2*R*,4*R*,5*S*)-2,4-Dimethyl-5-(benzyloxy)-6,8-nonadien-1-ol (46). A solution of 655 mg (1.69 mmol) of silyl ethers **45** in 0.5 mL of THF was treated with 3 mL of 1.0 M tetrabutylammonium fluoride in THF. Purification by chromatography on a 1 × 16 cm silica gel column with 20% ether–hexane as eluent afforded 336 mg (73% over 3 steps) of alcohol **46**: IR (film) ν 3350, 2950, 2900, 2850, 1600, 1460 cm^{-1}; ^1H NMR δ 0.83–0.94 (6 H, m, $CHCH_3$), 1.14–1.36 (2 H, m, CH_2), 1.74 and 1.83 (2 H, m and m), 3.46 (2 H, br m, CH_2OH), 3.57 (1 H, m, $CHOBn$), 4.32 and 4.58 (2 H, ABq, J_{AB} = 12.0 Hz, OCH_2Ph), 5.12 (1 H, d, J = 10.0 Hz, cis $C=CH_2$), 5.21–5.26 (1 H, dm, J = 17.0 Hz, trans $C=CH_2$), 5.59–5.65 (1 H, m, C=CH), 6.15–6.22 (1 H, m, C=CH), 6.34–6.43 (1 H, m, C=CH), 7.24–7.36 (5 H, m, aryl H). Anal. Calcd for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.71; H, 9.59.

(3*E*)-*rel*-(2*R*,4*R*,5*R*)- and (3*E*)-*rel*-(2*R*,4*R*,5*S*)-2,4-Dimethyl-5-(benzyloxy)-6,8-nonadienal (47). A 211-mg (0.77 mmol) sample of alcohol **46** was oxidized with 0.11 mL (1.23 mmol) of oxalyl chloride, 0.18 mL (2.46 mmol) of Me_2SO, and 0.75 mL (5.29 mmol) of triethylamine in a total of 8 mL of CH_2Cl_2.[21] Purification by chromatography on a 1 × 16 cm column of silica gel, eluting with 3.5% ether–hexane, afforded 192 mg (92%) of the aldehydes **47**: IR (film) ν 2950, 2900, 2850, 2700, 1720, 1600, 1460 cm^{-1}; ^1H NMR ($CDCl_3$) (400 MHz) δ 0.86 and 0.92 (3 H, d and d, J = 6.8 Hz, CH_3CH), 1.01–1.09 (3 H, m, CH_3CH), 1.40–1.61 (2 H, m, CH_2), 1.79 (1 H, m, CH_3CH), 2.38 (1 H, m, CH_3CH), 3.55 (dd, J = 8.3, 6.4 Hz), 3.60 (ddd, J = 8.7, 4.4, and 0.6 Hz; 1 H, $CHOBn$), 4.27 and 4.28 (1 H, d and d, J = 12.0 Hz, H of OCH_2Ph), 4.47–4.58 (1 H, m, H of OCH_2Ph), 5.10–5.25 (2 H, m, $C=CH_2$), 5.55–5.63 (1 H, m, C=CH), 6.15–6.22 (1 H, m, C=CH), 6.31–6.41 (1 H, m, C=CH), 7.23–7.35 (5 H, m, aryl H).

(2*E*,8*E*)-*rel*-(4*R*,6*R*,7*S*)- and (2*E*,8*E*)-*rel*-(4*R*,6*R*,7*R*)-Methyl 2,4,6-Trimethyl-7-(benzyloxy)-2,8,10-undecatrienoate (48). Aldehyde **47** (180 mg, 0.66 mmol) was homologated with 322 mg (0.93 mmol) of methyl α-(triphenylphosphorylidene)propionate in 1 mL of CH_2Cl_2 as described for the conversion of **10** to **14**. Purification by chromatography on a 1 × 16 cm column of silica gel with 4% ether–hexane as eluent afforded 223 mg (98%) of ester **48**: IR (film) ν 2950, 2900, 2850, 1705, 1650, 1600, 1460, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) (400 MHz) δ 0.85–0.98 (6 H, m, $CHCH_3$), 1.03–1.14 (2 H, m, CH_2), 1.48–1.67 (1 H, m), 1.74 and 1.76 (3 H, d and d, J = 1.5 Hz, vinyl CH_3), 2.43 and 2.56 (1 H, 8 lines), 3.54 (1 H, m, $CHOBn$), 3.70 and 4.71 (3 H, s, CH_3O), 4.27 and 4.29 (1 H, d, J = 12.1 Hz, H of OCH_2Ph), 4.54 and 4.57 (1 H, d, J = 12.1 Hz, H of OCH_2Ph), 5.09–5.23 (2 H, m, $C=CH_2$), 5.54–5.62 (1 H, m, C=CH), 6.10–6.19 (1 H, m, C=CH), 6.32–6.41 (1 H, m, C=CH), 6.49–6.57 (1 H, 16 lines, H3), 7.22–7.34 (5 H, m, aryl H). Anal. Calcd for $C_{22}H_{30}O_3$: C, 77.16; H, 8.83. Found: C, 77.05; H, 8.89.

(2*E*,8*E*)-*rel*-(4*R*,6*R*,7*S*)- and (2*E*,8*E*)-*rel*-(4*R*,6*R*,7*R*)-2,4,6-Trimethyl-7-(benzyloxy)-2,8,10-undecatrien-1-ol (49). A solution of 223 mg (0.65 mmol) of ester **48** was reduced with 1.43 mL (1.43 mmol) of 1.0 M DIBAH in hexanes as described for the reduction of **11** to **12**. Although the product, alcohol **49**, was normally used without further purification, an analytical sample was prepared by column chromatography on silica gel, eluting with 20% ether–hexane: IR (film) ν 3350, 2950, 2850, 1600, 1460 cm^{-1}; ^1H NMR ($CDCl_3$) (400 MHz) 0.82–0.94 (6 H, m, $CHCH_3$), 0.97–1.08 (2 H, m, CH_2), 1.24 and 1.31 (1 H, br s, OH), 1.37 and 1.46 (1 H, m), 1.57–1.61 (3 H, m, vinyl CH_3), 1.79 and 2.45 (1 H, m), 3.58 (1 H, m, CHOBn), 3.94 (2 H, br s, CH_2OH), 4.28 and 4.30 (1 H, d, J = 12.1 Hz, H of OCH_2Ph), 4.55 and 4.58 (1 H, d, J = 12.1 Hz, H of OCH_2Ph), 5.05–5.24 (2 H, m, $C=CH_2$), 5.55–5.67 (1 H, m, C=CH), 6.10–6.20 (1 H, m, C=CH), 6.32–6.42 (1 H, m, C=CH), 7.22–7.35 (5 H, m, aryl H). Anal. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 80.12; H, 9.67.

(2*E*,8*E*)-*rel*-(4*R*,6*R*,7*S*)- and (2*E*,8*E*)-*rel*-(4*R*,6*R*,7*R*)-2,4,6-Trimethyl-7-(benzyloxy)-2,8,10-undecatrienal (50). Trienol **49** (96 mg, 0.31 mmol) was oxidized with 54 μL (0.62 mmol of oxalyl chloride, 88 μL (1.24 mmol) of Me_2SO, and 0.39 mL (2.79 mmol) of triethylamine in 3 mL of CH_2Cl_2.[21] The product was purified by chromatography on a 1 × 12 cm column of silica gel with 5% ether–hexane as eluent providing 91 mg (92%) of the trienals **50**: IR (film) ν 2950, 2910, 2850, 2700, 1690, 1640, 1604, 1460 cm^{-1}; ^1H NMR ($CDCl_3$) (400 MHz) δ 0.88–1.01 (6 H, four d, J = 6.8 Hz, $CHCH_3$), 1.10–1.22 (2 H, m, CH_2), 1.55–1.80 (1 H, m), 1.66 and 1.68 (3 H, d, J = 1.4 Hz, vinyl CH_3), 2.65 and 2.77 (1 H, m), 3.56 (1 H, m, CHOBn), 4.28 (1 H, d, J = 12.0 Hz, H of OCH_2Ph), 4.57 and 4.60 (1 H, d, J = 12.0 Hz, H of OCH_2Ph), 5.10–5.27 (2 H, m, $C=CH_2$), 5.56–5.64 (1 H, m, C=CH), 6.12–6.29 (2 H, m, C=CH), 6.33–6.41 (1 H, m, H-3), 7.22–7.34 (5 H, m, aryl H), 9.36 (1 H, s, CHO). Anal. Calcd for $C_{21}H_{28}O_2$: C, 80.73; H, 9.03. Found: C, 80.75; H, 9.04.

***rel*-(4*R*,4a*R*,5*S*,7*S*,8*S*,8a*S*)- and *rel*-(4*R*,4a*R*,5*S*,7*S*,8*R*,8a*S*)-4,5,7-Trimethyl-8-(benzyloxy)-3,4,4a,5,6,7,8,8a-octahydronaphthalene-4-carboxaldehyde (51 and 52).** To a solution of 79 mg (0.25 mmol) of trienal **50** in 2.5 mL of CH_2Cl_2 was added 0.25 mL (0.25 mmol) of 1.0 M dimethylaluminum chloride in hexanes dropwise. The solution was warmed slowly to −13 °C and stirred for a total of 12 h. The reaction was quenched with saturated $NaHCO_3$, the mixture was warmed to room temperature and the product was isolated by ether extraction. Chromatography on a 1 × 16 cm column of silica gel with 6% ether–hexane as the eluent afforded 72 mg (91%) of enals **51** and **52**. Pure samples of these aldehydes were secured via oxidation of the purified alcohols **53** and **54** according to the previously described Swern procedure.[21]

51: IR (film) ν 2950, 2875, 1720, 1460, 1380 cm^{-1}; ^1H NMR δ 0.73 (3 H, d, J = 6.6 Hz, $CHCH_3$), 1.01 (3 H, d, J = 6.1 Hz, $CHCH_3$), 1.06

(3 H, s, C-4 CH_3), 1.24–1.80 and 2.16–2.47 (8 H, m), 3.23 (1 H, dd, J = 10.7, 5.7 Hz, CHOBn), 4.35 and 4.63 (2 H, ABq, J_{AB} = 11.4 Hz, OCH_2Ph), 5.63 (1 H, ddd, J = 10.1, 3.0, 1.2 Hz, H-2), 6.01 (1 H, br d, J = 10.2 Hz, H-1), 7.22–7.38 (5 H, m, aryl H), 9.46 (1 H, s, CHO). Anal. Calcd for $C_{21}H_{28}O_2$: C, 80.73; H, 9.03. Found: C, 80.62; H, 9.06.

52: IR (film) ν 2950, 2875, 1720, 1460, 1380 cm^{-1}; ^1H NMR δ 0.73 (3 H, d, J = 6.6 Hz, $CHCH_3$), 0.98 (3 H, d, J = 7.4 Hz, $CHCH_3$), 1.04 (3 H, s, C-4 CH_3), 1.39 (1 H, m), 1.40 (1 H, dm, J = 17.5 Hz), 1.60 (1 H, m), 1.75 (1 H, dd, J = 12.8, 5.0 Hz), 2.04 (1 H, t, J = 10.5 Hz, H4a), 2.20 (2 H, m), 2.29 (1 H, br d, J = 17.6 Hz), 3.39 (1 H, br s, CHOBn), 4.48 and 4.64 (2 H, ABq, J_{AB} = 12.3 Hz, OCH_2Ph), 5.41 (1 H, br d, J = 10.0 Hz, H-1), 5.66 (1 H, ddd, J = 10.0, 5.0, 2.6 Hz, H-2), 7.25–7.40 (5 H, m, aryl H), 9.49 (1 H, s, CHO). Anal. Calcd for $C_{21}H_{28}O_2$: C, 80.73; H, 9.03. Found: C, 80.62; H, 9.06.

***rel*-(4*R*,4a*R*,5*S*,7*S*,8*S*,8a*S*)- and *rel*-(4*R*,4a*R*,5*S*,7*S*,8*R*,8a*S*)-4,5,7-Trimethyl-8-(benzyloxy)-4-(hydroxymethyl)-3,4,4a,5,6,7,8,8a-octahydronaphthalene (53 and 54).** A solution of 47 mg (0.15 mmol) of aldehydes **51** and **52** was treated with 0.25 mL (0.25 mmol) of 1.0 M DIBAH in hexanes as described for the reduction of **11** to **12**. Purification by chromatography on a 1 × 16 cm dry-packed column of silica gel, eluting with 100 mL of 10%, 100 mL of 20%, and 100 mL of 30% ether–hexane, afforded 10 mg of alcohol **53**, 11 mg of a mixture of **53** and **54**, and 15 mg of alcohol **54** (combined yield 95%).

53: IR (film) ν 3400, 3025, 2950, 2875, 1460 cm^{-1}; ^1H NMR ($CDCl_3$) (400 MHz) δ 0.83 (3 H, s, C-4 CH_3), 1.02 (3 H, d, J = 7.1 Hz, $CHCH_3$), 1.06 (3 H, d, J = 6.4 Hz, $CHCH_3$), 1.11 (1 H, m), 1.35 (1 H, m), 1.53–1.66 (4 H, m), 1.71 (1 H, m), 2.22 (1 H, m), 2.31 (1 H, m), 3.22 (1 H, dd, J = 10.0, 5.0 Hz, CHOBn), 3.33, 3.72 (2 H, ABq, J_{AB} = 11.0 Hz, CH_2OH), 4.38, 4.62 (2 H, ABq, J_{AB} = 11.3 Hz, OCH_2Ph), 5.67 (1 H, dddd, J = 10.0, 5.0, 2.5, 2.5 Hz, H-2), 5.96 (1 H, bd, J = 10.0 Hz, H-1), 7.25–7.41 (5 H, m, Ar H); ^{13}C NMR ($CDCl_3$) (20 MHz) δ 205.1, 138.7, 128.4, 127.7, 127.5, 127.3, 122.4, 82.4, 70.5, 48.1, 47.6 41.1, 35.9, 32.4, 30.3, 28.3, 21.2, 12.8, 12.7. Anal. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 80.14; H, 9.65.

54: ^1H NMR ($CDCl_3$) (400 MHz) δ 0.82 (3 H, s, C-4 CH_3), 0.85–0.90 (1 H, m), 0.98 (3 H, d, J = 7.3 Hz, $CHCH_3$), 1.07 (3 H, d, J = 6.5 Hz, $CHCH_3$), 1.21–1.29 (2 H, m), 1.55 and 1.75 (3 H, m), 2.06 (1 H, m), 2.21 (1 H, m), 2.34 (1 H, br d, J = 17.7 Hz), 3.40 (1 H, dd, J = 2.5, 2.5 Hz, CHOBn), 3.39, 3.66 (2 H, ABq, J_{AB} = 11.0 Hz, CH_2OH), 4.50, 4.63 (2 H, ABq, J_{AB} = 12.4 Hz, OCH_2Ph), 5.41 (1 H, br d, J = 10.0 Hz, H-1), 5.66 (1 H, dddd, J = 10.0, 5.0, 2.5, 2.5 Hz, H-2), 7.23–7.39 (5 H, m, aryl H). Anal. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 80.38; H, 9.65.

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Registry No. 1, 66084-35-3; **2**, 66084-36-4; **3**, 98076-79-0; **5**, 55048-74-3; **7**, 101032-45-5; (±)-**8**, 101032-46-6; (±)-**9**, 101032-47-7; (±)-**10**, 101032-48-8; (±)-**11**, 101032-49-9; (±)-**12**, 101032-50-2; (±)-**13**, 101032-51-3; (±)-**14**, 105859-21-0; (±)-**15**, 101032-53-5; (±)-**16**, 101032-54-6; (±)-**17**, 101032-55-7; (±)-**18**, 101032-56-8; **19**, 105859-44-7; **20**, 105859-45-8; **21**, 105859-46-9; **22**, 105859-47-0; **23**, 105859-48-1; **24**, 105859-49-2; **25** (isomer 1), 105859-50-5; **25** (isomer 2), 105859-51-6; **26** (isomer 1), 105859-52-7; **26** (isomer 2), 105859-53-8; **27** (isomer 1), 105859-54-9; **27** (isomer 2), 105859-55-0; **28** (isomer 1), 105859-56-1; **28** (isomer 2), 105859-57-2; **29** (isomer 1), 105859-58-3; **29** (isomer 2), 105859-59-4; **30** (isomer 1), 105859-60-7; **30** (isomer 2), 105859-61-8; **31** (isomer 1), 105859-62-9; **31** (isomer 2), 105859-63-0; **32** (isomer 1), 105859-64-1; **33** (isomer 2), 105859-65-2; **33**, 105859-66-3; **34**, 105859-67-4; **35** (isomer 1), 105859-68-5; **35** (isomer 2), 105859-69-6; **36**, 105859-70-9; **37**, 105859-71-0; **38**, 105859-72-1; **39**, 105859-73-2; **40**, 105859-74-3; (±)-**41**, 101032-57-9; (±)-**42**, 101032-58-0; (±)-**43** (isomer 1), 101032-70-6; (±)-**43** (isomer 2), 101143-49-1; (±)-**44** (isomer 1), 101142-78-3; (±)-**44** (isomer 2), 101032-59-1; (±)-**45** (isomer 1), 101032-60-4; (±)-**45** (isomer 2), 101142-79-4; (±)-**46** (isomer 1), 101032-61-5; (±)-**46** (isomer 2), 101142-80-7; (±)-**47** (isomer 1), 101032-62-6; (±)-**47** (isomer 2), 101312-97-4; (±)-**48** (isomer 1), 101032-63-7; (±)-**48** (isomer 2), 101142-81-8; (±)-**49** (isomer 1), 101142-82-9; (±)-**49** (isomer 2), 101032-64-8; (±)-**50** (isomer 1), 101142-77-2; (±)-**50** (isomer 2), 101032-65-9; (±)-**51**, 101032-66-0; (±)-**52**, 101032-67-1; (±)-**53**, 101032-68-2; (±)-**54**, 101032-69-3; (±)-**57**, 105859-75-4; (±)-**58**, 105859-76-5; (±)-**59** (isomer 1), 105928-39-0; (±)-**59** (isomer 2), 105928-40-3; (±)-**60** (isomer 1), 105928-41-4; (±)-**60** (isomer 2), 105928-42-5; (±)-**61** (isomer 1), 105928-43-6; (±)-**61** (isomer 2), 105928-44-7; (±)-**62** (isomer 1), 105928-45-8; (±)-**62** (isomer 2), 105928-46-9; (±)-**63** (isomer 1), 105928-47-0; (±)-**63** (isomer 2), 105928-48-1; (±)-**64** (isomer 1), 105928-49-2; (±)-**64** (isomer 2), 105928-50-5; (±)-**65** (isomer 1), 105928-51-6; (±)-**65** (isomer 2), 105928-52-7; (±)-**66**, 105928-53-8; (±)-**67**, 105928-54-9; (±)-**68**, 105859-77-6; (±)-**69**, 105859-78-7; (±)-**70**, 105859-79-8; (±)-**71**, 105859-80-1; (±)-**72**, 105859-81-2; (±)-**73**, 105859-82-3; (±)-**74**, 105859-83-4; (±)-**75**, 105859-84-5; (±)-II (R^1 = R^3 = H; R^2 = Me), 105859-22-1; (±)-II (R^1 = H; R^2 = R^3 = Me), 105859-23-2; (±)-II (R^1 = R^2 = R^3 = Me), 105859-24-3; (±)-II (R^1 = R^3 = H; R^2 = Bn), 105859-25-4; (±)-II (R^1 = R^3 = H; R^2 = *t*-Bu), 105859-26-5; (±)-II (R^1 = H; R^2 = *t*-Bu; R^3 = Me), 105859-27-6; (±)-II (R^1 = R^3 = Me; R^2 = *t*-Bu), 105859-28-7; (±)-III (R^1 = R^3 = H; R^2 = Me), 105928-31-2; (±)-III (R^1 = H; R^2 = R^3 = Me), 105928-32-3; (±)-III (R^1 = R^2 = R^3 = Me), 105859-29-8; (±)-III (R^1 = R^3 = H; R^2 = Bn), 105928-33-4; (±)-III (R^1 = R^3 = H; R^2 = *t*-Bu), 105928-34-5; (±)-III (R^1 = H; R^2 = *t*-Bu; R^3 = Me), 105928-35-6; (±)-III (R^1 = R^3 = Me; R^2 = *t*-Bu), 105859-30-1; (±)-V (R^1 = R^3 = Me; R^2 = X = H), 105859-31-2; (±)-V (R^1 = R^2 = H; X = β-OMe; R^3 = Me), 105859-32-3; (±)-V (R^1 = R^2 = H; X = α-OMe; R^3 = Me), 105859-33-4; (±)-V (R^1 = H; X = β-OMe; R^2 = β-Me; R^3 = Me), 105859-34-5; (±)-V (R^1 = H; X = α-OMe; R^2 = β-Me; R^3 = Me), 105859-35-6; (±)-V (R^1 = H; X = β-OMe; R^2 = α-Me; R^3 = Me), 105859-36-7; (±)-V (R^1 = H; X = α-OMe; R^2 = α-Me; R^3 = Me), 105859-37-8; (±)-VI (R^1 = X = R^2 = R^3 = H), 105928-36-7; (±)-VI (R^1 = X = R^2 = H; R^3 = Me), 105928-37-8; (±)-VI (R^1 = R^3 = Me; R^2 = X = H), 105859-38-9; (±)-VI (R^1 = R2 = H; X = β-OMe; R^3 = Me), 105928-38-9; (±)-VI (R^1 = R^2 = H; X = α-OMe; R^3 = Me), 105859-39-0; (±)-VI (R^1 = H; X = β-OMe; R^2 = β-Me; R^3 = Me), 105859-40-3; (±)-VI (R^1 = H; X = α-OMe; R^2 = β-Me; R^3 = H), 105859-41-4; (±)-VI (R^1 = H; X = β-OMe; R^2 = α-Me; R^3 = Me), 105859-42-5; (±)-VI (R^1 = H; X = α-OMe; R^2 = α-Me; R^3 = Me), 105859-43-6; (±)-2,4-dimethyl-1,5-pentanediol, 54630-82-9; Dowex AG50W, 105881-81-0.

Supplementary Material Available: Experimental procedures and spectral data for Schemes II and IV (22 pages). Ordering information is given on any current masthead page.