Stereoselective Syntheses of the Nonactate Esters via Intramolecular Oxymercurations of Allenes

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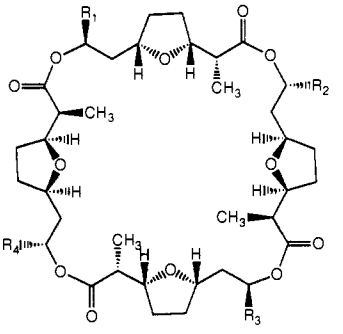
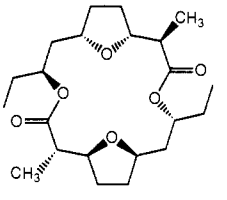
Abstract: The nactin antibiotic subunits (±)-nonactic acid, (±)-homononactic acid, and (±)-bishomononactic acid were synthesized as their methyl esters (**14**, **15**, **16**) by a route which forms the cis-2,5-disubstituted tetrahydrofuran ring moiety by a one-pot oxymercuration–transmetalation (with palladium)–methoxycarbonylation, which converts the γ-silyloxy allenes **27–29** to the 2(10)- or 2(11)-dehydrononactate methyl esters **31–33** with excellent (>98:<2) cis:trans stereoselectivity. The γ-silyloxy allenes were synthesized from the corresponding *anti*-1,3-diols **18–20**, which in turn were prepared by the reduction of the β-hydroxy ketone aldol products **23–25** using tetramethylammonium triacetoxyborohydride. Catalytic hydrogenation of the dehydrononactate intermediates yielded 50:50 mixtures of the title products and their C_2 epimers. A remarkable "chelation-controlled" reduction of the dehydrononactate **32** to primarily the "2-epi" product, using magnesium in methanol, was observed. The versatility of this synthetic route was demonstrated by the synthesis of the unnatural nonactate homologue (±)-methyl "trishomononactate" **17**.

The nactins (**1–9**) are a group of macrotetralides which occur in various *Streptomyces* species[1] and are renowned for their ionophoric properties,[2] antibiotic activity,[1,3] and unusual stereochemistry.[4] A number of syntheses of the subunit of nonactin, nonactic acid (**10**) (or its methyl ester), have been reported.[5] (Fewer syntheses of nonactin itself have been reported.[6]) To date, no syntheses of the nonactate homologues homononactic acid (**11**) and bishomononactic acid (**12**) have been reported. A facile synthetic route to such homologues for use in the construction of oligomeric macrolides is warranted by the notable miticidal activity of the tetramer of homononactate tetranactin (**5**)[7] and by the recent report of a cyclic dimer of homononactate, **13**, which possesses antifungal activity.[8] Furthermore, the known affinity of nonactin for complexing to ammonium ions[2] has prompted us to consider the possibility that chiral homologues of nonactin may bind to amines or alkylammonium ions enantioselectively. The "minor" nactins (**2–4** and **6–9**), which bear homo- or bishomononactate subunits, have not been extensively studied for their complexing properties or biological activity.

In this paper we report the first synthesis of (±)-methyl homononactate (**15**) and (±)-methyl bishomononactate (**16**) as well as the syntheses of (±)-methyl nonactate (**14**) and the unnatural homologue (±)-methyl "trishomononactate" (**17**) by a general



	R_1	R_2	R_3	R_4
1 (NONACTIN):	CH_3	CH_3	CH_3	CH_3
2 (MONACTIN):	CH_3	CH_3	CH_3	CH_2CH_3
3 (DINACTIN):	CH_3	CH_2CH_3	CH_3	CH_2CH_3
4 (TRINACTIN):	CH_3	CH_2CH_3	CH_2CH_3	CH_2CH_3
5 (TETRANACTIN):	CH_2CH_3	CH_2CH_3	CH_2CH_3	CH_2CH_3
6 (MACROTETRALIDE G):	CH_2CH_3	CH_3	$CH(CH_3)_2$	CH_3
7 (MACROTETRALIDE D):	CH_2CH_3	CH_3	CH_2CH_3	$CH(CH_3)_2$
8 (MACROTETRALIDE C):	CH_2CH_3	CH_3	$CH(CH_3)_2$	$CH(CH_3)_2$
9 (MACROTETRALIDE B):	CH_2CH_3	$CH(CH_3)_2$	CH_2CH_3	$CH(CH_3)_2$



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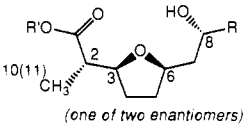

(one of two enantiomers)

10: R = CH_3, R' = H
11: R = CH_2CH_3, R' = H
12: R = $CH(CH_3)_2$, R' = H
14: R = CH_3, R' = CH_3
15: R = CH_2CH_3, R' = CH_3
16: R = $CH(CH_3)_2$, R' = CH_3
17: R = $C(CH_3)_3$, R' = CH_3

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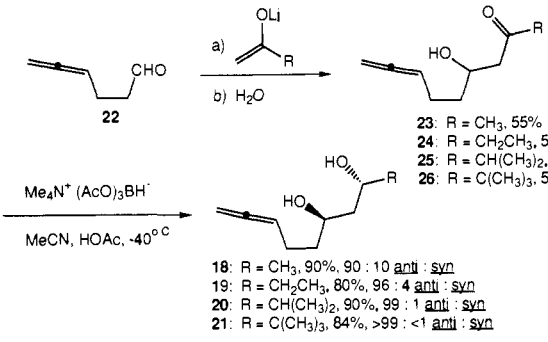
Scheme I[a]



[a] All compounds indicated are racemic.

route that features, as a key step, a stereoselective one-pot oxymercuration–transmetalation–methoxycarbonylation reaction sequence for forming the requisite cis-2,5-disubstituted tetrahydrofuran ring from a γ-silyloxy allene precursor.[9] It should be noted that this cyclization reaction forms methyl 2(10)- or 2(11)-dehydrononactate esters, structural analogues of the nonactates which may be useful starting materials for the syntheses of unsaturated nactin analogues having unique ionophoric and/or biological activities.

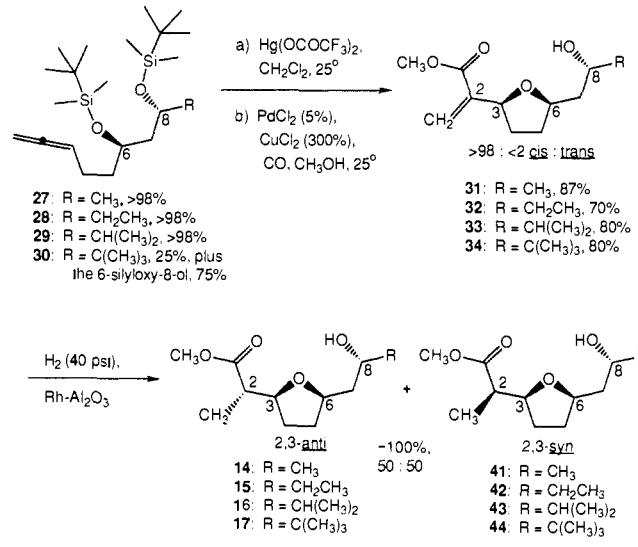
Results and Discussion

The key precursors to the nonactates **14–17** are the *anti*-1,3-diols **18–21**, respectively, which we synthesized by using the route indicated in Scheme I. Addition of the "kinetic" lithium enolates of acetone, 2-butanone, 3-methyl-2-butanone, and 3,3-dimethyl-2-butanone to 4,5-hexadienal (**22**) yielded, upon workup, the β-hydroxy ketones **23–26**, respectively. In the case where the enolate from 2-butanone was employed, a minor amount (17%) of the isomeric β-hydroxy ketone derived from the "thermodynamic" enolate was formed. The moderate yields observed for all four aldol products are due, at least in part, to the volatility of the aldehyde **22**, which imparted uncertainties into the experimental procedure for performing the condensation reactions.

Treatment of the β-hydroxy ketones **23–26** with tetramethylammonium triacetoxyborohydride under the conditions perfected by Evans and co-workers[10] resulted in the formation of the *anti*-1,3-diols **18–21** with excellent diastereoselectivities (Scheme I). We note that recipes exist for the highly stereoselective reduction of these β-hydroxy ketones to the corresponding *syn*-1,3-diols,[11] thus allowing one to synthesize 8-*epi*-nonactates for coupling into oligomers via an S_N2 displacement at C_8, as demonstrated to be effective in previous syntheses of nonactin.[6b,c]

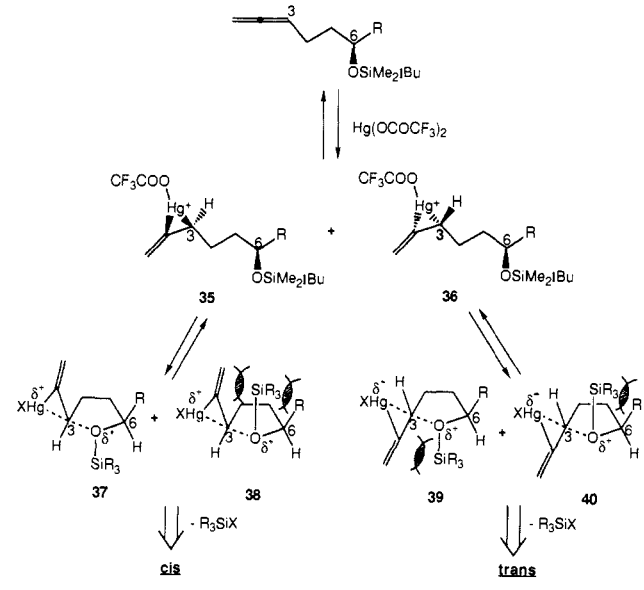
The anti configuration of the major 1,3-diol products **18–21** was indicated by the precedented stereoselectivity of the triacetoxyborohydride reagent,[10] by the relative ^{13}C NMR chemical shifts of the carbinol carbons for each diastereomer, which followed the precedented trend of "anti upfield from syn" (as indicated in Table I),[10,11c,e] and by the subsequent conversion of **18** to (±)-methyl nonactate, for which high-field NMR data on both natural and unnatural diastereomers has been reported.[6c]

Scheme II[a]



[a] All compounds indicated are racemic.

Scheme III[a]



[a] All compounds indicated are racemic.

The conversion of the purified diols **18–21** to the methyl nonactate homologues **14–17** proceeded as indicated in Scheme II. Treatment of each diol with an excess of *tert*-butylchlorodimethylsilane[12] produced the bis(trialkylsilyl)oxy allenes **27–30** in excellent yields. (For the more hindered diol **21**, a 3:1 monosilylated–bis-silylated product mixture was obtained and used for the subsequent step.) Intramolecular oxymercuration using mercuric trifluoroacetate, to form cyclized vinylmercuric trifluoroacetate intermediates,[13] and followed immediately by a transmetalation with palladium(II) chloride, under conditions which recycle the palladium(II) via reoxidation by cupric chloride (Scheme II), yielded the 2(10)- and 2(11)-dehydrononactates **31–34** in good yields and with high stereoselectivities for the cis-2,5-disubstituted tetrahydrofuran ring. *The stereoselectivity*

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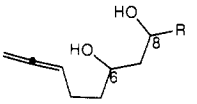
(13) Evidence for such intermediates was obtained by following the reaction between mercuric trifluoroacetate and **28**, in deuteriochloroform, by ^1H NMR spectroscopy. Signals for the two vinylic protons of the cyclic vinylmercuric complex, at 5.7 and 5.2 ppm, were clearly discernible, as were their ^1H–^{199}Hg couplings (J = 590 Hz for the signal at 5.7 ppm, J = 290 Hz for the signal at 5.2 ppm).

Table I. ^{13}C NMR Chemical Shifts for the Carbinol Carbons of 6,7-Octadiene-1,3-diol Derivatives[a]



	R = CH_3		R = CH_2CH_3		R = $CH(CH_3)_2$		R = $C(CH_3)_3$	
proton	anti[b]	syn	anti[b]	syn	anti[b]	syn	anti[b]	syn
C_6[c], δ (ppm)	68.84	72.12	68.56	71.96	68.77	72.04	69.11	72.11
C_8[c], δ (ppm)	65.59	68.93	70.64	73.96	73.87	77.44	76.05	80.16

[a] Measured at 50 MHz in deuteriochloroform (tetramethylsilane standard). [b] The major diastereomer obtained by the reduction of the β-hydroxy ketone with tetramethylammonium triacetoxyborohydride. [c] Nonactate numbering.

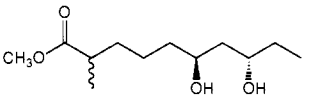
of this cyclization requires both the silyl ether and the initial oxymercuration step: when the "two-step" protocol (oxymercuration/transmetallation/alkoxycarbonylation) was applied to the diol **18**, and when a direct "one-step" oxypalladation–alkoxycarbonylation (using $PdCl_2$–$CuCl_2$ in methanol under carbon monoxide)[14] of either the diol **18** or the silyl ether **27** was performed, 50:50 cis:trans ratios were observed. Our previous studies with other γ-hydroxy allenes and derivatives imply that this phenomenon is general.[9]

It is apparent that the bulky trialkylsilyl group on the C_6 oxygen (nonactate numbering system) is "directing" the stereochemistry of the mercury-mediated cyclization of **27–30** in a manner analogous to that proposed by Bartlett, who pioneered the employment of silyl or alkyl groups on the nucleophilic oxygen to serve such a purpose in iodocyclizations of γ-hydroxy alkenes.[15] In our systems, initial complexation of the "internal" carbon–carbon double bond of the allene group by the mercury ion probably occurs at both faces of the double bond to form the syn and anti complexes **35** and **36**, respectively, as an equilibrium mixture, as shown in Scheme III.[16] Subsequent intramolecular backside nucleophilic attack by the silyloxy oxygen on C_3 would then proceed through transition states **37** or **38** from complex **35** and through transition states **39** or **40** from complex **36** (Scheme III). (We have approximated planar rings for **37–40**; in fact, an "envelope" geometry, with the oxygen at the "flap", is a more likely geometry. The conclusions are the same). Based on a straightforward qualitative analysis of gauche-type interactions between bulky groups in the transition states, it is easy to see that transition state **37** is the one lowest in energy. Thus, the complex **35** would cyclize via **37** to form the cis-2,5-disubstituted tetrahydrofuran faster than the complex **36** would cyclize to form the trans isomer, and concomitant rapid equilibration between **36** and **35** would allow for the eventual formation of virtually all-cis product as observed. The relatively bulky trialkylsilyl group plays a key role in this proposed mechanism.

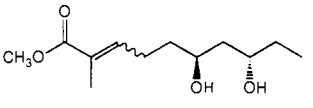
Why does the corresponding oxy*palladation* not exhibit such stereoselectivity? One possible explanation is that the π-complex between the allene group and palladium(II) (cf. **35** and **36**) and/or the approach trajectories of the oxygen toward the palladium-complexed allene (cf. **37–40**) are geometrically different from the corresponding mercury species in such a way (e.g. longer partial bonds, more obtuse "attack angles") that the energy differences between the various transition states becomes insignificantly small. A more straightforward reason is that the conditions for the oxypalladation—palladium(II) chloride with copper(II) chloride, in methanol—bring about the relatively rapid cleavage of *tert*-butyldimethylsilyl ethers. Indeed, we observed that the *tert*-butyldimethylsilyl ether derivative of 2-butanol, when monitored by ^1H NMR spectroscopy (observation of the signals for the methyl groups on the silicon atom), underwent desilylation at least 50 times faster in the presence of palladium(II) chloride, cupric chloride, and methanol ($t_{1/2} \sim 30$ min) than in the presence of mercuric trifluoroacetate in chloroform ($t_{1/2} > 24$ h). Therefore, it seems likely that the trialkylsilyl group that we rely upon for cis stereoselectivity is rapidly removed under the conditions for oxypalladation. The employment of more durable trialkylsilyl groups may avoid this problem and allow for the stereoselective syntheses of cis-2,5-disubstituted tetrahydrofurans via the oxypalladation of γ-silyloxy allenes. At this time, however, our two-step, "one-pot" protocol is practicable.

The cis geometry of the dehydrononactates **31–34** was indicated by comparison studies. The strong similarities between the NMR spectra (see the Experimental Section) of all four dehydrononactates (**31–34**) imply that they all have the same relative stereochemistry. The subsequent conversion of **31** to (±)-methyl nonactate having spectroscopic properties identical with that of the naturally derived material provides evidence for the cis geometry of the product **31** and, by analogy, products **32–34**.

As indicated in Scheme II, catalytic hydrogenation of the dehydrononactates **31–34** yielded equimolar mixtures of the 2,3-anti ("natural" configuration) and 2,3-syn ("2-epi" configuration) diastereomers of the nonactate esters, **14–17** and **41–44**, respectively. Extensive experimentation with various reducing agents and the dehydrononactate **32** did not result in any anti-selective reduction. Hydrogenation of **32** (under 1 atm of hydrogen) using palladium on charcoal or tris(triphenylphosphine)rhodium(I) chloride as the catalyst resulted in hydrogenolysis and hydrogenation to form the acyclic diol **45**. An attempt to achieve the conjugate reduction using lithium tri-*sec*-butylborohydride[17] yielded the acyclic unsaturated ester **46**



45 (racemic)



46 (racemic)

(approximately 50:50 *E*:*Z*, according to ^1H NMR). This result implies that reductions which proceed via the formation of an enolate species at C_2 result in eliminative ring opening prior to or during workup. Keinan's molybdenum(0)-catalyzed hydrosilation reaction failed to reduce **32** at all.[18] Attempts to isomerize the $\Delta^{2(11)}$ double bond of **32** to the $\Delta^{2(3)}$ ester **47**, whose nonactate homologue is known to undergo 2,3-anti-selective hydrogenation to methyl nonactate,[5i-k,6c] using rhodium(III) chloride in ethanol,[19] yielded only recovered starting material. Treatment of **32** with Noyori's hydridoiron reducing agent[20] gave a complex product mixture which consisted of less than 40% of an 85:15 2,3-syn–2,3-anti mixture of methyl homononactate diastereomers. Finally,

(14) These conditions are essentially the same as those reported for the analogous reaction of γ-hydroxyalkenes to form mixtures of tetrahydrofurans and tetrahydropyrans: Semmelhack, M. F.; Bodurow, C. *J. Am. Chem. Soc.* **1984**, *106*, 1496–1498.

(15) Rychnovsky, S. D.; Bartlett, P. A. *J. Am. Chem. Soc.* **1981**, *103*, 3963–3964. For a very good discussion of factors associated with the stereoselectivity of such cyclizations, see: Reitz, A. B.; Nortey, S. O.; Maryanoff, B. E.; Liotta, D.; Monahan, R. *J. Org. Chem.* **1987**, *52*, 4191–4202.

(16) Evidence exists for the formation of "mercuriocyclopropane" complexes like **35** and **36** by the reaction of allenes with mercuric acetate: Waters, W. L.; Kiefer, E. F. *J. Am. Chem. Soc.* **1967**, *89*, 6761–6268.

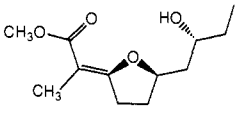
(17) Ganem, B.; Fortunato, J. M. *J. Org. Chem.* **1975**, *40*, 2846–2848.

(18) Keinan, E.; Perez, D. *J. Org. Chem.* **1987**, *52*, 2576–2580.

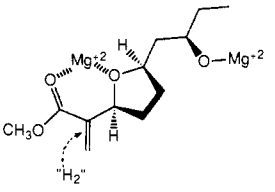
(19) Colquhoun, H. M.; Holton, J.; Thompson, D. J.; Twigg, M. V. *New Pathways for Organic Synthesis: Practical Applications of Transition Metals*; Plenum: New York, 1984; pp 183–187.

(20) Noyori, R.; Umeda, I.; Ishigami, T. *J. Org. Chem.* **1972**, *37*, 1542–1545.

the reduction of **32** using magnesium metal in methanol[21] resulted in the clean formation of an 80:20 2,3-syn–2,3-anti mixture of the homononactates. Apparently the magnesium(II) ions in the reaction medium chelate to the ester and tetrahydrofuran oxygens to form a cyclic complex like **48** which then favors the formal



47



48

addition of hydrogen to the least sterically crowded face of the alkene (attack from behind the plane of the paper in **48**) to yield the 2,3-syn product.[22] The stereoselectivity observed in the hydridoiron reduction could also be due to such a chelation model. To our knowledge, this observation represents the first example of "chelation control" in the reduction of α,β-unsaturated carbonyls by magnesium in methanol, and it may precedent the applicability of this facile reducing system to the stereoselective synthesis of polyoxygenated systems. In the present case, however, the observed stereoselectivity favors the unnatural ("2-epi") diastereomer of the nonactate esters.[23]

Each of the homologous nonactate esters **14–17** was separated from its respective C_2 epimer **41–44** by using high-performance liquid chromatography (HPLC). The assignment of the configuration of each diastereomer was based on ^{1}H NMR spectroscopy, as detailed NMR data are available for all eight diastereomers of methyl nonactate.[5e,6c] Table II lists HPLC retention times and the ^{1}H NMR chemical shifts for the carbomethoxy and 2-methyl signals for compounds **14–17** and **41–44**. These data indicate that ^{1}H NMR chemical shifts and, in this homologous series at least,[24] relative HPLC retention times follow consistent trends with the C_2 configuration of the products. Furthermore, the ^{1}H NMR data for all of our homologues is consistent with previously reported data for methyl nonactate and 2-*epi*-methyl nonactate (Table II) and distinct from the corresponding data for the C_2 epimers of the trans or the 8-epi diastereomers of methyl nonactate.[6c] This correlation, along with our evidence for the anti configuration of **18–21** and the cis configuration of **31–34**, clearly indicates that our synthetic route has yielded the natural diastereomers of (±)-methyl nonactate (**14**), (±)-methyl homononactate (**15**), (±)-methyl bishomononactate (**16**), and the "trishomononactate" homologue (**17**), along with the C_2 epimers (**41–44**) of these hydroxy esters.

Conclusions

A concise synthetic route to all of the natural (and one unnatural) nonactate esters has been achieved. Advantages of this route to the nonactates over others[5] include (1) its brevity (four steps from the aldehyde **22** to the methyl nonactate products), (2) its stereoselectivity (all steps, except for the last one, proceed with a sufficiently high selectivity that the separation of stereoisomers is not necessary in practice), and (3) its versatility (the route can be easily adapted for the syntheses of numerous analogues, as well as C_2 or C_8 epimers, of the nonactates (e.g., **17**)). Disadvantages include the observed lack of stereoselectivity in the reduction of the 2(10)-dehydrononactate intermediates (**31–34**) and low yields from the initial aldol reactions which form the β-hydroxy ketone intermediates **23–26**.

In addition to demonstrating the syntheses, for the first time, of the naturally occurring nonactate homologues **15** and **16**, this research has indicated the value of mercury- and palladium-mediated cyclizations of allenes for natural products syntheses[9,25,26] and has led to the discovery of a potentially useful "chelation-controlled" stereoselectivity reduction of a β-alkoxy-α-methylene ester by magnesium in methanol. Applications of the results from this research to the syntheses of substrate-specific macrotetralide complexing agents are in progress.

Experimental Section[27]

β-Hydroxy Ketones 23–26. General Procedure. To a stirring solution of 4.0 mmol of lithium diisopropylamide in tetrahydrofuran–hexanes at −78 °C, under a nitrogen atmosphere (prepared by adding 4.0 mmol of a hexane solution of *n*-butyllithium to a cooled solution of 0.56 mL (4 mmol) of diisopropylamine in 15 mL of dry tetrahydrofuran) was added a solution of 4.0 mmol of the appropriate ketone in 1 mL of dry tetrahydrofuran. After 15 min, a solution of approximately 4.4 mmol of 4,5-hexadienal[29] in 2–5 mL of dichloromethane–ether was added, via syringe, over a 10-min period. The solution was then stirred at −78 °C for 2 h, then quenched with 10 mL of water, and allowed to warm to room temperature. Workup yielded the crude β-hydroxy ketones which were purified by chromatography using 85:15 (v/v) hexane–ethyl acetate as the eluent.

(±)-4-Hydroxy-7,8-nonadien-2-one (23). After chromatography a 55% yield was obtained. ^{1}H NMR: δ 5.13 (m, 1 H), 4.68 (m, 2 H), 4.11 (m, 1 H), 2.6–2.4 (m, 2 H), 2.19 (s, 3 H), 2.17–2.07 (m, 2 H), 1.65–1.49 (m, 2 H). ^{13}C NMR: β 211.95, 209.81, 89.3, 75.00, 66.78, 49.92, 35.49, 30.55, 23.94. IR (cm^{-1}): 3440, 2928, 1955, 1705. LRMS (*m/e*): 154 (M^+, absent), 139 ($M^+ - CH_3$), 111 ($M^+ - COCH_3$), 97 ($M^+ - CH_2COCH_3$). LRFABMS (LiI matrix); *m/e* 161 (M + Li). HREIMS: *m/e* 96.0574 (M − acetone), 97.0651 (M − CH_2COCH_3).

(21) (a) Youn, I. K.; Yon, G. H.; Pak, C. S. *Tetrahedron Lett.* **1986**, *27*, 2409–2410. (b) Hudlicky, T.; Sinai-Zingde, G.; Natchus, M. G. *Tetrahedron Lett.* **1987**, *28*, 5287–5290.

(22) This model (**48**) is inspired by similar models for the selective addition of nucleophiles to the least hindered face of a carbonyl held in a cyclic chelate: Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 556–569.

(23) We have recently employed this methodology to its fullest advantage in the synthesis of the C_1–C_{11} portion of pamamycin 607, a novel nonactate homologue having the 2,3-syn geometry: Walkup, R. D.; Park, G. *Tetrahedron Lett.* **1988**, *29*, 5505–5508.

(24) This trend is also followed by the *R* = *n*-propyl homologue. See ref 23. For a similar correlation between stereochemical assignments and ^{1}H NMR/HPLC data in 2,5-disubstituted tetrahydrofurans, see: Hoye, T. R.; Suhadolnik, J. C. *J. Am. Chem. Soc.* **1987**, *109*, 4402–4403. We thank Professor Hoye for bringing this work to our attention.

(25) A number of intramolecular oxymercurations of allenes have been reported. However, our work (ref 9) was the first to utilize the organomercury intermediates for an alkoxycarbonylation. See: Audin, P.; Doutheau, A.; Gore, J. *Tetrahedron Lett.* **1982**, *23*, 4337–4340. Arseniyadis, S.; Gore, J. *Tetrahedron Lett.* **1983**, *24*, 3997–4000. Chilot, J. J.; Doutheau, A.; Gore, J.; Saroli, A. *Tetrahedron Lett.* **1986**, *27*, 849–852. Delair, T.; Doutheau, A. *Tetrahedron Lett.* **1986**, *27*, 2859–2860. Audin, P.; Doutheau, A.; Gore, J. *Bull. Soc. Chim. Fr.* **1984**, II-297–306. Chilot, J.-J.; Doutheau, A.; Gore, J. *Bull. Soc. Chim. Fr.* **1984**, II-307–316.

(26) The oxypalladation–alkoxycarbonylation reaction of allenes was pioneered by the groups of Alper and of Gallagher: Alper, H.; Hartstock, F. W.; Despeyroux, B. *J. Chem. Soc., Chem. Commun.* **1984**, 905–906. Lathbury, D.; Vernon, P.; Gallagher, T. *Tetrahedron Lett.* **1986**, *27*, 6009–6012.

(27) The reagents employed were purchased from Aldrich Chemical Co., Inc. (Milwaukee, WI) or Lancaster Synthesis, Ltd. (Windham, NH) and used as received, unless otherwise indicated. Dichloromethane was distilled from calcium hydride, and tetrahydrofuran was distilled from sodium benzophenone under nitrogen prior to usage. Other solvents were purified by simple distillation. Unless otherwise indicated, reaction workup consisted, in each case, of partitioning between diethyl ether and water followed by washing of the ether phases with saturated brine, then drying over magnesium sulfate, filtration, and concentration using a rotary evaporator. "Chromatography" refers to the "flash" chromatographic method[28] using silica gel and the indicated solvent system. HPLC chromatography (both analytical and preparative) was done with the indicated solvent system and flow rate on a system consisting of a Waters M45 pump, a Rheodyne injector, an Advanced Separations Technologies column (25 cm × 4 mm (i.d.)) packed with 10 μm silica gel, and a Waters 401 refractometer detector. Peak integrations were performed by using the cut-and-weigh method. NMR spectra were measured on an IBM AF-200 spectrometer in deuteriochloroform with tetramethylsilane as the standard. NMR chemical shifts are indicated in ppm downfield from TMS. IR spectra were measured by using a Nicolet MX-S spectrophotometer. Low-resolution mass spectra (LRMS) were measured on a Hewlett-Packard 5995 spectrometer. Elemental analyses were performed by Desert Analytics, Inc. (Tucson, AZ). Low-resolution FAB mass spectra (LRFABMS) and high-resolution electron-impact mass spectra (HREIMS) were measured by the Midwest Center for Mass Spectrometry.

(28) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

(29) Coates, R. M.; Senter, P. D.; Baker, W. R. *J. Org. Chem.* **1982**, *47*, 3597–3607. In practice, we prepared the aldehyde **22** from 4,5-hexadien-1-ol (Arseniyadis, S.; Gore, T.; Roumestant, M. L. *Tetrahedron* **1979**, *35*, 353–363) by stirring with pyridinium chlorochromate in dichloromethane–magnesium sulfate, followed by dilution with ether, and filtration through Florisil and concentration to a 2–5-mL volume. The volatility and heat sensitivity to this aldehyde precluded further purification.

(±)-5-Hydroxy-8,9-decadien-3-one (24). After chromatography, a 58% yield of **24** was obtained. ^{1}H NMR: δ 5.14 (m, 1 H), 4.68 (m, 2 H), 4.10 (m, 1 H), 2.6–2.4 (m, 4 H), 2.2–2.0 (m, 2 H), 1.6–1.4 (m, 2 H), 1.07 (t, 3 H, J = 7.3 Hz). ^{13}C NMR: δ 212.45, 208.50, 89.46, 75.16, 66.98, 48.52, 36.75, 31.52, 24.08, 7.54. IR (cm^{-1}): 3430, 2970, 1955, 1705. LRMS (m/e): 168 (M^+, absent), 139 ($M^+ - CH_2CH_3$), 111 ($M^+ - COCH_2CH_3$), 97 ($M^+ - CH_2COC_2H_5$).

In addition to the aldol product **24**, a 17% yield of **(±)-4-hydroxy-3-methyl-7,8-nonadien-2-one** was obtained after chromatography. It was a mixture of diastereomers and was not characterized beyond ^{1}H NMR spectroscopy. ^{1}H NMR: δ, 5.14 and 5.13 (m, 1 H), 4.68 (m, 2 H), 3.99 and 3.75 (m, 1 H), 2.7–2.5 (m, 1 H), 2.21 (s, 3 H), 2.2–2.0 (m, 2 H), 1.7–1.4 (m, 2 H), 1.16 and 1.15 (t, 3 H, J = 7.3 and 7.2 Hz).

(±)-5-Hydroxy-2-methyl-8,9-decadien-3-one (25). After chromatography, a 55% yield of **25** was obtained. ^{1}H NMR: δ 5.14 (m, 1 H), 4.68 (m, 2 H), 4.09 (m, 1 H), 2.7–2.5 (m, 3 H), 2.19–2.08 (m, 1 H), 1.66–1.49 (m, 2 H), 1.11 (d, 6 H, J = 6.9 Hz). ^{13}C NMR: δ 215.96, 208.50, 89.49, 75.13, 66.99, 46.47, 41.46, 35.50, 24.11, 17.97. IR (cm^{-1}): 3430, 2970, 1955, 1710. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49;, H, 9.9. Found: C, 71.19; H, 9.95. LRFABMS (LiI matrix): m/e 189 (M + Li). HREIMS: m/e 139.0755 ($M - C_3H_7$), 128.0838 ($M - C_4H_5 - H$), 121.0653 ($M - C_3H_7 - H_2O$).

(±)-5-Hydroxy-2,2-dimethyl-8,9-decadien-3-one (26). After chromatography, a 55% yield of **26** was obtained. ^{1}H NMR: δ 5.14 (m, 1 H), 4.68 (m, 2 H), 2.8–2.5 (m, 3 H), 2.14 (m, 2 H), 1.7–1.4 (m, 2 H), 1.15 (s, 9 H). ^{13}C NMR: δ 217.68, 208.49, 89.53, 75.11, 67.09, 44.35, 42.97, 35.44, 26.22, 24.14. IR (cm^{-1}): 3450, 1955, 1705. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.05; H, 10.46.

1,3-Diols 18–21. General Procedure. To a solution of 1.32 g (5.0 mmol) of tetramethylammonium triacetoxyborohydride in 4.0 mL of anhydrous acetonitrile at room temperature under nitrogen atmosphere was added 4.0 mL of anhydrous acetic acid. The mixture was cooled to −30 °C with a dry ice–30% calcium chloride slurry bath. The hydroxy ketone (1.0 mmol) in 1.0 mL of acetonitrile was then added via syringe. The reaction mixture was stirred at −30 °C for 7 h and then allowed to warm to room temperature slowly. After 15 h, the reaction mixture was added slowly to a mixture of ether and saturated aqueous sodium bicarbonate solution. The aqueous layer was extracted several times with ether. The combined organic layers were washed with saturated aqueous sodium bicarbonate solution, dried over magnesium sulfate, and concentrated. Each product was purified by chromatography using 60:40 (v/v) hexane–ethyl acetate as the eluent. The crude products were analyzed for their syn:anti ratios by HPLC (60:40 (v/v) hexanes–ethyl acetate at 1.0 mL/min). Pure samples of the syn and anti diastereomers, for spectroscopic characterization, were obtained by preparative HPLC.

(±)-*anti*-7,8-Nonadiene-2,4-diol (18). HPLC: t_R = 9.4 min. ^{1}H NMR: δ 5.12 (m, 1 H), 4.68 (m, 2 H), 4.16 (m, 1 H), 4.00 (m, 1 H), 2.07 (m, 2 H), 1.7–1.4 (m, 4 H), 1.24 (d, 3 H, J = 6.4 Hz). ^{13}C NMR: δ 208.3, 89.63, 74.94, 68.84, 65.59, 44.72, 36.82, 24.55, 23.68.

(±)-*syn*-7,8-Nonadiene-2,4-diol. HPLC: t_R = 7.5 min. ^{1}H NMR: δ 5.12 (m, 1 H), 4.68 (m, 2 H), 4.03 (m, 1 H), 3.90 (m, 1 H), 2.07 (m, 2 H), 1.7–1.4 (m, 4 H), 1.19 (d, 3 H, J = 6.2 Hz). ^{13}C NMR: δ 208.3, 89.53, 75.06, 72.12, 68.93, 44.70, 37.16, 24.15, 23.97.

(±)-*anti*-8,9-Decadiene-3,5-diol (19). HPLC: t_R = 6.8 min. ^{1}H NMR: δ 5.14 (m, 1 H), 4.68 (m, 2 H), 3.99 (m, 1 H), 3.86 (m, 1 H), 2.09 (m, 2 H), 1.7–1.4 (m, 6 H), 0.96 (t, 3 H, J = 7.4 Hz). ^{13}C NMR: δ 208.3, 89.57, 75.16, 70.64, 68.56, 41.79, 36.35, 30.15, 24.45, 10.06. IR (cm^{-1}): 3380, 2932, 1955. LRFABMS (LiI matrix) of a mixture of anti and syn diol **19**: m/e 177 (M + Li). HREIMS: m/e 142.1008 ($M - C_2H_4$), 123.0820 ($M - C_2H_5 - H_2O$), 111.0795 ($M - CH_3CH_2CHOH$).

(±)-*syn*-8,9-Decadiene-3,5-diol. HPLC: t_R = 5.5 min. ^{1}H NMR: δ 5.13 (m, 1 H), 4.69 (m, 2 H), 3.92 (m, 1 H), 3.80 (m, 1 H), 2.09 (m, 2 H), 1.7–1.4 (m, 6 H), 0.95 (t, 3 H, J = 7.4 Hz). ^{13}C NMR: δ 208.3, 89.42, 75.20, 73.96, 71.96, 37999, 36.23, 29.96, 23.54, 9.26.

(±)-*anti*-2-Methyl-8,9-decadiene-3,5-diol (20). HPLC: t_R = 7.0 min. ^{1}H NMR: δ 5.13 (m, 1 H), 4.67 (m, 2 H), 4.0 (m, 1 H), 3.7 (m, 1 H), 2.1 (m, 2 H), 1.7–1.5 (m, 5 H), 0.95 (d, 3 H, J = 6.7 Hz), 0.90 (d, 3 H, J = 6.8 Hz). ^{13}C NMR: δ 208.42, 89.57, 75.13, 73.87, 68.77, 39.34, 36.35, 33.71, 24.52, 18.56, 17.94. LRFABMS (LiI matrix) of a mixture of the anti and syn diol **20**: m/e 191 (M + Li). HREIMS of a mixture of the anti and syn diol **20**: m/e 169.1237 ($M - CH_3$), 154.0997 ($M - 2CH_3$), 149.1323 ($M - H_2O - OH$), 141.0904 ($M - C_3H_7$), 111.0805 ($M - (CH_3)_2CHCHOH$).

(±)-*syn*-2-Methyl-8,9-decadiene-3,5-diol. HPLC: t_R = 6.0 min. ^{1}H NMR: δ 5.13 (m, 1 H), 4.67 (m, 2 H), 3.9 (m, 1 H), 3.7 (m, 1 H), 2.1 (m, 2 H), 1.7–1.5 (m, 5 H), 0.92 (d, 3 H, J = 6.8 Hz). ^{13}C NMR: δ 208.53, 89.46, 77.44, 75.20, 72.04, 36.36, 35.03, 33.52, 23.60, 17.75.

(±)-*anti*-2,2-Dimethyl-8,9-decadiene-3,5-diol (21): HPLC t_R = 6.0 min. ^{1}H NMR: δ 5.13 (m, 1 H), 4.68 (m, 2 H), 3.98 (m, 1 H), 3.68 (m, 1 H), 2.1 (m, 2 H), 1.7–1.5 (m, 4 H), 0.90 (s, 9 H). ^{13}C NMR: δ 208.52, 89.61, 76.05, 75.17, 69.11, 37.04, 36.20, 34.41, 25.94, 24.40. LRFABMS of a mixture of the anti and syn diol **21**: m/e 199 (M + H). HREIMS of a mixture of the anti and syn diol **21**: m/e 180.1512 ($M - H_2O$), 163.1485 ($M - H_2O - DH$), 162.1407 ($M - 2H_2O$), 111.0811 ($M - (CH_3)_3CCHOH$).

(±)-*syn*-2,2-Dimethyl-8,9-decadiene-3,5-diol. HPLC t_R = 5.1 min. ^{1}H NMR: δ 5.13 (m, 1 H), 4.68 (m, 2 H), 3.99 (m, 1 H), 3.65 (dd, 1 H, J = 11.6 and 2.5 Hz), 2.1 (m, 2 H), 1.7–1.5 (m, 4 H), 0.90 (s, 9 H). ^{13}C NMR: δ 208.52, 89.46, 80.16, 75.17, 72.11, 36.43, 34.30, 32.97, 25.33, 23.64.

***tert*-Butyldimethylsilyl Derivatives of the Diols 27–30. General Procedure.** Each diol (0.5 mmol) was stirred in 4.0 mL of dry *N,N*-dimethylformamide with 0.10 g (1.5 mmol) of imidazole and 0.23 g (1.5 mmol) of *tert*-butylchlorodimethylsilane at room temperature, under a nitrogen atmosphere, for 24 h. In some runs, incomplete silylation of the diols **18–20** after this treatment was indicated by TLC analysis. In such cases, an additional 0.08 g (0.5 mmol) of the chlorosilane was added, and the mixture was stirred for an additional 12 h. (In the case of the diol **21**, a 75:25 (molar) mixture of the monosiloxane and the bissiloxane was obtained). Workup and chromatography (hexanes eluent) yielded material of sufficient purity to be carried on to the next step following a routine ^{1}H NMR analysis.

(±)-*anti*-2,4-Bis[(*tert*-butyldimethylsilyl)oxy]-7,8-nonadiene (27). This product was obtained in quantitative yield after chromatography. ^{1}H NMR: δ 5.12 (m, 1 H), 4.67 (m, 2 H), 3.89 (m, 1 H), 3.79 (m, 1 H), 2.06 (m, 2 H), 1.24 (m, 4 H), 1.14 (d, 3 H, J = 6.1 Hz), 0.88 (overlapping singlet and multiplet, 21 H), 0.06 (s, 12 H).

(±)-*anti*-3,5-Bis[(*tert*-butyldimethylsilyl)oxy]-8,9-decadiene (28). This product was obtained in a quantitative yield after chromatography. ^{1}H NMR: δ 5.12 (m, 1 H), 4.67 (m, 2 H), 3.77 (m, 1 H), 3.67 (m, 1 H), 2.04 (m, 2 H), 1.6–1.4 (m, 6 H), 0.88 (overlapping singlet and multiplet, 21 H), 0.05 (s, 12 H). IR (cm^{-1}): 2940, 1955.

(±)-*anti*-3,5-Bis[(*tert*-butyldimethylsilyloxy)]-2-methyl-8,9-decadiene (29). This product was obtained in a quantitative yield after chromatography. ^{1}H NMR: δ 5.12 (m, 1 H), 4.67 (m, 2 H), 3.76 (7, 1 H), 3.62 (m, 1 H), 2.01 (m, 2 H), 1.8–1.4 (m, 5 H), 0.9–0.8 (overlapping s and dd, 24 H), 0.05 (m, 12 H). IR (cm^{-1}): 2930, 1955.

Silylation of Diol 21. The silylation procedure yielded a mixture of the bis(*tert*-butylmethylsilyl) derivative **30** and the 6-silyloxy 8-ol derivative, in a 25:75 molar ratio, even when extended reaction times and additional silylating agent were used. This mixture was routinely used for the subsequent cyclization reaction. However, the two silylated derivatives could be easily separated by chromatography. The yield of the two silylated products together was quantitative.

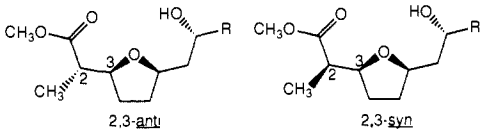
(±)-*anti*-3,5-Bis[(*tert*-butyldimethylsilyl)oxy]-2,2-dimethyl-8,9-decadiene (30). ^{1}H NMR: δ 5.12 (m, 1 H), 4.68 (m, 2 H), 3.85 (m, 1 H), 3.43 (dd, 1 H, J = 6.7 and 2.4 Hz), 2.02 (m, 2 H), 1.7–1.3 (m, 4 H), 0.89 (s, 9 H), 0.88 (s, 9 H), 0.84 (s, 9 H), 0.05 (m, 12 H). IR (cm^{-1}): 2915, 1950.

(±)-*anti*-5-[(*tert*-butyldimethylsilyl)oxy]-8,9-decadien-3-ol. ^{1}H NMR: δ 5.11 (m, 1 H), 4.69 (m, 2 H), 4.08 (m, 1 H), 3.60 (dd, 1 H, J = 7.9 and 4.7 Hz), 2.01 (m, 2 H), 1.8–1.5 (m, 4 H), 0.90 (s, 9 H), 0.89 (s, 9 H), 0.11 (s, 3 H), 0.09 (s, 3 H). IR (cm^{-1}): 3505, 2950, 1955.

Synthesis of $\Delta^{2(10)}$- or $\Delta^{2(11)}$-Dehydrononactate Esters 31–34. General Procedure. To a stirring solution of 0.5 mmol of the appropriate bis(silyloxy) derivative (or the mixture of mono- and bis(silyloxy) derivatives from the diol **21**) in 15 mL of dry dichloromethane was added 0.256 g (0.60 mmol) of mercuric trifluoroacetate. The mixture was stirred under a calcium chloride filled drying tube at room temperature for 2 h and then concentrated, by using a rotary evaporator, to an orange-brown residue. This residue was taken up into 15 mL of methanol, and then 0.256 g (1.50 mmol) of cupric chloride dihydrate and 0.0089 g (0.050 mmol) of palladium(II) chloride were added. The air space over the solution was purged with carbon monoxide, then a balloon filled with carbon monoxide was fitted to the neck of the flask, and the solution was allowed to stir at room temperature for 6 h. The black mixture was then filtered through a plug of silica gel with 10 mL of ether and then concentrated to a 2-mL volume on the rotary evaporator. Workup was completed in the usual manner, and then chromatography using 70:30 (v/v) hexanes–ethyl acetate yielded the pure esters. HPLC analysis (70:30 hexane–ethyl acetate at 1.0 mL/min) and NMR spectroscopy indicated that each dehydrononactate ester thus obtained was >98% diastereomerically pure.

(±)-Methyl 2(10)-Dehydrononactate (31). ^{1}H NMR: δ 6.23 (m, 1 H), 5.90 (m, 1 H), 4.72 (m, 1 H), 4.19 (m, 1 H), 4.10 (m, 1 H), 3.77 (s, 3 H), 2.3–1.5 (m, 6 H), 1.25 (d, 3 H, J = 6.3 Hz). ^{13}C NMR: δ 166.4, 141.96, 123.67, 77.32, 77.27, 65.56, 51.64, 43.64, 32.08, 30.96, 23.55.

Table II. Chromatographic and Selected ^{1}H NMR Data for Homologous Nonactate and 2-*epi*-Nonactate Esters



	R = CH_3		R = CH_2CH_3		R = $CH(CH_3)_2$		R = $C(CH_3)_3$	
	2,3-anti **14**	2,3-syn **41**	2,3-anti **15**	2,3-syn **42**	2,3-anti **16**	2,3-syn **43**	2,3-anti **17**	2,3-syn **44**
HPLC retention times (min)[a]	8.4[b]	6.8[b]	9.2[c]	7.2[c]	8.4[c]	6.8[c]	7.9[c]	6.2[c]
OCH_3, δ (ppm)	3.699[d]	3.683[e]	3.698	3.684	3.698	3.683	3.696	3.691
2-CH_3, δ (ppm)[f]	1.134[g]	1.215[h]	1.131	1.226	1.130	1.225	1.128	1.230

[a] See the Experimental Section for a description of the HPLC apparatus. [b] Eluent = 60:40 (v/v) hexanes–ethyl acetate at 1.0 mL/min. [c] Eluent = 70:30 (v/v) hexanes–ethyl acetate at 1.0 mL/min. [d] Lit.[6c] δ 3.696. [e] Lit.[6c] δ 3.683. [f] Doublets, J = 7.0 Hz. [g] Lit.[6c] δ 1.132. [h] Lit.[6c] δ 1.222.

(±)-Methyl 2(11)-Dehydrohomononactate (32). ^{1}H NMR δ 6.23 (m, 1 H), 5.90 (m, 1 H), 4.72 (m, 1 H), 4.21 (m, 1 H), 3.80, (m, 1 H), 3.77 (s, 3 H), 2.3–1.6 (m, 6 H), 1.54 (m, 2 H), 0.96 (t, 3 H, J = 7.4 Hz). ^{13}C NMR: δ 166.34, 141.74, 123.76, 77.27, 77.14, 70.66, 51.70, 41.24, 32.02, 30.85, 30.20, 10.05. IR (cm^{-1}): 3440, 2970, 1750, 1640. LRMS (*m/e*): 228 (M^+, absent), 199 ($M^+ - C_2H_5$), 197 ($M^+ - OCH_3$), 169 ($M^+ - CO_2CH_3$). Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.14; H, 8.83. Found: C, 62.73; H, 9.089

(±)-Methyl 2(11)-Dehydrobishomononactate (33). ^{1}H NMR: δ 6.23 (m, 1 H), 5.90 (m, 1 H), 4.72 (m, 1 H), 4.21 (m, 1 H), 3.76 (s, 3 H), 3.64 (m, 1 H), 2.3–1.5 (7, 7 H), 0.96 (d, 3 H, J = 7.1 Hz), 0.92 (d, 3 H, J = 7.2 Hz). ^{13}C NMR: δ 166.39, 141.90, 123.65, 77.52, 77.15, 73.95, 51.68, 38.87, 32.74, 32.16, 30.88, 18.63, 17.75. IR (cm^{-1}): 3440, 2950, 1710, 1630. LRMS (*m/e*): 242 (M^+, absent), 211 ($M^+ - OCH_3$), 1.9 ($M^+ - C_3H_7$), 183 ($M^+ - CO_2CH_3$). Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 63.78; H, 9.27. LRFABMS (LiI matrix): *m/e* 248 (M + Li). HREIMS: *m/e* 210.1260 (M – CH_3OH), 199.0970 (M – C_3H_7).

(±)-Methyl 9,9-Dimethyl-2(11)-dehydrohomononactate (34). ^{1}H NMR: δ 6.22 (m, 1 H), 5.90 (m, 1 H), 4.71 (m, 1 H), 4.23 (m, 1 H), 3.76 (s, 3 H), 3.58 (dd, 1 H, J = 9.7 Hz and 2.5 Hz), 2.3–1.5 (m, 6 H), 0.92 (s, 9 H). ^{13}C NMR: δ 166.42, 141.98, 123.57, 77.69, 77.00, 76.27, 71.68, 36.63, 34.66, 32.34, 30.76, 25.59. IR (cm^{-1}): 3440, 2950, 1710, 1625. LRMS (*m/e*): 256 (M^+, absent), 225 ($M^+ - OCH_3$), 199 ($M^+ - C_4H_9$), 197 ($M^+ - CO_2CH_3$). Anal. Calcd for $C_{14}H_{24}O_4$: C, 65.60; H, 9.44. Found: C, 65.02; H, 9.43. LRFABMS: *m/e* 257 (M + H). HREIMS: *m/e* 225.1500 (M – CH_3O), 224.1410 (M – CH_3OH), 199.0971 (M – C_4H_9).

Catalytic Hydrogenations of Dehydrononactates. General Procedure. A mixture of 0.1 mmol of the dehydrononactate and 20 mg of 5% rhodium-on-alumina catalyst in 5.0 mL of methanol was shaken at room temperature in a Parr hydrogenator under a 40 psi hydrogen atmosphere for 2 days. The reaction mixture was then filtered through a Celite plug with an ether rinse and concentrated to give a colorless liquid. In each case, a quantitative yield of the saturated product was obtained. The two diastereomers ("2-natural" (2,3-anti) and "2-epi" (2,3-syn)) were separated by preparative HPLC (see Table II for HPLC retention times).

(±)-Methyl Nonactate (14). Because this is a known, well-characterized compound,[6c] the data recorded here has been limited to ^{1}H NMR: δ 4.2–3.9 (m, 3 H), 3.70 (s, 3 H), 2.54 (m, 1 H), 2.1–1.5 (m, 6 H), 1.21 (d, 3 H, J = 6.3 Hz), 1.13 (d, 3 H, J = 7.0 Hz). Lit.:[6c] δ 4.2–3.9 (m, 3 H), 3.695 (s, 3 H), 2.54 (m, 1 H), 2.1–1.5 (m, 6 H), 1.20 (d, 3 H, J = 6.3 Hz), 1.13 (d, 3 H, J = 7.0 Hz).

(±)-Methyl 2-*epi*-Nonactate (41). Because this is a known, well-characterized compound,[6c] the data recorded here is limited to ^{1}H NMR: δ 4.2–3.9 (m, 3 H), 3.68 (s, 3 H), 2.59 (m, 1 H), 2.1–1.5 (m, 6 H), 1.22 (d, 3 H, J = 7.0 Hz), 1.21 (d, 3 H, J = 6.3 Hz). Lit.[5e] (CCl_4): δ 4.0 (m, 3 H), 3.62 (s, 3 H), 2.50 (m, 2 H), 2.0 (m, 2 H), 1.6 (m, 4 H), 1.19 (d, 3 H, J = 7 Hz), 1.12 (d, 3 H, J = 7 Hz).

(±)-Methyl Homononactate (15). ^{1}H NMR: δ 4.15 (m, 1 H), 3.99 (m, 1 H), 3.74 (m, 1 H), 3.70 (s, 3 H), 2.52 (m, 1 H), 2.1–1.5 (m, 8 H), 1.13 (d, 3 H, J = 7.0 Hz), 0.94 (t, 3 H, J = 7.3 Hz). ^{13}C NMR: δ 175.23, 80.97, 77.31, 70.36, 51.64, 45.23, 40.53, 30.53, 29.94, 28.78, 13.47, 10.09. LRMS (*m/e*): 230 (M^+, absent), 201 ($M^+ - C_2H_5$), 143 ($M^+ - CH_3CHCO_2CH_3$). Anal. Calcd for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63. Found: C, 62.31; H, 9.93.

(±)-Methyl 2-*epi*-Homononactate (42). ^{1}H NMR: δ 4.14 (m, 1 H), 3.99 (m, 1 H), 3.76 (m, 1 H), 3.68 (s, 3 H), 2.59 (m, 1 H), 2.1–1.4 (m, 8 H), 1.23 (d, 3 H, J = 7.0 Hz), 0.94 (t, 3 H, J = 7.3 Hz). ^{13}C NMR: δ 174.83, 80.43, 77.21, 70.28, 51.60, 44.67, 40.60, 30.67, 30.01, 28.78, 13.88, 10.05. Anal. Calcd for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63. Found: C, 62.35; H, 9.82.

(±)-Methyl Bishomononactate (16). ^{1}H NMR: δ 4.16 (m, 1 H), 3.99 (m, 1 H), 3.70 (s, 3 H), 3.55 (m, 1 H), 2.54 (m, 1 H), 2.0–1.5 (m, 7 H), 1.13 (d, 3 H, J = 7.0 Hz), 0.94 (d, 3 H, J = 6.8 Hz), 0.89 (d, 3 H, J = 6.8 Hz). ^{13}C NMR: δ 175.28, 80.92, 77.57, 73.68, 51.69, 45.26, 38.00, 33.51, 30.46, 28.88, 18.64, 18.01, 13.52. LRFABMS of a mixture of **16** and **43**: *m/e* 245 (M + H). HREIMS of a mixture of **16** and **43**: *m/e* 201.1128 (M – C_3H_7), 187.0971 (M – C_4H_9), 183.1022 (M – C_3H_7 – H_2O).

(±)-Methyl 2-*epi*-Bishomononactate (43). ^{1}H NMR: δ 4.15 (m, 1 H), 3.99 (m, 1 H), 3.68 (s, 3 H), 3.56 (m, 1 H), 2.59 (m, 1 H), 2.0–1.5 (m, 7 H), 1.23 (d, 3 H, J = 7.1 Hz), 0.94 (d, 3 H, J = 6.8 Hz), 0.90 (d, 3 H, J = 6.8 Hz). ^{13}C NMR: δ 174.90, 80.43, 77.49, 73.67, 51.63, 44.74, 38.05, 33.58, 30.57, 28.93, 18.66, 17.92, 13.97.

(±)-Methyl 9,9-Dimethylhomononactate (17). ^{1}H NMR: δ 4.17 (m, 1 H), 3.99 (m, 1 H), 3.70 (s, 3 H), 3.46 (m, 1 H), 2.52 (m, 1 H), 2.1–1.6 (m, 6 H), 1.13 (d, 3 H, J = 7.0 Hz), 0.89 (s, 9 H). ^{13}C NMR: δ 175.28, 80.64, 77.82, 75.82, 51.64, 45.26, 35.85, 34.52, 30.08, 28.94, 25.64, 13.48. LRFABMS of a mixture of **17** and **44**: *m/e* 259 (M + H). HREIMS of a mixture of **17** and **44**: *m/e* 240.1732 (M – H_2O), 201.1126 (M – C_4H_9), 183.1023 (M – C_4H_9 – H_2O).

(±)-Methyl 2-*epi*-9,9-Dimethylhomononactate (44). ^{1}H NMR: δ 4.14 (m, 1 H), 3.99 (m, 1 H), 3.69 (s, 3 H), 3.49 (m, 1 H), 2.58 (m, 1 H), 2.1–1.6 (m, 6 H), 1.23 (d, 3 H, J = 7.0 Hz), 0.90 (s, 9 H). ^{13}C NMR: δ 174.90, 80.25, 77.76, 75.86, 51.57, 44.78, 35.87, 34.51, 30.18, 29.11, 25.62, 14.01.

(±)-Methyl *anti*-6,8-Dihydroxy-2-methyldecanoate (45). Treatment of the dehydrononactate **32** with hydrogen gas (1 atm) in methanol in the presence of 0.001 equiv of palladium on carbon at room temperature overnight, followed by workup, resulted in the diol **45** in 80% crude yield. This material was not characterized beyond ^{1}H NMR spectroscopy. ^{1}H NMR: δ 3.90, (m, 1 H), 3.82 (pentet, 1 H, J = 6 Hz), 3.67 (s, 3 H), 3.03 (br s, 2 H), 2.42 (br sextet, 1 H), 1.7–1.3 (m, 10 H), 1.15 (d, 3 H, J = 7.0 Hz), 0.94 (t, 3 H, J = 7.0 Hz)9

(±)-(*E*)- and -(*Z*)-Methyl *anti*-6,8-Dihydroxy-2-methyl-2-decenoate (46). A solution of the dehydrononactate **32** was stirred in dry THF under nitrogen at –78 °C and 1.1 equiv of a solution of lithium tri-*sec*-butylborohydride was added via syringe. The reaction mixture was stirred at –78 °C for 1 h, then water was carefully added, and the mixture was warmed to room temperature and then worked up in the usual manner to yield **46** in 75% crude yield. This material was not characterized beyond ^{1}H NMR spectroscopy. ^{1}H NMR: δ 6.78 and 6.77 (t, 1 H, J = 7.0 Hz), 4.1 (br s, 2 H), 3.9 (m, 2 H), 3.73 (s, 3 H), 2.30 (br q, 2 H), 1.86 and 1.85 (s, 3 H), 1.7–1.4 (m, 6 H), 0.95 (t, 3 H, J = 7.0 Hz).

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94-0; **24** (isomer 3), 124605-15-8; **25**, 124604-95-1; **26**, 124604-96-2; *anti*-**27**, 124605-05-6; *anti*-**28**, 124605-06-7; *anti*-**29**, 124618-73-1; *anti*-**30**, 124618-74-2; *anti*-**30** (3-ol derivative), 124618-75-3; **31**, 124649-63-4; **32**, 124605-07-8; **33**, 124605-08-9; **34**, 124605-09-0; **41**, 56761-11-6; **42**, 124649-64-5; **43**, 124649-65-6; **44**, 124649-66-7; **45**, 124605-12-5; (*E*)-**46**, 124605-13-6; (*Z*)-**46**, 124605-14-7; CH_3COCH_3, 67-64-1; $CH_3CH_2COCH_3$, 78-93-3; $(CH_3)_2CHCOCH_3$, 563-80-4; $(CH_3)_3CCOCH_3$, 75-97-8.

Photodimerization of Cyclohexene and Methane by Decatungstate Anions: Molecular Orbital Theory

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Abstract: A molecular orbital study has been made of the photodimerization of cyclohexene by excited $W_{10}O_{32}^{4-}$, yielding 3,3′-dicyclohexene to explain the observations of Yamase. The overall process is radical monomer coupling. Radical formation by an adiabatic H transfer from cyclohexene to O^- on the O 2p to W 5d charge transfer photoexcited oxyanion is described. This process is highly activated, just as on metal oxide surfaces, because of the stability which comes when an electron from the CH bond reduces the hole in the oxyanion O 2p band during H abstraction. Since α-H abstraction is stabilized by the formation of the allylic π orbital, the product selectivity can be understood. Calculated H abstraction activation energies for olefinic, α, and β CH bonds in cyclohexene and for a CH bond in CH_4 are higher, but they are low enough that in the case of CH_4 it can be suggested that dimerization could be looked for in future experiments using photoactivated oxyanions. Based on the calculated electronic structures, it is possible to envision a nonadiabatic electron transfer to O^- during mild thermal collisions between a CH bond and the clusters yielding an organic radical cation followed by proton transfer at a later time. Polar solvents would enhance the probability for this mechanism.

In the last decade, photoredox reactions involving polyoxometalates or polyoxoanions have received increased attention because of their high selectivity as reagents or catalysts for the photooxidation of organic substances.[1-7] These materials are stable for a number of photocatalytic oxidation reactions upon exposure to visible or near-ultraviolet light. Photocatalytic processes involving polyoxometalates and organic substrates lead in general to the reduction of the polyoxometalates and the oxidation of the organic substrates.

The light absorption step involves electron transfer from O^{2-} to the cation set of empty orbitals, forming the excited polyoxometalate $(P^{n-})^*$. This species reacts with the hydrocarbon R–H to form radicals R• which dimerize. There are two likely mechanisms for the formation of R•. The first is H abstraction by $(P^{n-})^*$:

$$(P^{n-})^* + RH \rightarrow PH^{n-} + R^\bullet \qquad (1)$$

and the second is electron transfer from R–H to $(P^{n-})^*$ followed by proton addition:

$$\begin{aligned}(P^{n-})^* + RH &\rightarrow P^{(n+1)-} + RH^{\bullet+} \\ &\rightarrow P^{(n+1)-} + R^\bullet + H^+ \\ &\rightarrow PH^{n-} + R^\bullet \end{aligned} \qquad (2)$$

As has been discussed,[8,9] the operative mechanism may be different for different systems. Hydride and proton elimination are unlikely first steps to R• formation.[3]

Yamase and co-workers studied the photocatalytic dimerization of olefins in acetonitrile by tetrakis(tetrabutylammonium)-decatungstate(VI), $[NBu_4]_4[W_{10}O_{32}]$.[10] Accompanying dimer formation was the reduction of the decatungstate by H atoms. The photocatalytic dimerization of cyclohexene by $[W_{10}O_{32}]^{4-}$ led to the formation of 3,3′-dicyclohexene as the main product of the oxidation process. Many other molecules were studied, and when dimerization was not observed, it was because of preferential dehydrogenation of OH groups present in the molecules to form aldehydes or in some cases, because of steric hindrance. Typical examples of these two effects were benzyl alcohol and norbornadiene.[10]

The formation of O^- hole centers on metal oxide surfaces is known to facilitate the dimerization of hydrocarbons by H abstraction followed by radical coupling.[11-13] The active O^- sites have been prepared by different methods, including charge-transfer excitation from O^{2-} to the empty cation band, γ-irradiation defect formation, cation doping, and chemical reactions. Molecular orbital theory has explained this activity in terms of the reduction of surface O^- by an electron from the CH bond during H atom abstraction.[14-17] The O^- prevents the high initial closed-shell

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