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ELECTROPHILIC LACTONIZATION AS A TOOL IN ACYCLIC STEREOCONTROL

SYNTHESIS OF SERRICORNIN

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Abstract—Several electrophilic lactonization procedures have been explored as a means of functionalizing olefinic carboxylic acids with relative asymmetric induction. Iodolactonization of δ,ϵ-unsaturated acids under conditions of thermodynamic control exhibits good 1,2- and 1,3-, but not 1,4-induction in the formation of δ-lactones. Mercurilactonization proceeds with good stereocontrol in the formation of both γ- and δ-lactones (1,2-induction), but suffers from the difficulty of elimination during reductive demercuration; phenylselenolactonization with N-(phenylseleno)phthalimide is apparently kinetically controlled, affording high induction with **10**, a strongly sterically biased substrate leading to a δ-lactone, but not with **16**, which leads to a γ-lactone. In contrast, hydroxymethyllactonization proceeds with good stereocontrol in the case of **26**, the ester of **10**, but not with the analogous ester of **16**. The lactones resulting from cyclization of **10** and **13** were converted in stereospecific fashion into each of the stereoisomers of (±)-serricornin.

Electrophilic cyclization is a useful process for the regio- and stereocontrolled functionalization of both cyclic and acyclic unsaturated carboxylic acids.[1] With regard to acyclic systems, most investigations have focused on 1,2-relative asymmetric induction using iodine as the electrophile. We now report our studies on the extension of this process to cases involving 1,3- and 1,4-asymmetric induction in the formation of δ-lactones and to mercuri-, phenylseleno-, and hydroxymethyllactonization.

Iodolactonization of δ,ϵ-unsaturated acids

As we and others have reported, iodolactonization of a number of γ,δ- and δ,ϵ-unsaturated carboxylic acids under conditions of thermodynamic control manifests high 1,2-relative asymmetric induction from allylic substituents.[2,3] In view of the conformational flexibility of 5-membered ring systems, stereocontrol from homoallylic groups is not expected to be very high in the formation of δ-lactones from γ,δ-unsaturated acids.[2a,4] On the other hand, because of the pseudo chair-like conformation of δ-lactones, remote stereochemical relationships are well-defined and 1,3- and 1,4-relative asymmetric induction may be expected in their formation.

Under conditions of kinetic control (iodine in acetonitrile in the presence of $NaHCO_3$ as acid-scavenger), 4-methyl-5-hexenoic acid (**1**) shows a modest preference for formation of the less stable *cis*-lactone **2** (Table 1, entry 1). This is analogous to the behavior of related 3-substituted 4-pentenoic acids.[2a] Omission of sodium bicarbonate from the mixture allows equilibration of the *cis* and *trans* lactones to take place, and the expected diequatorial *trans* product **3** is highly favored (entry 2).[5]

As indicated in entry 4, moderate 1,3-asymmetric induction is observed on iodolactionization of 3-methyl-5-hexenoic acid (**4**) under conditions of thermodynamic control: the expected *cis* product **6** is produced with a selectivity of 6 : 1. With this substrate, there is no reversal in stereospecificity between the thermodynamically and kinetically controlled reaction conditions; the latter still favor the *cis*-product, albeit with reduced selectivity (entry 3).

We have also studied the possibility of 1,4-asymmetric indiction from a Me substituent at C-2, both alone and in combination with another Me at the allylic position (C-4). As the results in Table 1 indicate (entries 5–9), the C-2 Me group exerts no significant stereochemical influence. Under conditions of thermodynamic control, 2-methyl-5-hexenoic acid (**7**) leads to a 1.1 : 1 mixture of isomers; with the other substrates (**10** and **13**), the allylic substituent completely dominates the stereochemistry of cyclization (1,2-induction). In view of the fact that a Me substituent at C-2 is eclipsed with the CO group in the pseudo-equatorial position and encounters only one axial hydrogen (at C-4) in the pseudo-axial position, it is not surprising that no preference is shown. Interestingly, a greater preference for formation of the *trans* (diequatorial) isomer is obtained on kinetically-controlled iodolactionization of 2-methyl-5-hexenoic acid, but the selectivity is still a modest 1.8 : 1 (entry 5).

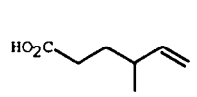
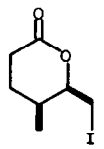
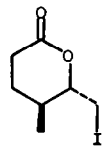
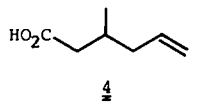
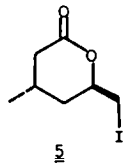
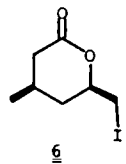
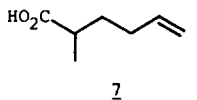
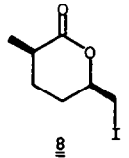
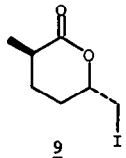
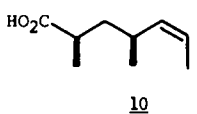
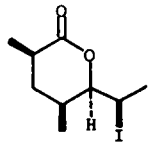
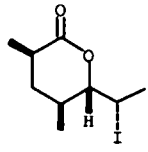
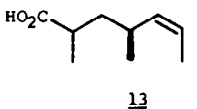
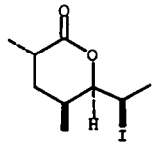
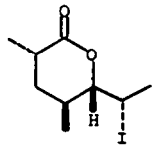
The stereostructures of the monomethyl iodolactones were readily assigned by ^{13}C-NMR, relying upon the upfield shifts consistently exhibited by the methyl, iodomethyl, and C-2, C-3, and C-4 carbons in the isomers with axial substituents, as displayed in Table 2.[6]

We have previously reported the use of an iodolactone which is related to **12** in a synthesis of the pheromone multistriatin;[2b] we describe below the conversion of lactone **15** to serricornin, the pheromone of the cigarette beetle.[7]

Stereocontrolled lactonization with other electrophiles

Mercurilactonization. Electrophilic cyclizations initiated by mercuric salts have been reported for a variety of olefinic alcohols and hemiacetals, and in some instances have been shown to proceed with excellent stereoselectivity.[1a,8,9] In contrast, there have

Table 1. Idolactonization of δ,ϵ-Unsaturated Acids

Entry	Substrate	Conditions[a]	Ratio of Products[b]		Yield[c] (%)
	 1		 2	 3	
1		K	2.3	1	83
2		T	1	15	77
	 4		 5	 6	
3		K	1	3	97
4		T	1	6	81
	 7		 8	 9	
5		K	1	1.8	78
6		T	1	1.1	68
	 10		 11	 12	
7		K	1	20	92
8		T	1	20	80
	 13		 14	 15	
9		T	1	20	69

[a] K = kinetic control: 3 eq. I_2, CH_3CN, $NaHCO_3$, 0 °C
T = thermodynamic control: 3 eq. I_2, CH_3CN, 0 °C

[b] Ratios determined by ^{13}C-NMR (entries 1-6) or capillary GC (entries 7-9).

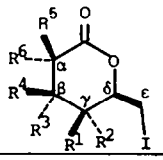
[c] Isolated yields of purified products

been only a few reports of mercurilactonizations,[10] and none which addresses the question of stereoselectivity in the cyclization of acyclic substrates.

Cyclization of 3-phenyl-4-pentenoic acid (**16**) and the δ,ϵ-unsaturated acid **10** with mercuric acetate in methanol leads to the mercurilactones **17** and **19**, respectively, in good yield and stereoselectivity (as indicated in Scheme 1). The stereochemistry of these cyclizations was readily demonstrated by reductive demercuration with sodium borohydride[11] and correlation of the products **18** and **20** with material obtained on tri(n-butyl)tin hydride reduction of the analogous iodolactones.[12]

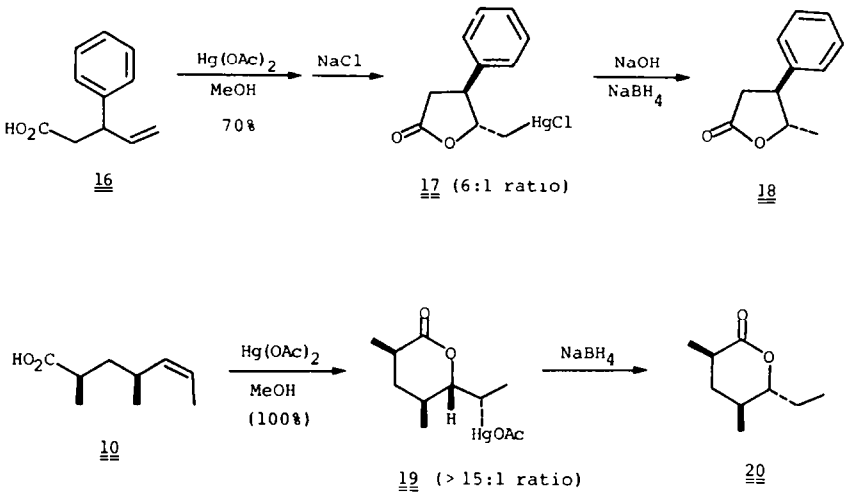
After mercuricyclization of unsaturated alcohols or other derivatives, a number of methods have been employed for demercuration, including electrophilic substitution with halogens[8b,13] and reduction with borohydride or sulfur reagents.[8a,9,14] Reductive demercuration appeared to us to be the most important from the point of view of extending the versatility of stereoselective lactonizations. However, a serious limitation in this regard is the propensity for the lactones to undergo reductive elimination under a variety of demercuration conditions, with reversion to the acyclic starting material. As indicated in Table 3, we explored a number of reagents and conditions, including sodium borohydride at various pH's[11]

Table 2. ^{13}C-NMR Chemical Shifts for Monomethyl δ-Lactones



Compound	Position of CH_3	(C=O)	Chemical Shift α^b	β^b	γ^b	δ	ε	CH_3
2	R^1	--	28.1	25.5	25.3	81.4	2.7	10.6
3	R^2	169.8	32.8	29.1	26.3	81.9	9.0	16.2
5	R^3	170.3	34.1	23.2	36.6	75.1	7.4	20.5
6	R^4	169.5	36.4	25.2	37.1	77.6	8.4	20.9
8	R^5	169.3	32.8	26.5	24.9	76.5	6.5	16.0
9	R^6	167.7	35.5	29.0	27.4	79.0	8.6	16.8

[a] Reported in ppm downfield from TMS, referenced to solvent $CDCl_3$ as 77.0 ppm.
[b] Some pairs of these assignments may be interchanged.



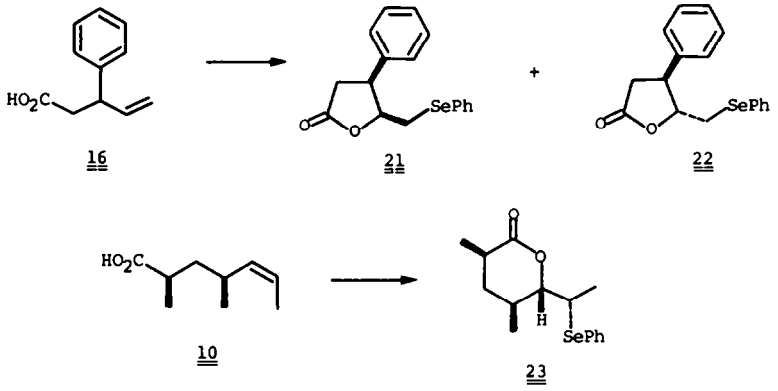
Scheme 1.

Table 3. Phenylselenolactonization of Unsaturated Acids

Entry	Conditions	Yield of Lactone 20[a]	Yield of Acid 10[b]
1	$NaBH_4$/MeOH/AcOH, 0 °C	0	(100%)
2	$NaBH_4$/MeOH/2 N NaOH, 0 °C	85%	15%
3	$NaBH_4$/MeOH, -78 °C	90%	10%
4	Na_2S/H_2O, 0 °C	0	(100%)
5	Na_2S/H_2O/2 N NaOH, 0 °C	0	(100%)
6	H_2 (50 psi)/$(\emptyset_3P)_3RhCl$/MeOH, 21 °C	0	(100%)
7	$(n\text{-}C_4H_9)_3SnH$/AIBN/toluene, 21 °C	66%	33%
8	$(n\text{-}C_4H_9)_3SnH$/MeOH, -78 °C	66%	33%

[a] All reactions carried out with 0.2 M substrate (19) in the indicated solvent.
[b] Ratios determined by VPC.

Table 4.



16 21 22

10 23

Entry	Substrate	Conditions	Ratio of Products[a]	Yield[b] (%)
1	16	PhSeCl, CH_2Cl_2, Et_3N -78°C	21/22, 1:2.7	54
2	16	PhSeFt,[c] CH_2Cl_2, p-TsOH -78 → 21 °C	21/22, 1:1	93
3	10	PhSeCl, CH_2Cl_2 -78°C	23 (15:1)	88
4	10	PhSeFt,[c] CH_2Cl_2 -78°C	23 (>15:1)	73

[a] Ratios determined by ^{13}C-NMR (entries 1,2) or capillary GC (entries 3,4)

[b] Isolated yields of purified products

[c] PhSeFt = N-(phenylseleno)phthalimide

hydrogen over Wilkinson's catalyst,[15] tri(n-butyl)tin hydride, and sodium sulfide.[9b,16] Reductive elimination was minimized in alkaline borohydride; however, it could not be avoided entirely.

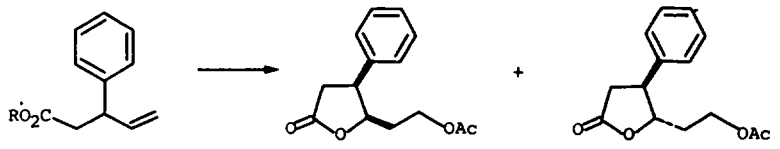
Phenylselenolactonization. Phenylselenyl reagents have been applied to a wide variety of cyclization reactions,[17] although they have not been systematically studied for the stereocontrolled lactonization of acyclic substrates. As the results in Table 4 indicate, phenylselenolactonization does not appear to be as generally applicable for relative asymmetric induction as the iodine-and mercuric ion-initiated processes are. Although the dimethyl substituted δ,ϵ-unsaturated acid **10** exhibits its usual preference for the all-equatorial product (entries 3 and 4), very modest selectivity is seen for 3-phenyl-4-pentenoic acid **16** (entries 1 and 2). In this latter case, conditions were chosen to facilitate thermodynamic control by acid-catalyzed equilibration (entry 2), but without success.[17c] Thermodynamic control has been reported by Sharpless for a phenylselenoetherification reaction,[18] and it may prove possible in a lactonization process under more vigorous conditions.

The phenylselenolactones were correlated with the analogous iodolactones by reduction of both series with tri(n-butyl)tin hydride. Lactone **23** on treatment with t-BuOOH at room temperature undergoes elimination as expected to give the allylic lactone **24**. Interestingly, the allylic lactone is not accessible from iodolactone **12**: base-induced elimination **12** affords the enol-lactone **25** preferentially.

24 25

Hydroxymethyllactonization. The Prins reaction is a well-established process for the *anti* addition of a carbon electrophile (most commonly protonated formaldehyde) and an oxygen nucleophile across a double bond.[19] In contrast to cyclizations initiated by iodine, mercury, or phenylselenium electrophiles, the step involving addition of the formaldehyde to the double bond is not likely to be reversible. For stereocontrol to be exerted over the stereochemistry and regiochemistry of a lactonization initiated under Prins conditions, simultaneous addition of the electrophile and the carboxyl group to the double bond would presumably be required. Moreover, one would expect only kinetic rather than thermodynamic control over the cyclization. Nevertheless, the potential ability to initiate an electrophilic lactonization

Table 5.



16: R = H
26: R = Me

27 28

Entry	Substrate	Conditions	Ratio,[a] 27/28	Yield[b] (%)
1	16	$(CH_2O)_n$, H_2SO_4, HOAc	1:3	64
2	16	1. $(CH_2O)_n$, $BF_3 \cdot Et_2O$, CH_2Cl_2 2. Ac_2O, pyridine	1:2	53
3	26	"	1:7	60

[a] Ratios determined by ^{13}C-NMR
[b] Isolated yields of purified products

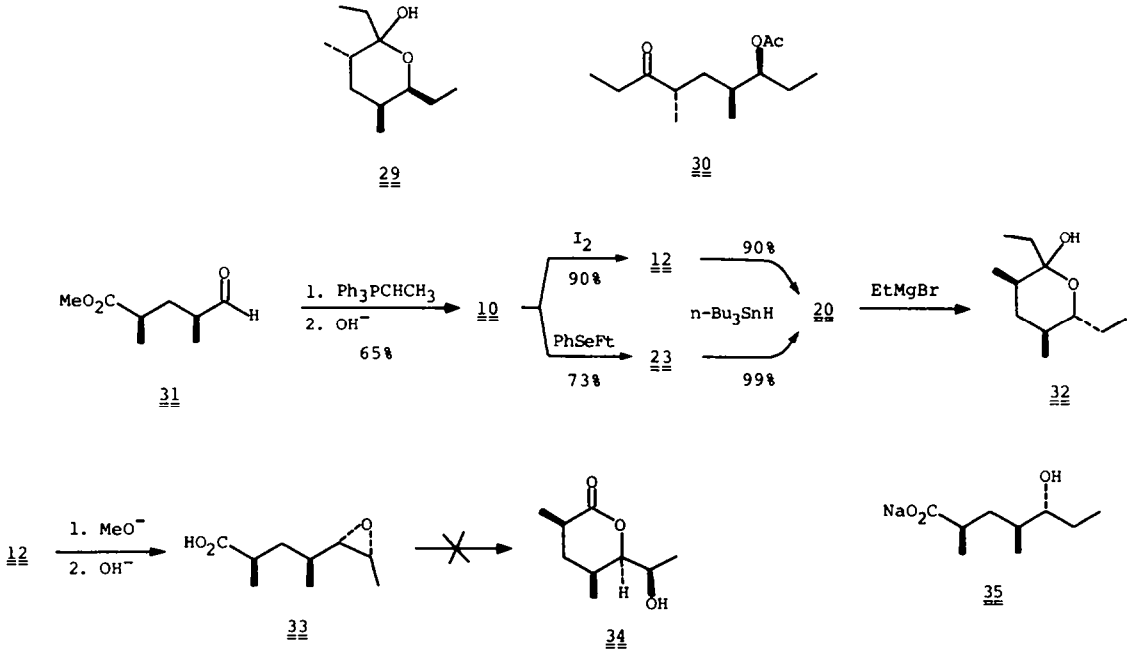
with a carbon electrophile made the process an appealing goal.

3-Phenyl-4-pentenoic acid (**16**) undergoes lactonization under classical Prins conditions (paraformaldehyde and sulfuric acid in acetic acid), giving a 3 : 1 mixture of *trans*/*cis* products **27** and **28** in 64% yield. Modified conditions involving boron trifluoride etherate in CH_2Cl_2 are less effective, as shown in Table 5. When these Lewis acid-catalyzed conditions are applied to the methyl ester **26**, a dramatic improvement in the stereoselectivity is seen: the *trans* isomer is favored over the *cis* by a ratio of 7 : 1.

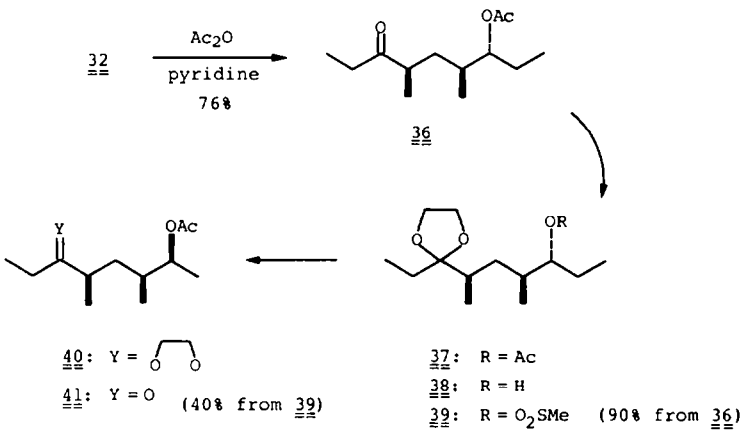
However, we were not able to generalize this procedure, as the results in Table 5 indicate. When applied to the dimethyl-substituted, δ,ϵ-unsaturated compound **10**, either in the form of the free acid or the methyl ester, a stereo- and regioisomeric mixture of lactones is obtained in low yield, in spite of the fact that this substrate is otherwise a very favorable one for lactonization.

Stereocontrolled total synthesis of (+) *serricornin acetate*

The cigarette beetle *Lasioderma serricone* (*F.*) produces as a pheromone the cyclic hemiacetal 29, known as serricornin.[7] The stereochemistry of serricornin, as its open-chain acetate **30**, has been shown by Mori *et al.* to be 4*S*,6*S*,7*S*.[20] Recently a number of partial and total syntheses of serricornin and its isomers have been reported.[7,20,21]



Scheme 2.



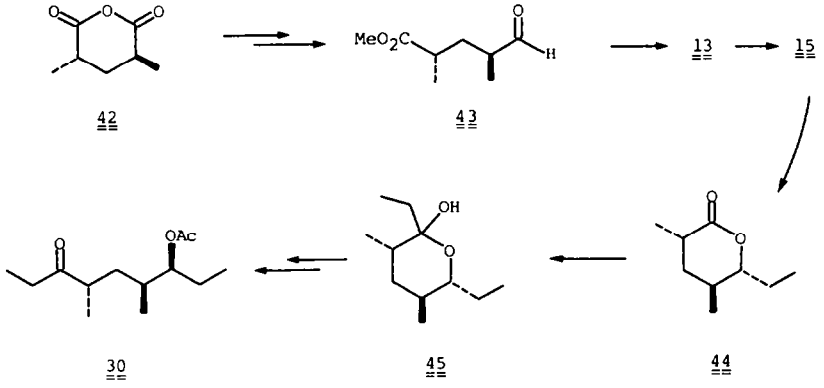
Scheme 3.

At the beginning of our work, the relative stereochemistry at C-4 had not been determined, hence it was of interest to study the cyclization of both diastereomers of 2,4-dimethyl-5-heptenoic acid. Although we envisaged that the lactonization reaction could be used to advantage to control the regio- and stereochemistry of the olefin functionalization process, we expected to obtain the incorrect relative configuration at the carbinol center. We therefore planned to invert this stereocenter to obtain the natural isomer.

Because of its ready availability from *meso*-2,4-dimethylglutaric anhydride,[27] the *R**,*S**-isomer **10** was used as the substrate in our initial exploration (Scheme 2). This material was prepared from the aldehyde ester **31**[9b,22] with ethylidenetriphenylphosphorane and consisted of a 13–15 : 1 mixture of *cis* and *trans* isomers. As indicated above, iodo- or selenolactonization of this material was accomplished in a highly stereoselective fashion. Tri(n-butyl)tin hydride reduction of either of these products afforded the all-equatorial lactone **20** in greater than 95% stereochemical purity. Treatment of this material in turn with ethylmagnesium bromide then provided hemiacetal **32**, a stereoisomer of the natural product.

Inversion of the relative configuration at the carbinol position (C7) proved to be difficult. We first explored a number of ways to invert the configuration at the lactone stage. Conversion of iodolactone **12** to the epoxy acid **33** was straightforward, although it was not possible to cyclize this material to the desired hydroxy lactone **34** with either acid or base catalysis.[2c] Our inability to effect the inversion by a second lactonization reaction presumably reflects the steric congestion that would develop from the pseudo-axial hydroxyethyl substituent in the transition state. An alternative strategy, to take hydroxy carboxylate **35**, derived from the reduced lactone **20** by alkaline hydrolysis, and relactonize it with inversion using diethyl azodicarboxylate/triphenylphosphine,[23] was also foiled: simple lactionization takes place upon neutralization of the salt, even in the presence of the redox-dehydration reagents.

We therefore turned our attention to opening the hemiacetal ring of **32** and inverting the C-7 OH by an intermolecular reaction.[24] The only ring-opening sequence which proved to be successful involved a number of steps: conversion of the hemiacetal **32** to the open chain acetate **36**, formation of the ethylene ketal **37**, and subsequent alkaline cleavage of the acetate moiety to give hydroxy ketal **38** (Scheme 3). Mitsunobu-type inversion[25] of hydroxyketal **38** failed, presumably because of the branched (and therefore hindered) nature of the carbinol center. However, conversion of **38** to the mesylate and displacement with cesium acetate in DMF[26] afforded the desired inverted ester **40** in 50% yield, along with a comparable amount (by GC analysis) of material resulting from elimination. A number of variations in



Scheme 4.

solvent and conditions were made without significantly altering the yield. Finally, acid-catalyzed cleavage of the ketal protecting group afforded the keto-acetate **41**, another stereoisomer of the material derived from serricornin.

With the conditions for cyclization and inversion worked out for the diastereomer, application of the sequence to dl-2,4-dimethylglutaric anhydride (**42**) was pursued (Scheme 4). The anhydride **42** is readily available by cyclization of the corresponding diacid[27] with DCC (95% yield). (Epimerization to a 1 : 1 mixture of **42** and the *meso*-anhydride is found when this cyclization is accomplished with acetic anhydride). Subsequent elaboration of the olefinic acid via aldehyde ester **43** and iodolactone **15** to give the simple lactone **44** proceeds as described for the diastereomeric material. This lactone can also be converted to the hemiacetal **45** by direct addition of ethylmagnesium bromide, although in this case some care has to be taken to avoid double addition to the CO group. Ring opening of **45**, protection of the ketone function, and inversion of the OH group also proceed as described for the diastereomeric series and in comparable yields. Finally, hydrolysis of the ketal affords acetate **30**, which exhibits NMR spectral properties identical to those reported for the acetate derived from natural serricornin.[20]

EXPERIMENTAL

General methods. Unless otherwise indicated: IR spectra were obtained in $CHCl_3$. ^{1}H-NMR spectra were measured in $CDCl_3$; data are presented as follows: chemical shift in ppm on the δ scale relative to internal TMS (multiplicity, number of hydrogens, coupling constant(s) in hertz). ^{13}C-NMR spectra were acquired in $CDCl_3$; chemical shifts are reported in ppm on the δ scale, relative to solvent $CDCl_3$ as 77.0 ppm. Extractive workups culminated in washing the organic layer with brine, drying over $MgSO_4$, and evaporating the solvent at reduced pressure on a rotary evaporator. Analytical gas chromatography was performed on a 6 ft × 1/8 in. column using helium as the carrier gas with OV-101 on 100–200 mesh gasChrom Q (OV-101) or a 0.2 mm × 12.5 m crosslinked dimethylsilane (capillary) column; preparative gas chromatography was performed on 6 ft × 1/4 in. SE-30 columns eluted with helium. Distillations were bulb-to-bulb, performed with a Büchi kugelrohrofen at the oven temperature and system pressure indicated. Chromatography was performed by the method of Still,[28] using the indicated eluting solvent.

Tetrahydro - 6 - (*iodomethyl*) - 5 - *methyl* - 2*H* - *pyran* - 2-*one*, **2** *and* **3**

General procedure for kinetically-controlled iodolactonization. To a mixture of 756 mg (9 mmol) of anhyd powered $NaHCO_3$ and 39 mg (0.30 mmol) of 4-methyl-5-hexenoic acid[29] in 1 ml of CH_3CN stirred at 0° was added 230 mg (0.91 mmol) of I_2. After 3 hr, the mixture was diluted with ether, washed with $Na_2S_2O_3$aq and water, and worked up to give 64 mg (83% yield) of **2** and **3** in a ratio of 2.3:1 IR 1725 cm^{-1}; ^{1}H-NMR δ 0.97 and 1.01 (two d, 3, assigned to *cis* and *trans* isomers, respectively), 1.2-2.3 (m, 3), 2.3-3.0 (m, 2), 3.1-3.9 (m, 3); ^{13}C-NMR: see Table 2. An analytical sample was prepared by preparative GC (170°C): (Found: C, 33.20; H, 4.44; I, 49.48. Calc. for $C_7H_{11}IO_2$: C, 33.09; H, 4.36; I, 49.95%.)

Tetrahydro - 6 - (*iodomethyl*) - 4 - *methyl* - 2*H* - *pyran* - 2-*one*, **5** *and* **6**

General procedure for thermodynamically-controlled iodolactonizations. To a soln of 175 mg (1.37 mmol) of 3-methyl-5-hexenoic acid[30] in 4 ml of CH_3CN stirred at 0° was added 1.04 g (4.1 mmol) of I_2. After 2.5 hr, the mixture was diluted with ether, washed with $Na_2S_2O_3$aq and $NaHCO_3$aq, and worked up to give 280 mg (81% yield) of **5** and **6** in a ratio of 1 : 6: IR 1725 cm^{-1}; ^{1}H-NMR (180 MHz) δ 0.97 1.07 (d, 3, J = 6), 1.30 (dq, 1, J = 2.4, 14.0), 1.7–2.3 (m, 3), 2.5–2.8 (m, 1), 3.24–3.44 (AB of ABX, 2, H_A = 3.32, H_B = 3.37, J_{AB} = 10.53, J_{AX} = 6.66, J_{BX} = 4.07), 4.26 (X of ABX, 1); signals for the minor isomer (**5**) appeared δ 1.13 (d) and 4.46 (X of ABX); ^{13}C-NMR: see Table 2. An analytical sample was prepared by preparative GC (190°): (Found: C, 32.90; H, 4.36; I, 49.94. Calc. for $C_7H_{11}IO_2$: C, 33.09; H, 4.36; I, 49.95%.)

Tetrahydro - 6 - (*iodomethyl*) - 3 - *methyl* - 2*H* - *pyran* - 2-*one*, **8** *and* **9**

Prepared as indicated above in 78% yield (kinetically-controlled) or 68% yield (thermodynamically-controlled): IR 1725 cm^{-1}; ^{1}H-NMR δ 1.21 and 1.28 (two d, 3, *cis* and *trans* isomers, respectively), 1.4–2.7 (m, 5), 3.3 (AB of ABX, 2), 4.25 (X of ABX, 1); ^{13}C-NMR: see Table 2. An analytical sample was prepared by preparative GC (190°): (Found: C, 32.85; H, 4.35; I, 49.72. Calc. for $C_7H_{11}IO_2$: C, 33.09; H, 4.36; I, 49.95%.)

(3R*, 5S*, 6S*, 1'S*)-*Tetrahydro* - 6 - (1-*iodoethyl*) - 3,5 - *dimethyl* - 2*H* - *pyran* - 2 - *one*, **12**

Prepared as indicated above in 92% yield (kinetically-controlled) or 80% yield (thermodynamically-controlled): IR 1734 cm^{-1}; ^{1}H-NMR δ 0.975 (d, 3), 1.29 (d, 3), 1.45–1.6 (m, 1), 1.9–2.0 (m, 1), 2.04 (d, 3, J = 7), 2.5–2.7 (m, 1) 2.97 (dd, 1, J = 1.3, 9.6), 4.32 (dq, 1, J = 1.35, 7.1). An analytical sample was prepared by chromatography (2 : 1 hexane–ether). (Found: C, 38.33; H, 5.38; I, 44.79. Calc. for $C_9H_{15}IO_2$: 38.32; H, 5.36; I, 44.98%.)

(2R*, 4S*, Z) - 2,4 - *Dimethyl* - 5 - *heptenoic acid* **10**

Prepared from **31**[22] in 65%overall yield by the same procedure as described below for the 2*R**, 4*R** diastereomer **13**. IR 3500-2400, 1700 cm^{-1}; ^{1}H-NMR δ 0.9 (d, 3), 1.1 (d, 3), 1.55, (dd, 3, J = 2.8, 7.5), 2.2–2.7 (m, 2), 4.8–5.4 (m, 2), 8.1–8.8 (br s, 1). An analytical sample was prepared by preparative GC (140°): (Found: C, 69.23; H, 10.24. Calc. for $C_9H_{16}O_2$: C, 69.21; H, 10.33%.)

(2*R**, 4*R**, *Z*) - 2,4 - *Dimethyl* - 5 - *heptenoic acid* **13**

Ethylidenetriphenylphosphorane was prepared from 1.44 g (3.87 mmol) of ethyltriphenylphosphonium bromide and 2.74 mL (3.78 mmol) of 1.41 M n-BuLi/hexane in 5 mL THF at 21°. The red ylide soln was added dropwise to a soln of 0.509 g (3.22 mmol) of **43** in 10 mL of THF at 0° until the red ylide color persisted (~ 85% of ylide added). HMPA (0.67 mL, 3.87 mmol) was added, and the soln was brought to 21° and kept for 18 hr. The mixture was partitioned between ether and H_2O and the aqueous layer was extracted with another portion of ether. After washing the combined organic layer with $NaHCO_3$aq, work up provided a pale yellow residue which was triturated with pentane and filtered to remove triphenylphosphine oxide. After evaporation, the resulting oil was dissolved in 3 mL of MeOH and 3 mL of 2N NaOH and heated at 65° for 30 min. The hydrolysis mixture was partitioned between ether and water, the aqueous layer was acidified and extracted with ether and worked up to give 0.21 g (41% yield) of **13** as a slightly yellow oil, pure by NMR analysis: IR 3400–2400, 1700 cm^{-1}; ^{1}H-NMR δ 0.95 (d, 3), 1.18 (d, 3), 1.25 (m, 1), 1.58 (d, 3, J = 6.5), 1.77 (ddd, 1, J = 5, 5.2, 12.5), 2.4–2.7 (m, 2), 5.1 (ddq, 1, j = 12.5, 12.5, ~0.5), 5.4 (m, 1). An analytical sample was prepared by preparative GC (150°): (Found: C, 69.11; H, 10.18. Calc. for $C_9H_{16}O_2$: C, 69.21 H, 10.33%.)

(3R*, 5R*, 6R*, 1'R*) - *tetrahydro* - 6 - (1-*iodoethyl* - 3,5-*dimethyl* - 2*H* - *pyran* - 2 - *one*, **15**

Prepared by the thermodynamically-controlled iodolac-

tonization procedure described above, in 69% yield: IR 1737 cm^{-1}; ^{1}H-NMR δ 0.98 (d, 3), 1.28 (d, 3), 1.65–1.85 (m, 2), 2.04 (d, 3), 2.05 (m, 1), 2.7 (m, 1), 2.95 (dd, 1, J = 1.6 9.6), 4.29 (dq, 1, J = 1.6, 7.1). An analytical sample was purified by chromatography (1 : 1 hexane–ether): m.p. 77–80° (Found: C, 38.44; H, 5.30; I, 45.15. Calc. for $C_9H_{15}IO_2$: C, 38.32; H, 5.36; I, 44.98%.)

(4R*, 5S*) - *Dihydro* - 5 - *methyl* - 4 - *phenyl* - 2(3*H*) - *furanone*, **18**

3-Phenyl-4-pentenoic acid **16**[31] was converted to the mercurilactone and demercurated as described below for **10**, giving **18** as a 6 : 1 mixture of *trans*:*cis* isomers in 45% overall yield: IR 1782 cm^{-1}; ^{1}H-NMR δ 1.45 (d, 3), 2.7–3.0 (m, 2), 3.24 (ddd, 1, J = 8.5, 11), 4.56 (dq, 1, J = 6, 8.5), 7.0–7.3 (m, 5); signals for the minor (*cis*) isomer were visible at δ 1.03 (d, 3), 3.78 (ddd, 1, J = 8, 8, 8), 4.94 (dq, 1, J = 6.5, 6.5). An analytical sample was prepared by chromatography (CH_2Cl_2). (Found: C, 75.05; H, 6.86. Calc. for $C_{11}H_{12}O_2$: C,74.97; H, 6.87%.)

(3R*, 5S*, 6S*, 1'S*) - 6 - (1 - *Acetoxymercuriethyl*) - *tetrahydro* - 3,5 - *di* - *methyl* - 2*H* - *pyran* - 2 - *one*, **19**

A soln of 50 mg (0.32 mmol) of **10** and 112 mg (0.34 mmol) of $Hg(OAc)_2$ in 3 mL of MeOH was stirred at 20° for 18 hr. The solvent was removed under reduced pressure, and the residual AcOH was swept out by evaporation from heptane three times. The product, obtained in quantitative yield was shown by ^{1}H-NMR analysis to be predominantly a single isomer, **19**: δ 1.05 (d, 3), 1.38 (d, 3), 1.4–1.5 (m, 3), 1.57 (m, 3), 2.06 (s, 3), 2.6 (m, 1), 2.96 (dq, 1, J = 1.5, 7.5), 4.06 (dd, 1, J = 1.5, 10). A signal for the minor isomer was visible at δ 4.3 (dd). No attempt was made to purify this material before it was subjected to the demercuration procedures.

(2R*, 4R*, 5R*) - 6 - *Ethyl* - *tetrahydro* - 3,5 - *dimethyl* - 2*H* - *pyran* - 2 - *one*, **20**

By deiodination of **12**. A soln of 1.39 g (4.9 mmol) of **12** and 1.95 ml (7.4 mmol) of tri(n-butyl)tin hydride in 75 ml of THF was stirred at 21° for 20 hr. The solvent was removed under reduced pressure and the residue was dissolved in 50 ml of CH_3CN and washed twice with 15–20 mL of cold hexane.[32] The hexane washes were back extracted with CH_3CN, the combined CH_3CN layer was evaporated, and the resulting oil was purified by chromatography (2:1 hexane–ether) to give 0.69 g (90% yield) of **20**: m.p. 32–35°; IR 1715 cm^{-1}; ^{1}H-NMR δ 0.95 (d, 3), 0198 (t, 3), 1.25 (d, 3), 1.2–1.4 (m, 1), 1.5–1.6 (m, 1), 1.6–1.9 (m, 3), 2.5 (m, 1), 3.9 (ddd, 1, J = 3.2, 7.2 10.1). An analytical sample was prepared by preparative GC. (Found: C, 68.95; H, 10.20. Calc. for $C_9H_{16}O_2$: C, 69.19, H, 10.32%.)

By demercuration of **19**. A soln of 160 mg (0.38 mmol) of **19** in 1 mL MeOH and 2 mL of 0.5 N NaOH was cooled to 0° and treated with 1.5 mL of 0.5 M $NaBH_4$ in 2 N NaOH, leading to an instantaneous precipitation of metallic Hg. After 30 min, the mixture was diluted with ether, centrifuged, washed with 2 N HCl and 5% $NaHCO_3$aq, and worked up to give 41 mg (69% yield) of a colorless oil which was shown by GC analysis to consist of **20** and **10** in a ratio of 85:15.

By deselenation of **23**. A soln of 148 mg (0.475 mmol) of **23**, 3 mg of azobisisobutyronitrile, and 0.25 mL (0.95 mmol) of tri(n-butyl)tin hydride in 6 mL of toluene was heated at reflux for 1 hr. After removal of the solvent at reduced pressure, the residue was purified by chromatography (2:1 hexane–ether) to give 73 mg (98% yield) of **20** as a colorless oil.

5 - (*Benzeneselenomethyl*) - *dihydro* - 4 - *phenyl* - 2(3*H*) - *furanone*, **21** and **22**

To a soln of 105 mg (0.60 mmol) of **16** and 2 mg of anhyd *p*-toluenesulfonic acid in 2 mL of CH_2Cl_2 at −78° was added 234 mg (0.775 mmol) of N-(phenylseleno)- phthalimide. The mixture was allowed to warm to 21° for 2 hr, diluted with CH_2Cl_2 and washed with 2 N NaOH, and worked up to give the crude product as a yellow oil. After chromatographic purification 183 mg (93% yield) of a 1:1 mixture of **21** and **22** was obtained. In a similar experiment, continued stirring of the selenolactone in the presence of 20 mole % of *p*-toluenesulfonic acid under the same conditions at 21° for 3 d led to a 92% recovery of starting material with an unaltered 1 : 1 ratio of isomers: IR 1780 cm^{-1}; ^{1}H-NMR δ 2.78 (m, 2), 3.1 (m, 2), 3.6 (m, 1), 4.62 (m, 1), 7.1 (m, 10); ^{13}C-NMR δ *trans* isomer **22**fi 20.59, 36.95, 85.02, 126.96–132.84, 174.64; *cis* isomer **21**: 27.48, 36.27, 43.94, 82.34. An analytical sample was prepared by distillation (223°/0.1 torr). (Found: C, 61.85; H, 4.92. Calc. for $C_{17}H_{16}O_2Se$: C, 61.64; H, 4.86%.)

(3R*, 5S*, 6S*, 1'S*) - *Tetrahydro* - 3,5 - *dimethyl* - 6 - (1 - *phenyseleno* - *methyl* - 2*H* - *pyran* - 2 - *one*, **23**

By a procedure similar to that described above, 60 mg (0.384 mmol) of **10** was converted to 87 mg (73% yield) of the oily **23** after chromatography (1:1 hexane–ether): IR 1725 cm^{-1}; ^{1}H-NMR δ 0.92 (d, 3), 1.3 (d, 3), 1.4–1.5 (m, 1), 1.65 (d, 3), 1.9, (m, 1, 2.25–2.45 (m, 1), 2.5 (m, 1), 3.4, (dq, 1, J = 1.4, 7.3), 3,97 (dd, 1, J = 1.4, 10.2). A signal for a minor isomer appeared at δ 4.27 (dd, J = 2.7, 12.1). (Found: C, 58.01; H, 6.39. Calc. for $C_{15}H_{20}O_2Se$: C, 57.87; H, 6.48%.)

5 - (2 - *Acetyloxyethyl*) - *dihydro*- -4 - *phenyl* - 2(3*H*) - *furanone*, **27** *and* **28**

A mixture of 200 mg (1.05 mmol) of **26**, 44 mg (1.47 mmol) of paraformaldehyde, and 0.17 mL (1.22 mmol) of BF_3.etherate in 4 mL of CH_2Cl_2 was stirred at 21° for 24 hr. Another 0.17-mL of BF_3.etherate was then added and the mixture was heated at reflux for an additional 37 hr, at which point the starting material was consumed. The mixture was diluted with CH_2Cl_2, washed with $NaHCO_3$aq, and worked up to give 202 mg of crude hydroxylactone as an oil. For analysis this material was acetylated directly with 0.12 ml (1.26 mmol) of Ac_2O, 0.16 mL (1.16 mmol) of Et_3N, and a catalytic amount of 4-(dimethylamino)pyridine in 8 mL of ether. After washing the mixture with water and working up in the usual way, 169 mg (59% yield of **27** and **28** was obtained as an oil in the ratio of 1:7: IR (film) 1780, 1740 cm^{-1}; ^{1}H-NMR δ 2.0 (m, 2), 2.00 (s, 3), 2.90 (m, 2), 3.30 (dddd, 1), 4.2 (m, 2), 4.6 (m, 1), 7.1 (br s, 5); ^{13}C-NMR δ 32.70, 32.77, 36.95, 47.33, 60.34, 83.11, 126.9–129.6 (several carbons), 170.31, 174.77; peaks attributable to the minor isomer appeared at δ 20.39, 30.49, 35.29, 43.98, 60.63, 80.12. (Found: C, 67.70; H, 6.52. Calc. for $C_{14}H_{16}0_4$: C, 67.73; H, 6.50%.)

(4R*, 6S*, 7R*) - 7 - *Acetyloxy* - 4,6 - *dimethyl* - 3 - *nonanone* **36**

Treatment of 91 mg (0.58 mmol) of **20** with EtMgBr as described below for **44** afforded 101 mg (93% yield) of **32**. This material was acetylated with Ac_2O and 4-dimethylaminopyridine in pyridine, also as described below, to give 96 mg (73% overall yield) of **36** as a colorless oil: IR 1715 cm^{-1}; ^{1}H-NMR δ 0.86 (t, 6), 1.05 (t, 3), 1.1 (d, 3), 1.5–1.7 (m, 3), 1.8–1.9 (m, 1), 2.06 (s, 3), 2.35–2.6 (m, 2), 2.6–2.73 (m, 1), 4.63–4.73 (m, 1); ^{13}C-NMR δ 7.64, 9.81, 15.71, 17.87, 20.91, 23.26, 33.97, 35.43, 43.79, 78,82, 170.78, 214.59. (Exact mass: Found, 168.1519. Calc. for $C_{13}H_{24}O_3$-CH_3CO_2H: *m/z* 168.1515.)

(4R*, 6S*, 7R*) - 7 - *Acetyloxy* - 3,3 - *ethylenedioxy* - 4,6-*dimethyl* - 3 - *nonanone*, **37**

Prepared as described below for the (4*R**, 6*R**, 7*S**)-diastereomer, in 87% yield: IR 1715 cm^{-1}, ^{1}H-NMR δ 0.8–0.9 (m, 12), 1.1–1.8 (m, 8), 2.06 (s, 3), 3.95 (m, 4), 4.7 (m, 1). (Exact mass: Found, 278.1984. Calc. for $C_{15}H_{28}O_4$: *m/z* 278. 1988.)

(4R*, 6S*, 7R*) - 3,3 - *Ethylenedioxy* - 7 - *hydroxy* - 4,6 - *dimethyl* - 3 - *nonanone*, **38**

Prepared as described below for the (4*R**, 6*S**, 7*R**)-diastereomer, in 97% yield: IR 3300 cm^{-1}; ^{1}H-NMR δ 0.9–1.0 (m, 12), 1.2–1.8 (m, 9), 3.4 (m, 1), 3.9 (m, 4). (Exact mass: Found, 201.1493. Calc. for $C_{13}H_{26}O_3$-C_2H_5: *m/z* 201.1491.)

(4R*, 6S*, 7R*) - 3,3 - *Ethylenedioxy* - 7 - *methanesulfonyloxy* - 4,6 - *dimethyl* - 3 - *nonanone*, **39**

Prepared as described below for the (4*R**, 6*R**, 7*S**)-diastereomer, in 98% yield: IR 1335, 1175 cm^{-1}; ^{1}H-NMR δ 0.87 (t, 3), 0.95–1.05 (m, 9), 1.4–1.8 (m, 7), 2.13 (m, 1), 3.02 (s, 3), 3.94 (m, 4), 4.6 (m, 1). An analytical sample was prepared by chromatography 1 : 1 hexane–ether). (Found: C, 54.28; H, 8.98; 10.23. Calc. for $C_{14}H_{28}O_5S$: C, 54.52; H, 9.15; S, 10.39%.)

(4R*, 6S*, 7S*) - 7 - *Acetyloxy* - 3,3 - *ethylenedioxy* - 4,6 - *dimethyl* - 3 - *nonanone*, **40**

Prepared as described below for the (4*R**, 6*R**, 7*R**)-diastereomer, in 46% overall yield from **38**: IR 1715 cm^{-1}; ^{1}H-NMR δ 0.8–0.95 (m, 12), 2.05 (s, 3), 3.9–4.0 (m, 4), 4.7–4.8 (m, 4). An analytical sample was purified by chromatography (2/1 hexane/ether). (Found: C, 66.30; H, 10.34. Calc. for $C_{15}H_{28}O_4$: C, 66.14; H, 10.36.%.)

(4R*, 6S*, 7S*) - 7 - *Acetyloxy* - 4,6 - *dimethyl* - 3 - *nonanone*, **41**

Prepared as described below for the (4*R**, 6*R**, 7*R**)-diastereomer, in quantitative yield IR 1720, 1715 cm^{-1}; ^{1}H-NMR δ 0.875 (t, 3), 0.885 (d, 3), 1.033 (t, 3), 1.064 (d, 3), 1.3–1.8 (m, 5), 2.065 (s, 3), 2.45 (m, 2), 2.7 (m, 1), 4.75 (ddd, 1, J = 3.8, 5.4, 7.9); ^{13}C-NMR δ 7.80, 10.14, 14.59, 17.34, 24.17, 33.52, 34.31, 36.31, 43.30, 77.75. (Exact mass: Found, 228.1728. Calc. for $C_{13}H_{24}O_3$: 228.1725.)

d,l-2,4-*Dimethylglutaric anhydride*, **42**

To a soln of 100 mg (0.624 mmol) of d,l-2,4-dimethylglutaric acid[27] in 2 mL of CH_3CN at 21° was added a soln of 142 mg (0.686 mmol) of dicyclohexylcarbodiimide in 3 mL of CH_3CN, causing an immediate ppt of dicyclohexylurea. After 1 hr, the urea was removed by filtration, the filtrate was evaporated, and the residue was triturated with ether to extract the anhydride. After evaporation of the ether layer, the crude anhydride was distilled (85–87°/1.8 torr) to give 86 mg (97% yield) of a colorless oil which solidified on standing: m.p. 34–36°; IR 1805, 1760 cm^{-1}; ^{1}H-NMR δ 1.4 (d, 6), 1.9 (t, 2), 2. (m, 2). (Found: C, 59.03; H, 7.03. Calc. for $C_7H_{10}O_3$: C, 59.15; H, 7.09%.)

Methyl (2R*, 4R*) - 2,4 - *dimethyl* - 5 - *oxopentanoate*, **43**

A soln of 156 mg (1.1 mmol) of the *d,l*-**42** in 2 mL of MeOH was heated under reflux for 3 hr, allowed to stand at 21° for 18 hr, and evaporated, and the residue was distilled (110–115°/4 torr) to give 190 mg (99% yield) of the monoester as a colorless oil: IR 3400–2400, 1720 (br) cm^{-1}; ^{1}H-NMR δ 1.2 (two d, 6), 1.8 (t, 2), 2.54 (m, 2), 3.68 (s, 3). (Found: C, 55.44; H, 8.18. Calc. for $C_8H_{14}O_4$: C, 55.16; H, 8.10%.)

To a 2.517 g-sample (14.45 mmol) of the monoester, prepared in a similar way, was added 1.89 mL (21.7 mmol) of oxalyl chloride over a 10 min period at 0°. After 3 hr at 0° and 4 hr at 21°, the mixture was distilled under vacuum (62–65°/0.8 torr) to give 2.53 g (91% yield) of the ester-acid chloride. A 1.25 g sample (6.49 mmol) of this material was dissolved in 10 mL of THF and added to a flask which had previously been purged with N_2, charged with 113 mg of 10% Pd/C, 0.76 mL of 2,6-lutidine, and 20 mL of THF, and flushed with H_2. After 5 hr of agitation under H_2, the mixture was filtered through Celite and concentrated under reduced pressure. The crude product was dissolved in ether, washed with 1N HCl and with 5% $NaHCO_3$aq, worked up in the usual manner and then distilled (59–61/0.8 torr) to give 705 mg (67% yield) of **43** as a colorless oil: IR 2720, 1726 cm^{-1}; ^{1}H-NMR δ 1.16 d, 3), 1.18 (d, 3), 1.4–1.9 (m, 2), 2.38–2.5 (m, 1), 2.5–2.62 (m, 1), 3.68 (s, 3), 9.6 (d, 1). (Found: C, 60.42; H, 8.59. Calc. for $C_8H_{14}0_3$: C, 60.74; H, 8.92%.)

(2R*, 4R*, 5S*) - 6 - *Ethyl* - *tetrahydro* - 3,5 - *dimethyl* - 2*H* - *pyran* - 2 - *one*, **44**

A soln of 1.28 g (4.5 mmol) of **15** and 1.78 ml (6.75 mmol) of tri(n-butyl)tin hydride in 70 mL of THF was kept at 21 for 18 hr. After dilution with 50 mL of CH_3CN, the mixture was washed twice with cold hexane.[32] The hexane layers were back-extracted with CH_3CN, the combined CH_3CN layer was evaporated and the malodorous residue was purified by chromatography (2 : 1 hexane–ether) to give 675 mg (97% yield) of **44** as a colorless oil: IR 1725 cm^{-1}; ^{1}H-NMR δ 1.00 (d, 3), 1.03 (t, 3), 1.22 (d, 3), 1.5–1.9 (m, 5), 2.65 (m, 1), 3.87 (ddd, 1, J = 2.4, 8.4, 10.2). (Found: C, 68.96; H, 10.26. Calc. for $C_9H_{16}O_2$: c, 69.19; H, 10.32%.)

(4R*, 6R*, 7S*) - 7 - *Acetyloxy*- - 4,6 - *dimethyl* - 3 - *nonanone*

A soln of 229 mg (1.47 mmol) of **44** in 40 mL of ether at −78° was treated with 0.65 mL of a 2.7 M soln (1.76 mmol) of EtMgBr in ether, leading to the formation of a dense white ppt. After brief warming to 21°, the mixture was cooled to −78° before 2 mL of sat'd NH_4Claq was added. After warming again, the mixture was partitioned between ether (10 mL) and water (2 mL). The aqueous phase was extracted with ether, and the combined organic phase was worked up to give the crude **45**. This material was acetylated directly with 0.40 mL (4.3 mmol) of Ac_2O and a catalytic amount of 4-(dimethylamino)pyridine in 2 mL of pyridine at 21° for 18 hr. Water (0.5 mL) was added, and after 30 min the mixture was diluted with ether, the organic phase was washed with 5% $NaHCO_3$aq and worked up. The product was purified by chromatography (2 : 1 hexane–ether) to give 39 mg of recovered **44** and 210 mg (76% overall yield, based on unrecovered starting material) of the keto-acetate: IR 1715 cm^{-1}; ^{1}H-NMR δ 0.862 (d, 3), 0.877 (t, 3), 1.036 (d, 3), 1.057 (t, 3), 1.3–1.8 (m, 5), 2.053 (3, 3), 2.45–2.55 (m, 3), 4.73 (ddd, 1, J = 5.6, 6.6, 10). ^{13}C-NMR δ 7.79, 10.01, 15.25, 16.10, 21.14, 23.24, 33.70, 34.30, 34.90, 43.50, 78.87. An analytical sample was purified by preparative GC (160°). (Found: C, 68.33; H, 10.39. Calc. for $C_{13}H_{24}O_3$: C, 68.38; H, 10.59%.)

(4R*, 6R*, 7S*) - 7 - *Acetyloxy* - 3,3 - *ethylenedioxy* - 4,6-*dimethyl* - 3 - *nonanone*

To a soln of 35.4 mg (0.155 mmol) of the keto-acetate and 96 mg (0.47 mmol) of ethylene glycol bis(trimethylsilyl)ether in 4 mL of CH_2Cl_2 at −20° was added 3 drops of trimethylsilyl triflate.[33] After 7 hr, the soln was warmed to 0°, the reaction was quenched with 0.25 mL of pyridine, and the mixture was washed with 5% $NaHCO_3$aq. The aqueous layer was back-extracted with three 15 mL portions of CH_2Cl_2, and the combined organic layer was worked up to give 41 mg (91% yield) of the ketal as an oil. ^{1}H-NMR analysis indicated that it was sufficiently pure to be carried on to the next step. IR 1715 cm^{-1}; ^{1}H-NMR δ 0.84–0.94 (m, 12), 1.2–1.8 (m, 8), 2.057 (s, 3), 3.9 (m, 4), 4.7 (m, 1). (Exact mass: Found, 272.1978. Calc. for $C_{15}H_{28}O_4$: 272.1987.)

(4R*, 6R*, 7S*) - 3,3 - *Ethylenedioxy* - 7 - *hydroxy* - 4,6 - *dimethyl* - 3 - *nonanone*

A soln of 120 mg (0.44 mmol) of the ketal and 0.88 mL of 2N NaOH (1.76 mmol) in 6 mL of MeOH was heated at 60° for 18 hr. The mixture was diluted with water and extracted three times with CH_2Cl_2, and the organic layer was worked up to give 100 mg (98% yield) of hydroxy-ketal as an oil, pure by TLC and ^{1}H-NMR: IR 3590, 3460 cm^{-1}; ^{1}H-NMR δ 0.85–1.0 (m, 12), 1.2–1.9 (m, 8), 3.34 (m, 1), 3.9 (m, 4).

(Exact mass: Found, 201.1495. Calc. for $C_{13}H_{26}O_3$-C_2H_5: 201.1491.)

(4R*, 6R*, 7S*) - 3,3 - *Ethylenedioxy* - 7 - *methanesulfonyloxy* - 4,6 - *dimethyl* - 3 - *nonanone.*

To a soln of 127 mg (0.55 mmol) of the hydroxy-ketal and 0.25 mL (1.79 mmol) of Et_3N in 12 mL of CH_2Cl_2 at 0° was added 0.13 mL (1.65 mmol) of methanesulfonyl chloride. After 1 hr at 0° and 2 hr at 21°, 5 mL of water was added and the layers were separated. The aqueous phase was extracted twice with CH_2Cl_2, and the combined organic phase was worked up in the usual manner. The crude product was purified by chromatography (1 : 1 ether–hexane to give 158 mg (93% yield) of the mesylate as a colorless oil: IR 1335, 1175 cm^{-1}; ^{1}H-NMR δ 0.84–1.0 (m, 12), 1.15–1.2 (m, 8), 3.017 (s, 3), 3.9 (m, 4), 4.55 (m, 1). (Found: C, 54.39; H, 8.99; S, 10.14. Calc. for $C_{14}H_{28}O_5S$: C, 54.52; H, 9.15; S, 10.39%.)

(4R*, 6R*, 7R*) - 7 - *Acetyloxy* - 3,3 - *ethylenedioxy* - 4,6-*dimethyl* - 3 - *nonanone*

A mixture of 14.7 mg (0.048 mmol) of the ketal-mesylate and 27 mg (0.143 mmol) of cesium acetate in 1 mL of DMF was heated at 80° For 1 hr. The solvent was removed under reduced pressure and the residue was dissolved in CH_2Cl_2, washed with $NaHCO_3$aq, and worked up to give a mixture of the desired product and elimination products. This material was purified by chromatography (3 : 1 hexane–ether) to give 6.6 mg (51% yield) of the acetoxy–ketal as a colorless oil: IR 1715 cm^{-1}; ^{1}H-NMR δ 0.84–0.90 (m, 12), 1.1–1.85 (m, 8), 2.053 (s, 3), 3.95 (m, 4), 4.72 (m, 1). (Found: C, 65.88; H, 10.11. Calc. for $C_{15}H_{28}O_4$: C, 66.14; H, 10.36;%.)

(4R*, 6R*, 7R*) - 7 - *Acetyloxy* - 4,6 - *dimethyl* - 3 - *nonanone*, **30**

A soln of 27.2 mg (0.99 mmol) of the acetoxy–ketal, 0.2 mL of water, and 1 mg of *p*-toluensulfonic acid in 1 mL of acetone was heated at 45° for 14 hr. After partitioning between CH_2Cl_2 and water, back-extracting the aqueous layer, and working up the combined organic layer in the usual way, 23 mg (100% yield) of (±)serricornin acetate was obtained, pure by ^{1}H-NMR: IR 1715 cm^{-1}; ^{1}H-NMR δ 0.86 (overlapping d and t, 6), 1.048 (overlapping d and t, 6), 1.2–1.7 (m, 5), 2.059 (s, 3), 2.46 (m, 2), 2.63 (m, 1), 4.75 (m, 1); ^{13}C-NMR δ 7.84, 10.15, 14.39, 16.60, 24.10, 33.59, 34.26, 35.81, 43.45, 78.08, 215.06. (Found: C, 68.57; H, 10.26. Calc. for $C_{13}H_{24}O_3$: C, 68.38; H, 10.59%.)

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