Stereocontrolled Routes to Functionalized [1,8-*bc*]Naphthopyran. A Study on the Total Synthesis of Quassinoids and Tetrahydronaphthalene Antibiotics[1,2]

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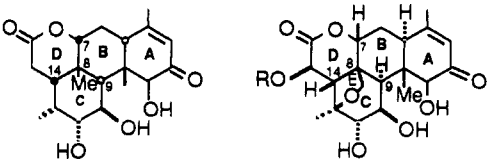
The intramolecular Diels–Alder reactions of (4*E*,6*E*)-1-(5,6-dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-4,6-octadienes have been examined with a planned synthesis of quassinoids, chlorotricholides, and mevinic acids. The intramolecular Diels–Alder reactions of 1-(5-oxo-2*H*-pyran-2-yl)-2-methyloctа-4,6-dien-3-ones preferentially afforded products possessing a trans-ring junction. For 1-(2*H*-pyran-2-yl)-2-methyl-3-[(thexyldimethylsilyl)oxy]-4,6-octadienes the cyclization was controlled by the methyl at C-2 and led to cis-fused or trans-fused derivatives. The reactions were performed under thermal Lewis acid catalyzed and sonochemical conditions with no changes in the reaction selectivity and reaction yields. However, IMDA of **10b** in the presence of silica gel produced a dramatic change in the course of the reaction.

In recent years much effort has been devoted to the preparation of perhydronaphthalene in connection with the total synthesis of biologically active naturally occurring derivatives[3] like mevinic acids, kijanolides, or chlorotricholide. The intramolecular Diels–Alder cyclization (IMDA)[4] has proven exceptionally useful to synthesize perhydronaphthalenes with a high degree of stereochemical control. As a part of our ongoing interest in synthetic and biological applications[5] of keto unsaturated C-glycosides[6-8] we envisioned the preparation of octahydronaphthalene by IMDA of 1-(5-oxo-2*H*-pyran-2-yl)-4,6-octadienes. We reasoned that the constraint induced by the C-glycosidic bond will control the cyclization in a highly selective fashion. Moreover, such a strategy could be applied to the synthesis of more complex polycyclic systems like the

Chart I



BCD moiety of quassinoids. Quassinoids[9] are a class of naturally occurring derivatives which have elicited considerable medicinal[10] and synthetic interest[11] because of their wide spectrum of biological activity. A characteristic feature common to quassinoids is the presence of a naphthopyran with a β-methyl or a β-(hydroxymethyl) group in the C-8 position with a cis relationship with H-7 and H-14 protons and a BC trans-ring junction (Chart I). We believe that the BCD ring could be built in a single step by an intramolecular Diels–Alder cycloaddition[12] of β-substituted 1-(5,6-dihydro-5-oxo-2*H*-pyran-2-yl)-4,6-octadienes. The success of such a strategy would depend on the degree to which the trienes undergo Diels–Alder cyclization in an exo fashion. Precedent for a cyclic dienophile[13] suggested that the tridecatriene would prefer to undergo cycloaddition *via* the exo transition state, thus forming the naphthopyran which would possess the required trans geometry.

Intermolecular Diels–Alder reactions involving a β-substituted dienophile are reputedly difficult. Moreover, with

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the exception of a recent report, intramolecular Diels–Alder reactions involving a six-membered ring are essentially unexplored. In that report Fallis et al.[14] succeeded in the synthesis of longifolene by an IMDA involving a *β-substituted* unsaturated δ-lactone. This encouraging result prompted us to embark on a systematic study of the cyclization[15,16] of 1-(5-oxo-2*H*-pyran-2-yl)-2-methyl-4,6-octadienes to set out the scope and limitation of this approach. During the course of our investigation we observed highly stereoselective IMDA leading to trans fused or highly strained cis fused naphthopyrans. Moreover, our results established that the stereoselectivity of the reactions was controlled by the C-2 pyran and by the C-2 and C-3 positions of the tether. Finally, we found that the reaction was independent of the conditions with the exception of the silica gel assisted IMDA of **10b** which afforded **17d** with an AB trans-ring junction.

Synthesis of 1-(5,6-Dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-4,6-octadien-3-ones (5a and 5b). Recent work in our laboratory has led to the development of a short preparation of 1-(5-oxo-2*H*-pyran-2-yl)-4,6-octadienes. This procedure combined our synthesis of 2,3-unsaturated keto C-glycosides[8] with that of dienones using modified Knoevnagel methodology.[17] As indicated in Scheme I treatment of 3,4-di-*O*-acetyl-D-xylal (**1**) with 2-[(thexyldimethylsilyl)oxy]-3-methyl-3-butene, in the presence of zinc bromide, and then direct deacetylation of the crude C-glycoside with sodium methoxide led to the alcohol **2** in 78% yield. Conversion of **2** to the silyloxy derivative **3** was performed with hexamethyldisilazane in the presence of a catalytic amount of saccharin.[18] Next, transformation of **3** to the (*E,E*)-2-methyl-4,6-octadien-3-one **4** was carried out by treating the lithium enolate of **3** with crotonaldehyde and trimethylsilyl chloride. Treatment of the crude (silyloxy)octadiene with citric acid afforded the 1-(5,6-dihydro-5-hydroxy-2*H*-pyran-2-yl)-2-methyl-4,6-octadien-3-one. At this stage, the C-2 (*S*) isomer **4b** ($J_{1,2}$ = 3.9 and 10 Hz) crystallized from diisopropyl ether allowing the isolation of **4a** and **4b** in 48% and 26.5% yields, respectively. The presence of conjugated double bonds was confirmed by the 300-MHz ^{1}H NMR spectrum with olefinic resonances between δ 6.11 and 7.19. These signals indicated the presence of conjugated olefinic protons with an *E* 4,5 double bond (**4a**, $J_{4,5}$ = 15.5 Hz; **4b**, $J_{4,5}$ = 15.4 Hz). Finally the dioxo-C-glycosides **5a** and **5b** were easily prepared in 66% yield by oxidation of **4a** and **4b** using pyridinium dichromate in the presence of 4-Å molecular sieves[19] (70%).

Preparation of 1-(5,6-Dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-3-[(thexyldimethylsilyl)oxy]-4,6-octadienes (10a and 10b). To prepare naphthopyrans with different functionalities at C-3 and C-7 (Chart II) we chose to investigate the chemistry of 3-[(thexyldimethylsilyl)oxy]-4,6-octadienes. This choice was dictated by the work of Marshall et al.[3q] which demonstrated the strong directing effect of such a bulky silyloxy group. The synthesis of the 4,6-octadienes **10a** and **10b** was straightforward (Scheme I) and involved the reduction of the acetylated derivatives of **4a** and **4b** with sodium borohydride in the presence of cerium chloride heptahydrate at −78 °C.[20] Examination of the ^{1}H and ^{13}C NMR spectra indicates that the reduction of **6a** proceeds with no selectivity affording **7a** as a 1:1 mixture of (3*R*)- and (3*S*)-2-methyl-4,6-octadien-3-ols in 100% yield. In contrast to this reaction the quantitative reduction of **6b** was highly stereoselective. Examination of the ^{1}H NMR spectrum of **7b** revealed the presence of a single product. However, the ^{13}C NMR spectrum showed the presence of a small amount of the other isomer. The synthesis was completed by the protection of the 3-hydroxy group (thexyldimethylsilyl chloride/DMAP in DMF), followed by the deacetylation (MeONa, MeOH) of the 5-*O*-acetyl ester. The corresponding alcohols **9a** and **9b** were oxidized with PDC in the presence of 4-Å molecular sieves to yield, respectively, the 1-(5,6-dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-3-[(thexyldimethylsilyl)oxy]-4,6-octadienes (**10a** and **10b**) (three steps 75% yield).

Synthesis of 1-(5,6-Dihydro-3-methyl-5-oxo-2*H*-pyran-2-yl)-2-methyl-4,6-octadien-3-one (14). We also carried out the preparation of the 5,6-dihydro-3-methyl-5-oxo-2*H*-pyranyl dienone **14**, of C-glycoside designed to investigate the feasibility of the introduction by an IMDA of the quaternary center characteristic of the BCD ring of quassinoids. We sought to develop an oxidative rearrangement strategy of a tertiary silyoxy ether for the enone formation. In this approach (Scheme II) silylation of the 4-(2,3-dihydro-3-methyl-3-hydroxy-2*H*-pyran-2-yl)-3-methyl-2-butanone (**11**)[8] is followed by the condensation with crotonaldehyde to provide the (*E,E*)-diene **13** in 60% yield. Oxidative rearrangement to **14** occurred in 60% yield when **13** was treated with PCC in the presence of 3-Å molecular sieves.

Study on the Preparation of Naphtho[1,8-*bc*]pyran-3(2*H*,3a*H*)-ones by Diels–Alder Intramolecular Cyclization of 1-(5,6-Dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-4,6-octadien-3-ones. Our initial results have focused on the Diels–Alder cyclization under thermal conditions. The naphtho[1,8-*bc*]pyran-3,7(2*H*,3a*H*)-diones **15a** and **15b** were prepared by heating a toluene solution of **5a** or **5b** in the presence of hydroquinone at 180 °C (Scheme I). In each case the reaction yielded a single product which was isolated by crystallization. The structure of **15a** was established by ^{1}H NMR, ^{13}C NMR, and ^{1}H COSY spectra. All data agree with the hexahydronaphtho[1,8-*bc*]pyran-3(2*H*,3a*H*)-one structure. The formation of the cyclohexene ring C (Chart II) was evidenced by the resonances at δ 2.41 and 2.62 assigned to H-9b and H-3a and by the two olefinic resonances at δ 5.7 and 5.92 assigned to H-5 and H-6. The AB and AC cis-ring junctions were dictated by the $J_{3a,9b}$ = 4.8 Hz and the $J_{9a,9b}$ = 1.7 Hz coupling constants. In addition, these values clearly show the cis relationship between the H-9a, H-9b, and H-3a protons. The BC trans-ring fusion was supported by the $J_{6a,9b}$ = 12.3 Hz coupling constant. Examination of the H-8 resonance at δ 2.87 revealed the chair conformation of the cycle B and the equatorial orientation of the C-8 (*R*) methyl. Finally, the syn relationship between the H-4 and H-6a protons was deduced from the 2D NOESY spectra which indicated a cross peak between H-4, H-3a, and H-9b. The 300-MHz

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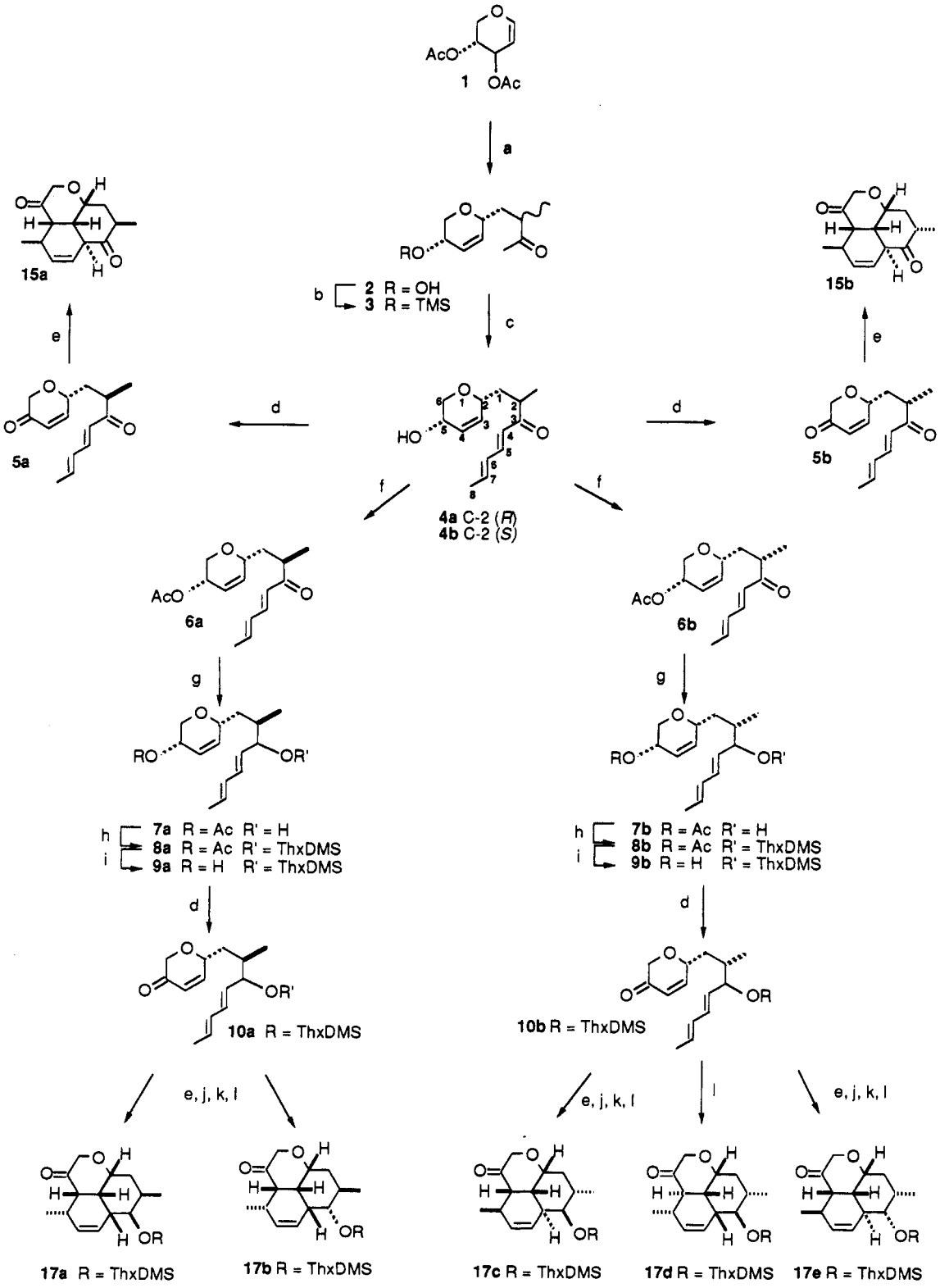
Scheme I[a]



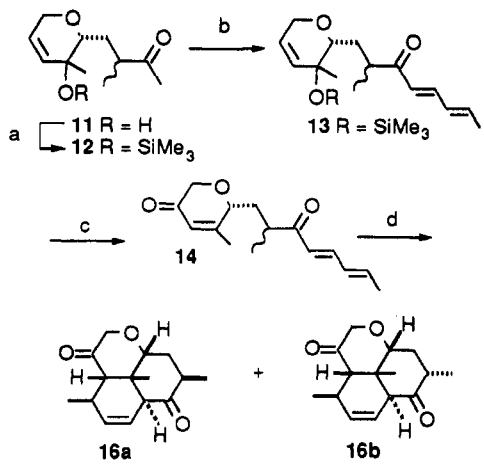
[a] Key: (a) 2-[(thexyldimethylsilyl)oxy]-3-methyl-3-butene $ZnBr_2$ 0 °C 2 h → rt 1 h, MeONa, MeOH rt; (b) hexamethyldisilazane saccharin $C_2H_4Cl_2$, rt; (c) LDA, −78 °C 15 min, crotonaldehyde, TMSCl −78 °C, 5 min → DBU reflux, citric acid, EtOH, rt, 70%; (d) PDC 4-Å, MS CH_2Cl_2; (e) toluene, 180 °C overnight; (f) Ac_2O, pyridine, DMAP, CH_2Cl_2; (g) $NaBH_4$, $CeCl_3$, MeOH, −78 °C, 10 min; (h) ThxDMSCl, imidazole, DMF, overnight, rt; (i) MeONa, MeOH, rt; (j) Lewis acids; (k) ultrasound, neat, 100 °C; (l) SiO_2 toluene, 100 °C.

^{1}H NMR spectrum of **15b** indicates a similar structure. As expected, the $J_{8,9}$ = 5.3 and 6.5 Hz coupling constants were consistent with the axial orientation of the C-8 (*S*) methyl.

The IMDA were also performed under catalytic conditions; however, either Lewis acid catalysis or solid support assistance (Al_2O_3, SiO_2) led only to the degradation of the 1-(5,6-dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-4,6-octadien-3-ones **5a** and **5b**.

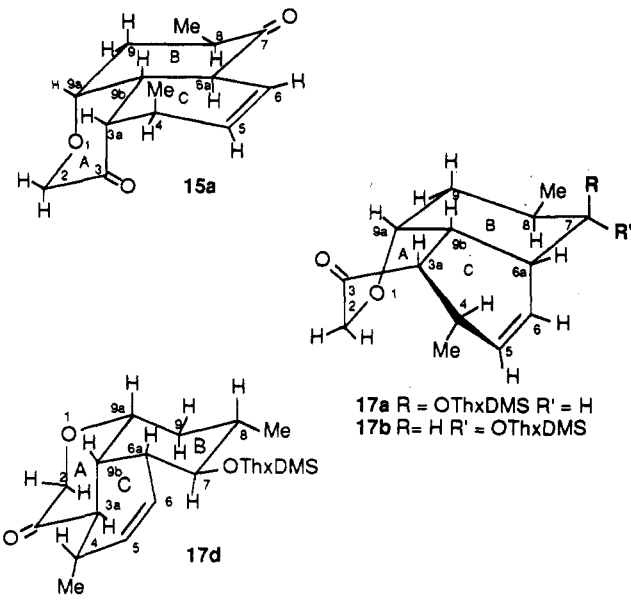
Synthesis of the Hexahydro-4,8,9b-trimethylnaphtho[1,8-*bc*]pyran-3,7(2*H*,3a*H*)-diones (16a and 16b). Attention was next turned to the cyclization of the

Scheme II[a]



[a] Key: (a) hexamethyldisilazane, saccharin, $C_2H_4Cl_2$, rt; (b) LDA, −78 °C, 15 min, crotonaldehyde, TMSCl, −78 °C, 5 min → DBU reflux 1.5 h, PCC 3A MS, CH_2Cl_2, 70%, 24 h; (d) toluene, 180 °C, overnight.

Chart II



β-substituted 5-oxo-2*H*-pyran **14** (Scheme II). Heating a sample of **14** in toluene solution at 180 °C afforded a mixture of naphthopyran diones **16a** and **16b** which were isolated by flash chromatography. The detailed ^1H NMR study of **16a** and **16b** was undertaken. This study shows a structure closely similar to **15a** and **15b**. The relative stereochemistry was determined by analysis of the proton–proton coupling constants and NOE experiments. A NOE between the C-9b methyl group and H-3a, H-9a established the cis AB and BC ring-junctions. On the other hand, irradiation of the methyl at C-9b and the H-6a proton shows no NOE. These results were consistent with a BC trans-ring junction. This assignment was ascertained by the detection of a NOE between H-6a and the axial methyl at C-8 for **16b**.

Preparation of the Octahydro-4,8-dimethyl-7-[(thexyldimethylsilyl)oxy]naphtho[1,8-*bc*]pyran-3(2*H*,3a*H*)-ones (17a–c,e). Heating **10a** and **10b** at 180 °C in the presence of hydroquinone in a sealed tube afforded after purification the two naphthopyrans **17a** and **17b** in 59.5% overall yield in a 1:2 ratio (Scheme I). Examination of the 300-MHz NMR spectra of **17a** and **17b** revealed an endo cyclization. The key in this analysis lay in the observation of the $J_{6a,9b}$ (**17a**, J = 6.7 Hz; **17b**, J = 6.5 Hz) and $J_{9a,9b}$ coupling constants (**17a**, J = 2.9 Hz; **17b**, J = 3.1 Hz). These data indicated a cis relationship between H-9a, H-9b and H-6a consistent with AB and BC cis-ring junctions. Despite a large $J_{3a,9b} \approx 10.2$ Hz coupling constant, the AC ring junction was also cis as evidenced by the existence of a cross peak on the NOESY spectra. This connection through space was confirmed by NOE difference spectroscopy. The equatorial orientation of H-6a was ascertained by the small value of $J_{6a,7}$ (**17a**, J = 2.9 Hz; **17b**, J = 4.8 Hz). Moreover, this constant and $J_{7,8}$ (**17a**, J = 2 Hz; **17b**, J = 10.5 Hz) established the 7(*R*) configuration for **17a** and the 7(*S*) configuration for **17b**. Analysis of the H-8, H-9, and H-9a resonances supported a chair conformation for the B cycle (Chart II). Examination of the Dreiding molecular model revealed that only one structure with the pyran ring in a flattened chair conformation and the cyclohexene ring in a boat conformation was consistent with the NMR data. Molecular model analysis indicated the possibility of another structure compatible with a chair conformation for the B cycle, a trans diaxial relationship between H-3a and H-9b, and an AC trans-ring junction. However, this structure does not fit with most of the coupling constants and could not explain the strong NOE between H-3a and H-9b.

In contrast to these results the IMDA of **10b** led to the naphthopyrans **17c** (56%) and **17e** (15%) by an exo cycloaddition. The rationale of this analysis lay in the examination of the H-6a resonances which revealed a large $J_{9b,6a}$ = 11.4 Hz coupling constants. In addition, the stereochemistry of the carbon at C-7 could be assigned as (*R*) for **17c** ($J_{6a,7}$ = 1.2 Hz) and (*S*) for **17e** ($J_{6a,7}$ = 10 Hz).

We also studied the preparation of the 7-[(thexyldimethylsilyl)oxy]naphthopyran under several catalytic conditions. First, we investigated Lewis acid catalysis. It was found that the best results were recorded when the reaction was carried out using a 0.44 M solution of (menthyloxy)aluminum dichloride[21] in CH_2Cl_2 at room temperature. Under this condition the same naphthopyrans were recovered in yields and ratios identical to the thermal reaction. Treatment of the tridecatrienes in CH_2Cl_2 at 0 °C with ethylaluminum dichloride (1 M solution in hexane, 0.2–0.9 equiv) was found also to be effective but led in some cases to lower yield. Attention was next turned to ultrasound-assisted cyclization.[22] The reaction was performed using the oily C-glycosides neat at 100 °C. In this case also the reaction afforded after 24 h the cycloaddition products, but no change in the yields and in the product ratio could be observed. Finally reactions were run with silica gel[23] assistance. Treatment of the neat C-glycosides at room temperature gave no cyclization. However, silica gel assisted IMDA were completed within 2 h when the reactions were carried out in hexane or toluene at 100 °C. Once more no change in the selectivity could found with the exception of the C-glycosides **10b**. When **10b** was subjected to silica gel catalysis three products were isolated, **17c**, **17e** and a majority of a new derivative **17d**. Examination of the 300-MHz ^1H NMR spectrum

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indicates that the junction for the A and C rings is trans whereas the B and C rings possess a cis junction (Chart II). The rational of this assignation lay in the $J_{6a,9b} = 5$ Hz coupling constants and in the very large value observed for $J_{3a,9b} = 13.5$ Hz which was consistent with a trans relationship between H-3a and H-9b. These data and the examination of the H-7 and H-9 signals at δ 1.92 and 3.18 supported a chair conformation for the A and B ring and a half-chair conformation for C. This assignment was secured by the correlations between H-7, H-9 axial, H-3a and H-2 axial observed on the NOESY spectrum.

Finally, we have prepared naphthopyrans **27a**, **27b**, and **28a–e** enantiomeric of compounds **15a**, **15b**, and **17a–e** to study the synthesis of mevinolin and dehydromevinolin. As for the (*R*)-(5,6-dihydro-5-oxo-2*H*-pyran-2-yl) derivatives these naphthopyrans were readily prepared from dienone enantiomers of **4a** and **4b** synthesized in three steps from 3,4-di-*O*-acetyl-L-xylal (see supplementary material).

Discussion and Conclusions

Examination of the results indicates clearly that the selectivity of the intramolecular Diels–Alder cyclization of the 1-(5,6-dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-4,6-octadienes was controlled by stereochemistry at the C-2 and C-3 position of the tether and by the C-2 pyran carbon. In addition the presence of the bulky silyloxy group at C-3 seemed to have no influence. As expected, the cycloaddition shows a total facial selectivity leading to naphthopyrans with cis-fused AB and AC rings.

In recent years, molecular mechanics has developed into an important tool for the prediction and the interpretation of the Diels–Alder reaction. Among several studies we were interested in the analysis of our experimental results by the product-oriented approach used by Marshall[3q] et al. According to Houk's calculation[24] that demonstrated high sp^3 character for the terminal centers of the diene, Marshall has shown that the stereochemistry of the cyclization could be predicted from transition states resembling reaction products. As a starting point we constructed exo and endo structures using Chem3D[25] (Figure 1).

According to the ^{1}H NMR data, the A ring was input as a chair and the C ring as a half-chair for the exo transition state. The endo transition state was built with an A ring half-chair and a C ring boat. In both cases the B ring tether was place in either a chair or a twist-boat conformation. These structures were subjected to energy minimization analysis using the MM2 force field. The calculated energies are summarized in Table I. Our first calculations were performed on the endo and the exo transition states with the tether in a chair conformation (Table I, columns A and C). In each case the exo transition state was lower in energy than the endo transition state. These results are in good accord with most of the experimental data but do not agree with the endo cycloadditions recorded for **17a–c**. Calculations done on the transition states with a twist-boat tether (Table I, columns B and D) led to the same difference of energy. On the other hand, examination of columns B and C for

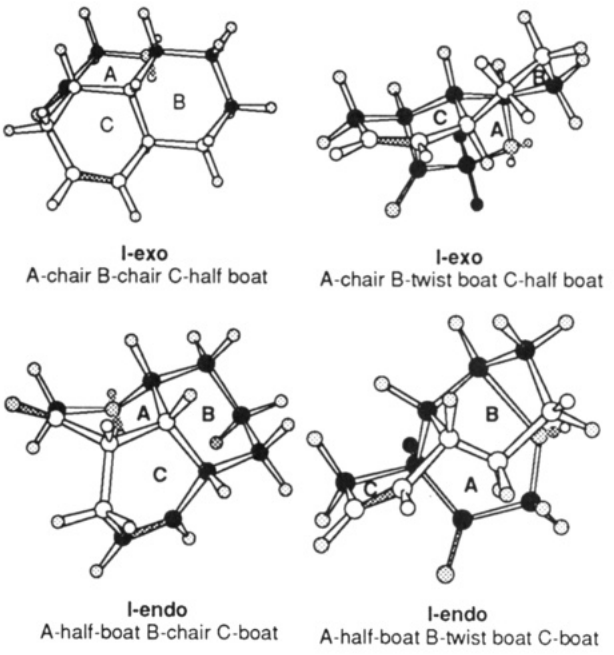

Figure 1. Prototype structures for Diels–Alder transition states.

Table I. Calculated Energies for Cyclization Products[a]

		A	B	C	D
entry	products	exo chair	exo twist boat	endo chair	endo twist boat
1	**I**	20.83	26.53	28.99	31.65
2	**15a**	26.39	29.40	32.27	36.80
3	**15b**	29.13	30.10	35.33	37.73
4	**16a**	32.04	34.37	34.94	40.43
5	**16b**	34.78	38.24	37.80	41.52
6	**17a**	32.02	44.53	39.76	47.25
7	**17b**	34.64	41.24	40.63	47.02
8	**17c**	33.40	44.54	44.23	50.22
9	**17e**	35.27	41.79	46.22	51.76

[a] Energy in kcal/mol.

the (thexyldimethylsilyl)oxy derivatives (entries 6–9) shows energies in excellent agreement with experimental findings. These data were strongly consistent with the idea of a cycloaddition by an endo process with the bridging ring in a chairlike conformation for the C-8 (*R*) naphthopyrans **17a** and **17b** and an exo twist-boat transition state for **17e**. As could be expected from experimental results the exo twist boat and the endo chair transition states for **17b** differed from less than 0.3 kcal/mol (entry 8). These values agree with the formation of an endo product in the presence of silica gel and the isolation of an exo derivative in the other experimental conditions. Thus, the effect of the silicagel could be depicted as favoring the endo chair transition state and catalyzing the formation of **17d** by an enolization at C-3a.

In conclusion, we have demonstrated that the cycloaddition of 1-(5,6-dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-4,6-octadienes led to naphtho[1,8-*bc*]pyran-3(2*H*,3a*H*)-ones with a complete facial selectivity. The dioxo octadienes led only to naphthopyrans with a BC trans-ring junction whereas 3-(silyloxy)octadienes afforded cis or trans derivatives. This methodology provides a short route to naphthopyrans with a stereochemistry related to mevinolin and dehydromevinolin. Adducts **15b** and **17e** are potential building blocks for the preparation of tetronolide or kijanolide. Finally, we have shown that the IMDA can be performed with 5,6-dihydro-3-methyl-5-oxo-

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

(25) Cambridge Scientific Computing, Inc., Cambridge, MA.

2H-pyran-2-yl derivatives affording in one step naphthopyrans with a stereochemistry close to the BCD ring of quassinoids.

Experimental Section

General Techniques. NMR spectra were recorded at 300.13 MHz for proton and 75.47 MHz for carbon with tetramethylsilane as internal standard. THF and toluene were distilled from sodium benzophenone ketyl. Dichloromethane and acetonitrile were distilled from P_2O_5 and stored over 4-Å molecular sieves. All reactions were monitored by thin-layer chromatography carried out on 0.25-mm E. Merck silica gel plate by using UV light or an ethanolic anisaldehyde acid–heat as developing agent. E. Merck silica gel 60 (particle 0.04–0.063 mm) was used for flash column chromatography.[26] Microanalyses were performed by the Laboratoire central de Microanalyse du CNRS, Vernaison, France. All reactions were run under nitrogen in flame-dried glassware with magnetic stirring.

[R-(R*,R*S*),5α]-4-(5,6-Dihydro-5-hydroxy-2H-pyran-2-yl)-3-methyl-2-butanone (2). To a suspension of dry zinc bromide (11.47 g, 51.00 mmol) in CH_2Cl_2 (63.75 mL) at 0 °C under nitrogen was added dropwise, for 2 h, a dichloromethane solution (63.75 mL) of diacetyl xylal (5.104 g, 25.50 mmol) and 2-[(thexyldimethylsilyl)oxy]-3-methyl-3-butene (8.074 g, 30.60 mmol). The resulting brown suspension was stirred at 0 °C for 1 h and then filtered through a sintered funnel. The filtrate was diluted with CH_2Cl_2 (350 mL) and then shaken with a mixture of a saturated solution of $NaHPO_4$ (63.75 mL) and a saturated solution of $NaHSO_4$ (25.5 mL) until discoloration. The organic phase was washed successively with a saturated solution of $NaHCO_3$ (50 mL) and brine (50 mL) and then dried ($MgSO_4$). After removal of the solvent the crude product was dissolved in methanol (50 mL) and then treated with sodium methoxide (12.75 mL, 2 N in methanol, 25.5 mmol). After 1 h solid NH_4Cl (1.53 g) was added, and the reaction mixture was stirred for 15 min, diluted with diethyl ether (51 mL), filtrated, and finally concentrated under vacuum. Purification of the resulting oil by flash chromatography (30% acetone in hexane/dichloromethane (1:1)) afforded the 4-(5,6-dihydro-5-hydroxy-2H-pyran-2-yl)-3-methyl-2-butanone (2): oil (3.66 g, 77.8%); $[\alpha]^{20}_D$ +126° (c 0.78 $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.85 (d, 0.99 H, J = 7.1 Hz, Me C-3(S)), 0.88 (d, 1.98 H, J = 6.8 Hz, Me C-3 (R)), 1.15 (ddd, 0.66 H, J = 3.4, 6.8, and 14.2 Hz, H-4(R)), 1.29 (ddd, 0.33 H, J = 4, 9.2, and 14.2 Hz, H-4(S)), 1.82 (m, 0.33 H, H-4(S)), 1.82 (s, 1.98 H, H-1(R)), 1.83 (s, 0.99 H, H-1(S)), 1.89 (ddd, 0.66 H, J = 6.6, 10 and 14.2 Hz, H-4(R)), 2.55 (ddq, 0.66 H, J = 6.6, 6.8, and 6.8 Hz, H-3(R)), 2.64 (ddq, 0.33 H, J = 4, 7.1, and 9.6 Hz, H-3(S)), 3.31 (dd, 0.33 H, J = 7.1 and 10.9 Hz, H-6(S)), 3.34 (dd, 0.66 H, J = 7.5 and 10.8 Hz, H-6(R)), 3.85 (dddd, 0.66 H, J = 1.8, 2.3, 3.4, and 10 Hz, H-2(R)), 3.94 (ddd, 0.66 H, J = 1.1, 5.2, and 10.8 Hz, H-6(R)), 3.97 (ddd, 0.33 H, J = 1.1, 5.1, and 10.9 Hz, H-6(S)), 3.97 (m, 0.33 H, H-2(S)), 4.10 (dddd, 0.66 H, J = 1.5, 2.3, 5.2, and 7.5 Hz, H-5(R)), 4.15 (dddd, 0.33 H, J = 1.5, 2.2, 5.1, and 7.1 Hz, H-5(S)), 5.40 (ddd, 0.66 H, J = 1.5, 1.8, and 10.3 Hz, H-4 pyran (R)), 5.43 (ddd, 0.33 H, J = 1.5, 1.8, and 10.3 Hz, H-4 pyran (S)), 5.81 (dddd, 0.33 H, J = 1.1, 2.2, 2.2, and 10.3 Hz, H-3 pyran (S)), 5.82 (dddd, 0.66 H, J = 1.1, 2.3, 2.3, and 10.3 Hz, H-3 pyran (R)); ^{13}C NMR ($CDCl_3$) δ 16.48 and 17.51 (q, C-3'), 28.51 and 28.76 (q, C-1), 36.52 and 36.98 (t, C-4), 42.7 and 43.39 (d, C-3), 62.42 (d, C-5), 67.76 and 68.21 (t, C-6), 71.61 (d, C-2 pyran), 128.32 and 128.57 (d, C-4 pyran), 131.69 (d, C-3 pyran), 212.55 (s, C-2). Anal. Calcd for $C_{10}H_{16}O_3$, $0.25H_2O$: C, 63.64; H, 8.81. Found: C, 63.12; H, 8.75.

[R-(R*,R*S*),5α]-4-(5,6-Dihydro-5-[(trimethylsilyl)oxy]-2H-pyran-2-yl)-3-methyl-2-butanone (3). To a solution of 4-(5,6-dihydro-5-hydroxy-2H-pyran-2-yl)-3-methyl-2-butanone (2) (3.56 g, 19.32 mmol) in dichloroethane (38.64 mL) was added hexamethyldisilazane (4.48 mL, 16.93 mmol) and saccharin (0.070 g, 0.28 mmol). After 1 h ethanol was added (1.93 mL) and then the solution was filtered, evaporated under reduced pressure, and finally distilled with dichloroethane (10 mL). The resulting oil was used without further purification.

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

[R-(R*,R*),5α-(E,E)]-1-(5,6-Dihydro-5-hydroxy-2H-pyran-2-yl)-2-methyl-4,6-octadien-3-one (4a) and [R-(R*,S*),3α-(E,E)]-1-(5,6-Dihydro-5-hydroxy-2H-pyran-2-yl)-2-methyl-4,6-octadien-3-one (4b). To a solution of diisopropylamine (3.25 mL, 23.21 mmol) in THF (24.175 mL) was added at 0 °C butyllithium (14.2 mL 1.6 M in hexane, 22.82 mmol). After 15 min the solution was cooled to −78 °C, and then slowly a solution of 4-[5,6-dihydro-5-[(trimethylsilyl)oxy]-2H-pyran-2-yl]-3-methyl-2-butanone (3) (4.96 g, 19.34 mmol) in THF (1 mL) was added. After 15 min a mixture of crotonaldehyde (1.76 mL, 21.27 mmol) and trimethylchlorosilane (2.68 mL, 21.27 mmol) was added slowly. Then the reaction mixture was removed from the cooling bath, and DBU (0.58 g, 4.64 mmol) was added. The solution was heated at reflux for 3 h, and then the solvent was removed slowly under vacuum to avoid foaming. The residue was partitioned between dichloromethane (50 mL) and Na_2HPO_4 (50 mL). The aqueous layer was extracted with dichloromethane (2 × 25 mL). The combined organic solutions were dried ($MgSO_4$) and then evaporated to yield a yellow oil. This oil was dissolved in a mixture of ethanol (30 mL) and water (5 mL), and citric acid ((0.386 g, 0.24 mmol) was added. The solution was stirred for 2 h and then ethanol (5 mL) was added and the solvent removed. After purification by flash chromatography (30% acetone in hexane/dichloromethane (1:1)) **4b** was isolated by crystallization (diisopropyl ether). When all the crystalline material has been recovered, evaporation of the mother liquor gave pure **4a** as yellow oil.

4a: 2.19 g (48%); oil; $[\alpha]^{20}_D$ +107° (c = 0.63 $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.13 (d, 1 H, J = 6.9 Hz, H-2'), 1.44 (ddd, 1 H, J = 3.6, 7.5, and 14.3 Hz, H-1), 1.87 (dd, 3 H, J = 0.8 and 5.1 Hz, H-8), 2.01 (ddd, 1 H, J = 6, 9.8, and 14.3 Hz, H-1), 3.01 (ddq, 1 H, J = 6, 6.9, and 7.4 Hz, H-2), 3.41 (dd, 1 H, J = 5.8 and 11.4 Hz, H-6), 4 (ddd, 1 H, J = 0.8, 4.2, and 11.4 Hz, H-6 pyran), 4.10 (dddd, 1 H, J = 1.1, 2.2, 3.6, and 9.8 Hz, H-2 pyran), 4.14 (dddd, 1 H, J = 2.2, 2.9, 4.2, and 5.8 Hz, H-5 pyran), 5.73 (ddd, 1 H, J = 1.1, 2.2, and 10.4 Hz, H-4 pyran), 5.88 (dddd, 1 H, J = 0.8, 2.2, 2.9, and 10.4 Hz, H-3), 6.11 (dd, 1 H, J = 0.8 and 15.5 Hz, H-4), 6.19–6.22 (m, 2 H, H-6 and H-7), 7.19 (m, 1 H, H-5); ^{13}C NMR ($CDCl_3$) δ 16.61 (q, C-2'), 18.72 (q, C-8), 36.77 (t, C-1), 39.94 (d, C-2), 62.50 (d, C-5 pyran), 67.94 (t, C-6 pyran), 71.39 (d, C-5 pyran), 126.45 (d, C-4 pyran), 128.46 (d, C-4 pyran), 130.33 (d, C-6), 131.64 (d, C-3 pyran), 140.37 (d, C-7), 143.13 (d, C-5), 204.01 (s, C-3). Anal. Calcd for $C_{14}H_{20}O_3$, $0.5H_2O$: C, 68.57; H, 8.57. Found: C, 68.85; H, 8.53.

4b: 1.21 g (26.5%); mp 106–108 °C; $[\alpha]^{20}_D$ +1° (c 0.4, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.12 (d, 3 H, J = 7 Hz, H-2'), 1.49 (ddd, 1 H, J = 3.9, 10, and 14.1 Hz, H-1), 1.88 (ddd, 3 H, J = 0.7, 0.7, and 4.9 Hz, H-8), 1.97 (ddd, 1 H, J = 3.3, 10, and 14.1 Hz, H-1), 3.11 (ddq, 1 H, J = 3.9, 7, and 10 Hz, H-2), 3.37 (dd, 1 H, J = 6.68 and 11.2 Hz, H-6 pyran), 3.96 (ddddd, 1 H, J = 1, 1.3, 2.1, 3.3, and 10 Hz, H-2 pyran), 4.00 (ddd, 1 H, J = 0.9, 4.7, and 11.2 Hz, H-6 pyran), 4.44 (ddddd, 1 H, J = 1, 2.1, 3, 4.7, and 6.7 Hz, H-5 pyran), 5.75 (ddd, 1 H, J = 1.3, 2.1, and 10.3 Hz, H-4 pyran), 5.86 (dddd, 1 H, J = 0.9, 2.1, 3, and 10.3 Hz, H-3), 6.14 (dd, 1 H, J = 0.7 and 15.4 Hz, H-4), 6.18–6.24 (m, 2 H, H-6 and H-7), 7.21 (dddd, 1 H, J = 0.7, 6, 10.3, and 15.4 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ 18.33 (q, C-2'), 18.75 (q, C-8), 37.43 (t, C-1), 39.50 (d, C-2), 62.73 (d, C-5 pyran), 68.17 (t, C-6 pyran), 71.77 (d, C-2 pyran), 127.04 (d, C-4 pyran), 128.14 (d, C-4), 130.36 (d, C-6), 132.40 (d, C-3 pyran), 140.18 (d, C-7), 143.33 (d, C-5), 204.18 (s, C-3). Anal. Calcd for $C_{14}H_{20}O_3$, $0.25H_2O$: C, 69.83; H, 8.58. Found: C, 69.86; H, 8.40.

Oxidation of 2-Methyl-1-(5,6-dihydro-5-hydroxy-2H-pyran-2-yl)-4,6-octadien-3-ones. To a solution of 2-methyl-1-(5,6-dihydro-5-hydroxy-2H-pyran-2-yl)-octa-4,6-dien-3-one (0.7 g, 2.96 mmol) in dichloromethane (14.8 mL) was added 4-Å molecular sieves (2.96 g) and PDC (1.16 g, 3.11 mmol). After 1.5 h the solution was filtered over a Celite pad. Then the black solid was washed with dichloromethane (15 mL). The solvent was removed under vacuum, and then the resulting black residue was purified by chromatography (flash 15% ethyl acetate in hexane/dichloromethane (1:1)) to yield 0.46 g (70%) of the dioxo derivatives.

[R-(R*,R*)-(E,E)]-1-(5,6-Dihydro-5-oxo-2H-pyran-2-yl)-2-methyl-4,6-octadien-3-one (5a): $[\alpha]^{20}_D$ +89.50° (c = 0.1 MeOH); ^1H NMR ($CDCl_3$) δ 1.12 (d, 3 H, J = 7 Hz, H-2'), 1.60 (ddd, 1 H, J = 4, 7.31, and 14.2 Hz, H-1), 1.80 (br d, 3 H, J = 4.8 Hz, H-8),

2.07 (ddd, 1 H, J = 6.2, 9.4, and 14.2 Hz, H-1), 3.00 (ddq, 1 H, J = 6.2, 7.02, and 7.3 Hz, H-2), 3.97 (dd, 1 H, J = 1.7 and 16.3 Hz, H-6 pyran), 4.16 (d, 1 H, J = 16.3 Hz, H-6 pyran), 4.25 (m, 1 H, H-2 pyran), 6.02 (dd, 1 H, J = 2.01 and 10.4 Hz, H-4 pyran), 6.07 (d, 1 H, J = 15.4 Hz, H-4), 6.14 (m, 2 H, H-6 and H-7), 6.83 (dd, 1 H, J = 2 and 10.4 Hz, H-3 pyran), 7.11 (dd, 1 H, J = 9.7 and 15.4 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ 16.74 (q, C-2′), 18.71 (q, C-8), 36.46 (t, C-1), 39.68 (d, C-2), 70.85 (d, C-2 pyran), 71.52 (t, C-6 pyran), 126.18 (d, C-4), 126.75 (d, C-4 pyran), 130.23 (d, C-7), 140.74 (d, C-6), 143.42 (d, C-5), 151.40 (d, C-3 pyran), 204.54 (s, C-3). Anal. Calcd for $C_{14}H_{20}O_3$, $0.75H_2O$: C, 67.88; H, 7.88. Found: C, 68.23; H, 7.52.

[*R*-(*R,*S**)-(*E*,*E*)]-1-(5,6-Dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-4,6-octadien-3-one (5b)**: $[\alpha]^{20}_D$ +91° (c = 0.1 MeOH); ^{1}H NMR ($CDCl_3$) δ 1.16 (d, 3 H, J = 7.2 Hz, H-2′), 1.63 (ddd, 1 H, J = 3.5, 10.3, and 14 Hz, H-1), 1.89 (dd, 3 H, J = 0.8 and 4.6 Hz, H-8), 2.17 (ddd, 1 H, J = 3.2, 10.3, and 14 Hz, H-1), 3.18 (ddq 1 H, J = 3.5, 7.2, and 10.3 Hz, H-2), 4.00 (dd, 1 H, J = 1.8 and 16.3 Hz, H-6 pyran), 4.21 (dd, 1 H, J = 0.8 and 16.3 Hz, H-6 pyran), 4.21 (ddddd, 1 H, J = 1.9, 1.9, 2.5, 3.2, and 10.3 Hz, H-2 pyran), 6.10 (ddd, 1 H, J = 0.7, 2.5, and 10.4 Hz, H-4 pyran), 6.13 (dq, 1 H, J = 0.7 and 15.6 Hz, H-4), 6.21–6.25 (m, 2 H, H-6 and H-7), 6.94 (dd, 1 H, J = 1.9 and 10.5 Hz, H-3 pyran), 7.22 (dd, 1 H, J = 10.2 and 15.6 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ 18.51 (q, C-2′), 18.87 (q, C-8), 37.35 (t, C-1), 39.44 (d, C-2), 71.12 (d, C-2 pyran), 71.66 (t, C-6 pyran), 126.67 (d, C-4), 126.94 (d, C-4 pyran), 130.38 (d, C-7), 141.06 (d, C-6), 143.69 (d, C-5), 152.01 (d, C-3 pyran), 203.53 (s, C-3). Anal. Calcd for $C_{14}H_{20}O_3$, 0.75 H_2O: C, 67.88; H, 7.88. Found: C, 68.22; H, 7.47.

Acetylation of the 1-(5,6-Dihydro-5-hydroxy-2*H*-pyran-2-yl)-2-methyl-4,6-octadien-3-ones (4a and 4b). To a solution of 1-(5,6-dihydro-5-hydroxy-2*H*-pyran-2-yl)-2-methyl-4,6-octadien-3-one (1.28 g, 5.42 mmol) in dichloromethane (13.55 mL) was added pyridine (0.876 mL, 10.84 mmol), acetic anhydride (0.767 mL, 8.13 mmol), and a catalytic amount of DMAP. After 2 h the solvent was removed under vacuum, and then the residue was distilled twice with toluene. The resulting oil was used without further purification.

Reduction of the 1-[5-(Acetyloxy)-5,6-dihydro-2*H*-pyran-2-yl]-2-methyl-4,6-octadien-3-ones (6a and 6b). [2*R*-[2α-(*R,*R***S**),5α]-(*E*,*E*)]-1-[5-(Acetyloxy)-5,6-dihydro-2*H*-pyran-2-yl]-2-methyl-4,6-octadien-3-ol (7a).** 1-[5-(Acetyloxy)-5,6-dihydro-2*H*-pyran-2-yl]-2-methyl-4,6-octadien-3-one (**6a**) (3.3 g, 12 mmol) and $CeCl_3$, $7H_2O$ (4.47 g, 12 mmol) were dissolved in methanol (120 mL). The solution was cooled at −78 °C, and then $NaBH_4$ (0.498 g, 13.19 mmol) was added portionwise over a period of 10 min. The solvent was removed under vacuum, and then the solution was partitioned between diethyl ether (599.5 mL) and water, transferred to a separatory funnel, extracted with a saturated $NaHCO_3$ solution (3 × 120 mL) and brine (120 mL), and dried ($MgSO_4$). The solvent was removed under vacuum, and then the residual oil was purified by chromatography (flash 40% ethyl acetate in hexane/dichloromethane (1:1)) to yield 3.26 g (98%) 1-[5-(acetyloxy)-5,6-dihydro-2*H*-pyran-2-yl]-2-methyl-4,6-octadien-3-ol (**7a**) as a 1.1 mixture of (3*R*) and (3*S*) isomers: $[\alpha]^{20}_D$ +219° (c 0.573 $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.94 (d, 3 H, J = 6.8 Hz, H-2′), 1.2–1.3 (m, 1 H, H-1), 1.74 (ddd, 1 H, J = 5.2, 10.5, and 15.5 Hz, H-1), 1.76 (dd, 3 H, J = 1.6 and 6.7 Hz, H-8), 1.8 (m, 1 H, H-2), 2.08 (s, 3H, CH_3CO), 3.55 (dd, 0.5 H, J = 5.7 and 11.3 Hz, H-6 pyran), 3.56 (dd, 0.5 H, J = 5.7 and 11.3 Hz, H-6 pyran), 3.94 (dd, 0.5 H, J = 3.00 and 6.5 Hz, H-3), 4.04 (dd, 0.5 H, J = 2.9 and 7.1 Hz, H-3), 4.06 (dd, 1 H, J = 4.2 and 11.3 Hz, H-6 pyran), 4.24 (m, 1 H, H-2 pyran), 5.18 (m, 1 H, H-5 pyran), 5.54 (dd, 0.5 H, J = 2.9 and 7.1 Hz, H-4), 5.55 (dd, 0.5 H, J = 3 and 6.5 Hz, H-4), 5.67 (dd, 0.5 H, J = 6.7 and 14.7 Hz, H-7), 5.69 (dq, 0.5 H, J = 6.7 and 14.7 Hz, H-7), 5.82 (ddd, 1 H, J = 2.4, 3, and 10.5 Hz, H-4 pyran)), 5.88 (ddd, 1 H, J = 0.9, 1.9 and 10.5 Hz, H-3 pyran), 6.02 (ddq, 0.5 H, J = 1.6, 10.3, and 14.7 Hz, H-6), 6.03 (ddq, 0.5 H, J = 1.6, 10.3, and 14.7 Hz, H-6), 6.18 (ddd, 0.5 H, J = 2.9, 10.3, and 14.8 Hz, H-5), 6.20 (ddd, 0.5 H, J = 3, 10.3, and 14.8 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ 15.28 and 15.29 (q, C-2′), 18.09 (q, C-8), 21.08 (q, CH_3CO), 35.62 (d, C-2), 36.17 (t, C-1), 64.42 (t, C-6 pyran), 64.97 (d, C-3), 71.38 and 71.84 (d, C-5 pyran), 76.23 and 76.65 (d, C-2 pyran), 123.52 (d, C-4 pyran), 129.65 and 129.80 (d, C-7), 130.97, 131.4, 131.69 and 131.95 (d, C-4, C-5 and C-6), 135.15 (d, C-3 pyran) 170.65 (s, CH_3CO). Anal. Calcd for $C_{16}H_{24}O_4$, $0.25H_2O$: C, 67.45; H, 8.65. Found: C, 67.53; H, 8.82.

[2*R*-[2α(*S,*S***R**),5α]-(*E*,*E*)]-1-[5-(Acetyloxy)-5,6-dihydro-2*H*-pyran-2-yl]-2-methyl-4,6-octadien-3-ol (7b).** Addition of NaBH4 (0.223 g, 5.92 mmol) to a mixture of **6b** (1.48 g, 5.38 mmol) and $CeCl_3$ $7H_2O$ (2.004 g, 5.38 mmol) dissolved in methanol (54 mL) gave 1.47 g (99%) of **7b**: $[\alpha]^{20}_D$ +79.72° (c = 0.439 $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.94 (d, 3 H, J = 7.1 Hz, H-2′), 1.48 (ddd, 1 H, J = 6.2, 8.6, and 14.5 Hz, H-1), 1.72 (ddd, 1 H, J = 4.6, 6.8, and 14.5 Hz, H-1), 1.76 (br dd, 3 H, J = 1.5 and 6.8 Hz, H-8), 1.89 (dddq, 1 H, J = 4, 6.2, 6.8, and 7.1 Hz, H-2), 2.08 (s, 3 H, CH_3CO), 3.56 (dd, 1 H, J = 6.5 and 11.7 Hz, H-6 pyran), 4.10 (dd, 1 H, J = 4.9 and 11.7 Hz, H-6 pyran), 4.15 (ddd, 1 H, J = 3.7, 4, and 6.5 Hz, H-3), 4.30 (ddddd, 1 H, J = 1.9, 2.2, 2.2, 4.6, and 8.6 Hz, H-2 pyran), 5.23 (ddddd, 1 H, J = 1.2, 2.2, 2.8, 4.9, and 6.5 Hz, H-5 pyran), 5.57 (dd, 1 H, J = 6.5 and 15.1 Hz, H-4), 5.70 (dq, 1 H, J = 6.8 and 14.8 Hz, H-7), 5.83 (ddd, 1 H, J = 2.2, 2.8, and 10.2 Hz, H-4 pyran), 5.91 (ddd, 1 H, J = 1.2, 1.8, and 10.2 Hz, H-3 pyran), 6.07 (ddq, 1 H, J = 1.5, 10.2, and 14.8 Hz, H-6), 6.21 (ddd, 1 H, J = 3.7, 10.2, and 15.1 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ 15.12 (q, C-2′), 18.03 (q, C-8), 21.01 (q, CH_3CO), 35.50 (d, C-2), 36.51 (t, C-1), 64.70 (d, C-5 pyran), 64.89 (t, C-6 pyran), 71.67 (d, C-2 pyran), 74.90 (d, C-3), 123.80 (d, C-4 pyran), 129.40 (d, C-7), 130.93 (d, C-3 pyran), 131.35 (d, C-4 and C-6), 134.29 (d, C-5), 170.55 (s, CH_3CO). Anal. Calcd for $C_{16}H_{24}O_4$,$0.25H_2O$: C, 67.45; H, 8.65. Found: C, 67.41; H, 8.41.

Preparation of the 1-(5,6-Dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-3-[(thexyldimethylsilyl)oxy]-4,6-octadienes (10a and 10b). In a flame-dried round-bottom flask was placed successively 1-(5-hydroxy-5,6-dihydro-2*H*-pyran-2-yl)-2-methyl-3-[(thexyldimethylsilyl)oxy]-4,6-octadiene (2.0 g, 7.21 mmol), imidazole (1.96 g, 28.84 mmol), dimethylformamide (5 mL), thexyldimethylsilyl chloride (1.52 g, 10.1 mmol), and a catalytic amount of (dimethylamino)pyridine. After one night the solution was diluted with hexane (80 mL) and then washed with water (2 × 40 mL). The organic solution was dried ($MgSO_4$) and then the solvent was removed to yield an oil which was dissolved in methanol (14.38 mL). This solution was treated with sodium methoxide (3.60 mL, 2 N in methanol, 7.2 mmol) for 1 h. Then solid NH_4Cl (0.43 g) was added. The mixture was stirred (15 min) and diluted with diethyl ether (20 mL), and the solids were removed by filtration. The solvent was evaporated under vacuum, and then the resulting oil was dissolved in dichloromethane (20 mL). To this solution was added 4-Å molecular sieves (3.20 g) and PDC (1.45 g, 3.86 mmol), and after 1.5 h the solution was diluted with diethyl acetate (32 mL) and then filtered over celite. The pad was washed with diethyl acetate (20 × 20 mL). The solvent was removed under vacuum, and then the resulting black residue was purified by chromatography (flash 20% ethyl acetate in hexane/dichloromethane (1:1)) to yield 0.84 g (74.96%) of 1-(5,6-dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-3-[(thexyldimethylsilyl)oxy]-4,6-octadiene.

[*R*[*R(*R**,*RS**)]-(*E*,*E*)]-1-(5,6-Dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-3-[(thexyldimethylsilyl)oxy]-4,6-octadiene (10a)**: $[\alpha]^{20}_D$ +51.36° (c 0.073 $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.037 (s, 3 H, SiMe), 0.07 (s, 3 H, SiMe), 0.80–0.97 (m, 9 H, H-2′ and CH_3C), 1.32 (ddd, 1 H, J = 3.7, 10.8 and 15.10 Hz, H-1), 1.64 (q, J = 6.7 Hz, $CHCH_3$), 1.75 (br d, 3 H, J = 7.1 Hz, H-8), 1.86 (m, 2 H, H-1 and H-2), 3.99 (m, 1 H, H-3), 4.06 (br d, 1 H, J = 16.6 Hz, H-6 pyran), 4.25 (d, 0.5 H, J = 16.6 Hz, H-6 pyran), 4.26 (d, 0.5 H, J = 16.6 Hz, H-6 pyran), 4.39 (m, 0.5 H, H-2 pyran), 4.47 (m, 0.5 H, H-2 pyran), 5.49 (m, 1 H, H-4), 5.66 (dq, 1 H, J = 7.1 and 14.1 Hz, H-7), 5.97–6.10 (m, 2 H, H-5 and H-6), 6.10 (dd, 1 H, J = 2.2 and 10.4 Hz, H-4 pyran), 6.94 (dd, 0.5 H, J = 1.8 and 10.4 Hz, H-3 pyran), 6.96 (dd, 0.5 H, J = 1.8 and 10.4 Hz, H-3 pyran); ^{13}C NMR ($CDCl_3$) δ −2.92 (q, SiMe), −2.11 (q, SiMe), 14.66 (q, C-2′), 18.08 (q, C-8), 20.37 (q, CCH_3), 25.05 (s, CH_3), 34.12 (d, $CHCH_3$), 36.07 (t, C-1), 36.28 (d, C-2), 70.71 (t, C-6 pyran), 71.51 (d, C-2 pyran), 77.28 (d, C-3), 128.46 (d, C-4), 129.09 (d, C-7), 131.07 (d, C-5 and C-6), 131.42 (d, C-4 pyran), 152.77 (d, C-3 pyran), 195.01 (s, C-3). Anal. Calcd for $C_{22}H_{38}O_3Si$: C, 69.79; H, 10.12. Found: C, 70.37; H, 10.20.

[*R*-[*R(*S**,*R***S**)]-(*E*,*E*)]-1-(5,6-Dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-3-[(thexyldimethylsilyl)oxy]-4,6-octadiene (10b)**: $[\alpha]^{20}_D$ +26.31° (c = 0.19 $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.05 (s, 3 H, SiMe), 0.08 (s, 3 H, SiMe), 0.88 (d, 3 H, J = 7 Hz, H-2′),

0.90 (d, 3 H, J = 6.7 Hz, CCH_3), 0.94 (d, 3 H, J = 6.7 Hz, CCH_3), 1.45 (ddd, 1 H, J = 6.6, 8.2, and 14.8 Hz, H-1), 1.65 (q, J = 6.7 Hz, $CHCH_3$), 1.76 (br dd, 3 H, J = 1.5 and 6.5 Hz, H-8), 1.78–1.89 (m, 2 H, H-1 and H-2), 4.08 (dd, 1 H, J = 1.8 and 16.4 Hz, H-6 pyran), 4.08 (ddd, 1 H, J = 1.5, 4.01, and 6.8 Hz, H-3), 4.28 (dd, 1 H, J = 0.5 and 16.4 Hz, H-6 pyran), 4.42 (m, 1 H, H-2 pyran), 5.49 (dd, 1 H, J = 6.8 and 14.6 Hz, H-4), 5.68 (dq, 1 H, J = 6.5 and 14.3 Hz, H-7), 6.04 (ddd, 1 H, J = 1.5, 10.3, and 14.3 Hz, H-6), 6.12 (dd, 1 H, J = 2.3 and 10.3 Hz, H-4 pyran), 6.12 (ddd, 1 H, J= 1.5, 10.3, and 14.6 Hz, H-5), 6.98 (dd, 1 H, J = 1.8 and 10.3 Hz, H-3 pyran); ^{13}C NMR ($CDCl_3$) δ −2.96 (q, SiMe), −2.05 (q, SiMe), 15.94 (q, C-2′), 18.1 (q, C-8), 20.26 (q, CCH_3), 20.38 (q, CCH_3), 25.05 (s, CH_3), 34.12 (d, $CHCH_3$), 36.47 (t, C-1), 36.64 (d, C-2), 71.09 (t, C-6 pyran), 72.67 (d, C-2 pyran), 76.29 (d, C-3), 128.38 (d, C-4), 129.20 (d, C-7), 131.21 (d, C-4 and C-5), 130.92 (d, C-6), 152.19 (d, C-3 pyran), 195.01 (s, C-3). Anal. Calcd for $C_{22}H_{38}O_3Si$: C, 69.79; H, 10.12. Found: C, 69.50; H, 10.03.

(2*R*)-4-[2,3-Dihydro-3-methyl-3-[(trimethylsilyl)oxy]-2*H*-pyran-2-yl]-3-methyl-2-butanone (12). A solution of 4-(2,3-dihydro-3-hydroxy-3-methyl-2*H*-pyran-2-yl)-3-methyl-2-butanone (11) (1.07 g, 5.98 mmol), hexamethyldisilazane (1.52 mL, 7.18 mmol) and saccharin (0.02 g, 0.08 mmol) in dichloroethane (10 mL) was heated overnight at 40 °C. The solution was filtered, evaporated under reduced pressure, and finally distilled with dichloroethane (10 mL). The resulting oil was used without further purification.

[2*R*-(*E*,*E*)]-1-[2,3-Dihydro-3-methyl-3-[(trimethylsilyl)-oxy]-2*H*-pyran-2-yl]-2-methyl-4,6-octadien-3-one (13). To a solution of diisopropylamine (0.89 mL, 6.36 mmol) in THF (15 mL) was added at 0 °C butyllithium (3.96 mL 1.6 M in hexane, 22.82 mmol). After 15 min the solution was cooled to −78 °C, and then slowly a solution of 1-[2,3-dihydro-3-[(trimethylsilyl)oxy]-3-methyl-2*H*-pyran-2-yl]-3-methyl-2-butanone (12) (0.86 g, 3.18 mmol) in THF (0.5 mL) was added. After 15 min a mixture of crotonaldehyde (0.32 mL, 3.81 mmol) and trimethylchlorosilane (0.58 mL, 4.6 mmol) was added slowly. Then the reaction mixture was removed from the cooling bath and DBU (0.48 mL, 3.18 mmol) was added. The solution was heated at 75 °C for 1.5 h, and then the solvent was removed slowly under vacuum to avoid foaming. The residue was partitioned between dichloromethane (10 mL) and Na_2HPO_4 (10 mL). The aqueous layer was extracted with dichloromethane (2 × 10 mL). The combined organic solution was dried ($MgSO_4$) and then evaporated to yield a yellow oil. Purification by flash chromatography (8% ethyl acetate in hexane) gave 13 (0.61 g 60%): $[\alpha]^{20}_D$ + 58.75° (methanol, c = 1); ^{1}H NMR ($CDCl_3$) δ 1.0 (d, 3H, J = 6.8 Hz, H-2′), 1.1 (s, 3H, H-3′), 1.45 (ddd, 0.7 H, J = 3, 10.2, and 14.1 Hz, H-1 (*R*)), 1.62 (ddd, 0.3H, J = 1.9, 8.3, and 14.2 Hz, H-1 (*S*)), 1.8 (dd, 1H, J = 0.9 and 5.2 Hz, H-8), 1.9 (m, 1H, H-1 (*R*,*S*)), 2.9 (m, 0.3H, H-2 (S)), 2.95 (m, 0.7H, H-2 (*R*)), 3.1 (m, 0.7H, H-2 pyran (*R*)), 3.15 (m, 0.3H, H-2 pyran (*S*)), 3.85 (dd, 1H, J = 2.2 and 16.3 Hz, H-6 pyran), 4.1 (dd, 1H, J = 2.2 and 16.3 Hz, H-6 pyran), 5.7 (m, 2H, H-4 and H-5 pyran), 6.05 (d, 1H, J = 14.4 Hz, H-4), 6.1 (dq 1H, J = 5.2 and 15.1 Hz, H-7), 6.15 (dd, 1H, J = 10.2 and 15.1 Hz, H-6), 7.12 (ddq 1H, J = 0.9, 10.2, and 14.4 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ 13.06 (q, C-2′), 16.06 (q, C-8 (*R*)), 16.31 (q, C-8 (*S*)), 24.23 (q, C-3′ (*S*)), 24.40 (q, C-3′ (*R*)), 29.67 (t, C-1 (*S*)), 30.4 (t, C-1 (*R*)), 36.83 (d, C-2 (*R*)), 37.78 (d, C-2 (*S*)), 62.91 (t, C-6 pyran), 65.64 (s, C-3 pyran (*S*)), 66.81 (s, C-3 pyran (*R*)), 77.63 (d, C-2 pyran (*S*)), 77.69 (d, C-2 pyran (*R*)), 124.21 (d, C-4), 125.17 (d, C-5 pyran), 128.04 (d, C-4 pyran), 129.62 (d, C-6), 137.26 (d, C-6 (*S*)), 137.66 (d, C-6 (*S*)), 140.20 (d, C-7 (*S*)), 140.50 (d, C-7 (*R*)), 202.07 (s, C-3 (*S*)), 202.82 (s, C-3 (*R*)).

[*R*-(*R,*R**,*S**)-(*E*,*E*)]-(5,6-Dihydro-3-methyl-4-oxo-2*H*-pyran-2-yl)-2-methyl-4,6-octadien-3-one (14).** To a solution of 1-[2,3-dihydro-3-methyl-3-[(trimethylsilyl)oxy]-2*H*-pyran-2-yl]-2-methyl-4,6-octadien-3-one (13) (0.522 g, 1.65 mmol) in dichloromethane (5 mL) was added 4-Å molecular sieves (1.05 g) and PCC (1.067 g, 4.95 mmol). The solution was stirred overnight, diluted with diethyl ether, and finally filtered over a Celite pad. The black solid was carefully washed with ethyl acetate (15 mL). The solvent was removed under vacuum, and then the resulting black residue was purified by chromatography (flash 10% ethyl acetate in hexane) to yield the dioxo derivatives 14 (0.285 g, 60%): $[\alpha]^{20}_D$ + 8.75° (c = 1 $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.18 (d, 3 H, J = 7.1 Hz, H-2′), 1.6 (ddd, 0.6 H, J = 3, 11.1 and 14.1 Hz, H-1 (*R*)), 1.7 (ddd, 0.4 H, J = 3, 8.6, and 14.4 Hz, H-1 (*S*)), 1.9 (d, 3 H, J = 5 Hz, H-8), 1.95 (d, 1.2 H, J = 1.5 Hz, H-3′ (*S*)), 1.98 (d, 1.8 H, J = 1.5 Hz, H-3′ (*R*)), 2.10 (ddd, 0.4 H, J = 5.2, 11.4, and 14.4 Hz, H-1 (*S*)), 2.25 (ddd, 0.6 H, J = 2.8, 10.5, and 14.1 Hz, H-1 (*R*)), 3.1 (ddq, 0.4 H, J = 7.1, 10.5, and 11.4 Hz, H-2 (*S*)), 3.2 (ddq, 0.6 H, J = 7.1, 8.6, and 11.4 Hz, H-2(*S*)), 3.97 (dd, 1 H, J = 1.2 and 16.3 Hz, H-6 pyran), 4.1 (m, 0.6 H, H-2 pyran (*R*)), 4.00 (dd, 1 H, J = 1.01 and 16.3 Hz, H-6 pyran); 4.25 (m, 0.4 H, H-2 pyran (*S*)), 5.95 (ddq, 1 H, J = 1, 1.2, and 1.8 Hz, H-4 pyran), 6.15 (d, 1 H, J = 15.1 Hz, H-4), 6.2 (m, 2 H, H-6 and H-7), 7.2 (ddd, 1 H, J = 6.1, 11, and 16.6 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ 16.34 (q, C-2′), 18.79 (q, C-8), 20.1 (q, C-3′), 33.67 (t, C-1 (*S*)), 34.24 (t, C-1 (*R*)), 39.54 (d, C-2 (*R*)), 40.31 (d, C-2 (*S*)), 68.36 (t, C-6 pyran (*S*)), 68.89 (t; C-6 pyran (*R*)), 71.77 (s C-3 pyran (*S*)), 72.68 (s C-3 pyran (*R*)), 74.51 (d, C-2), 124.04 (d, C-4), 128.33 (d, C-4 pyran (*S*)), 128.99 (d, C-4 pyran (*R*)), 130.26 (d, C-6), 141.00 (d, C-5), 143.59 (d, C-7), 194.39 (s, C-5 pyran), 203.58 (s C-3).

Cyclization of 1-(5,6-Dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-4,6-octadien-3-ones. A solution of 1-(5,6-dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-4,6-octadien-3-ones (0.155 g, 0.64 mmol) and hydroquinone (0.002 g, 0.03 mmol) in toluene (15.36 mL) was degassed under argon and then transferred in a silylated 60 mL SVL tube and heated at 180 °C overnight. Removal of the solvent and then crystallization (methanol) gave the pure 4,6a,8,9,9a,9b-hexahydro-4,8-dimethylnaphtho[1,8-*bc*]pyran-3,7-(2*H*,3a*H*)-dione.

[3a*S*-3aα,4β,6aβ,8β,9aα,9bα]-4,6a,8,9,9a,9b-Hexahydro-4,8-dimethylnaphtho[1,8-*bc*]pyran-3,7(2*H*,3a*H*)-dione (15a): 0.098 g (63%); mp 117–120 °C; $[\alpha]^{20}_D$ +95° (c 0.1, methanol); ^{1}H NMR ($CDCl_3$) δ 1.01 (d, 3 H, J = 7.6 Hz, H-4′), 1.05 (d, 3 H, J = 6.7 Hz, H-8′), 1.74 (ddd, 1 H, J = 2.9, 13, and 14.2 Hz, H-9), 2.41 (ddd, 1 H, J = 1.7, 4.8, and 12.3 Hz, H-9b), 2.42 (ddd, 1 H, J = 2.8, 6.4, and 14.2 Hz, H-9), 2.62 (dddd, 1 H, J = 0.9, 1, 1, and 4.8 Hz, H-3a), 2.87 (ddddq, 1 H, J = 0.7, 1.1, 6.4, 6.69, and 13 Hz, H-8), 3.06 (ddddq, 1 H, J = 1, 1.9, 2.4, 3.9, and 7.5 Hz, H-4), 3.31 (ddddd, 1 H, J = 1.1, 1.9, 2.4, 2.8, and 12.3 Hz, H-6a), 4.12 (dd, 1 H, J = 1 and 14.8 Hz, H-2), 4.20 (d, 1 H, J = 14.8 Hz, H-2), 4.23 (ddd, 1 H, J = 1, 2.8, and 2.9 Hz, H-9a), 5.61 (dddd, 1 H, J = 0.9, 2.8, 3.9, and 10.3 Hz, H-5), 5.97 (ddd, 1 H, J = 1.9, 1.9, and 10.3 Hz, H-6); ^{13}C NMR ($CDCl_3$) δ 14.02 (q, C-4′), 20.92 (q, C-8′), 25.99 (d, C-9b), 39.78 (d, C-4), 40.16 (d, C-9), 42.50 (d, C-6a), 43.45 (d, C-8), 53.44 (d, C-3a), 73.80 (t, C-2), 73.94 (d, C-9a), 120.95 (d, C-6), 131.90 (d, C-5), 205.36 (s, C-7), 209.92 (s, C-3). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.76; H, 7.73. Found: C, 71.72; H, 7.89.

[3a*S*-3aα,4β,6aβ,8α,9aα,9bα]-4,6a,8,9,9a,9b-Hexahydro-4,8-dimethylnaphtho[1,8-*bc*]pyran-3,7(2*H*,3a*H*)-dione (15b): 0.093 g (60%); mp 115–116 °C; $[\alpha]^{20}_D$ 0° (c 0.6 $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.03 (d, 3 H, J = 7.5 Hz, H-4′), 1.29 (d, 3 H, J = 7.2 Hz, H-8′), 2.02 (ddd, 1 H, J = 3.9, 5.3, and 14.8 Hz, H-9), 2.27 (ddd, 1 H, J = 6.3, 6.5, and 14.8 Hz, H-9), 2.49 (ddd, 1 H, J = 2.6, 5.02, and 12.7 Hz, H-9b), 2.54 (ddddq, 1 H, J = 1.1, 1.1, 5.3, 6.5, and 7.2 Hz, H-8), 2.69 (dddd, 1 H, J = 0.9, 0.9, 0.9, and 5 Hz, H-3a), 3.06 (ddddq, 1 H, J = 0.9, 1.9, 2.1, 3.6, and 7.5 Hz, H-4), 3.28 (ddddd, 1 H, J = 1.1, 1.9, 2.1, 2.6, and 12.7 Hz, H-6a), 4.05 (dd, 1 H, J = 1 and 15.1 Hz, H-2), 4.16 (d, 1 H, J = 15.1 Hz, H-2), 4.36 (dddd, 1 H, J = 0.9, 2.6, 3.9, and 5.3 Hz, H-9a), 5.67 (dddd, 1 H, J = 1, 2.6, 3.6, and 10.3 Hz, H-5), 5.98 (dddd, 1 H, J = 0.9, 1.7, 1.9, and 10.3 Hz, H-6); ^{13}C NMR ($CDCl_3$) δ 18.96 (q, C-4′), 20.70 (q, C-8′), 25.92 (d, C-9b), 35.19 (t, C-9), 39.73 (d, C-4), 40.66 (d, C-6a), 42.03 (d, C-8), 52.34 (d, C-3a), 73 (t, C-2), 73.81 (d, C-9a), 120.67 (d, C-6), 132.20 (d, C-5), 206.73 (s, C-7), 211.67 (s, C-3). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.76; H, 7.73. Found: C, 71.78; H, 7.89.

IMDA of 1-(5,6-Dihydro-3-methyl-5-oxo-2*H*-pyran-2-yl)-2-methyl-4,6-octadien-3-one. A solution of 1-(5,6-dihydro-3-methyl-5-oxo-2*H*-pyran-2-yl)-2-methyl-4,6-octadien-3-one (14) (0.080 g, 0.32 mmol) and hydroquinone (0.003 g, 0.04 mmol) in toluene (12 mL) was degassed under argon and then transferred in a silylated 60-mL SVL tube and heated at 180 °C overnight. Removal of the solvent and then chromatography (5% ethyl acetate in hexane/dichloromethane (1:1)) gave 0.012 g (15%) of [3a*S*-3aα,4β,6aβ,8β,9aα,9bα]-4,6a,8,9,9a,9b-hexahydro-4,8,9b-trimethylnaphtho[1,8-*bc*]pyran-3,7(2*H*,3a*H*)-dione (**16a**) and 0.032 g (40%) of [3a*S*-3aα,4β,6aβ,8α,9aα,9bα]-4,6a,8,9,9a,9b-Hexahydro-4,8,9b-trimethylnaphtho[1,8-*bc*]pyran-3,7(2*H*,3a*H*)-dione (**16b**).

[3a*S*-3aα,4β,6aβ,8β,9aα,9bα]-4,6a,8,9,9a,9b-Hexahydro-4,8,-9b-trimethylnaphtho[1,8-*bc*]pyran-3,7(2*H*,3a*H*)-dione (16a): $[\alpha]^{20}_D$ +63° (*c* = 0.64 methanol); ^{1}H NMR ($CDCl_3$) δ 0.95 (d, 3 H, *J* = 0.4 Hz, H-9b'), 1.05 (d, 3 H, *J* = 6.6 Hz, H-4'), 1.15 (d, 3 H, *J* = 7.7 Hz, H-8'), 2.04 (ddd, 1 H, *J* = 3.1, 12.6, and 14.4 Hz, H-9), 2.27 (ddd, 1 H, *J* = 0.62, 0.8, and 0.9 Hz, H-3a), 2.31 (ddd, 1 H, *J* = 2.6, 7.2, and 14.4 Hz, H-9), 2.8 (ddddq, 1H, *J* = 0.9, 1.4, 7.1, 7.7, and 12.7 Hz, H-8), 3.28 (ddddq 1 H, *J* = 0.9, 2.8, 2.9, 2.9, and 6.7 Hz, H-4), 3.35 (dddq 1 H, *J* = 0.5, 1.1, 2.00, and 2.9 Hz, H-6a), 3.9 (dddd, 1 H, *J* = 0.8, 0.9, 2.6, and 3.1 Hz, H-9a), 4.15 (dd, 1 H, *J* = 0.9 and 16.7 Hz, H-2), 4.25 (dd, 1 H, *J* = 0.9 and 16.7 Hz, H-2'), 5.6 (dddd, 1 H, *J* = 0.6, 2.9, 2.9 and 10.3 Hz, H-6). Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.11. Found: C, 72.70; H, 7.95.

[3a*S*-3aα,4β,6aβ,8α,9aα,9bα]-4,6a,8,9,9a,9b-Hexahydro-4,8,-9b-trimethylnaphtho[1,8-*bc*]pyran-3,7(2*H*,3a*H*)-dione (16b): $[\alpha]^{20}_D$ + 56° (*c* = 0.5 methanol); ^{1}H NMR ($CDCl_3$) δ 0.91 (d, 3 H, *J* = 0.4 Hz, H-9b'), 1.15 (d, 3 H, *J* = 7.8 Hz, H-4'), 1.35 (d, 3 H, *J* = 7.5 Hz, H-8'), 2.01 (dddd, 1 H, *J* = 0.7, 1.5, 2.7, and 16.1 Hz, H-9), 2.25 (ddd, 1 H, *J* = 0.7, 0.9, and 1.1 Hz, H-3a), 2.41 (ddd, 1 H, *J* = 4.1, 7.2, and 16.1 Hz, H-9), 2.56 (ddq, 1 H, *J* = 1.5, 7.2, and 7.5 Hz, H-8), 3.30 (ddddq, 1 H, *J* = 1.15, 2.75, 3, 3.4, and 7.8 Hz, H-4), 3.55 (ddd, 1 H, *J* = 1.8, 2.7, and 3 Hz, H-6a), 3.95 (ddd, 1 H, *J* = 0.7, 2.7, and 4.1 Hz, H-9a), 4.15 (dd, 1 H, *J* = 0.9 and 14.8 Hz, H-2), 4.25 (dd, *J* = 0.9 and 14.8 Hz, H-2'), 5.2 (dddd, 1 H, *J* = 0.7, 2.7, 3.4, and 10.3 Hz, H-5), 6.01 (dddd, 1 H, *J* = 0.7, 1.9, 2.7, and 10.3 Hz, H-6). Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.11. Found: C, 72.60; H, 7.90.

IMDA of 1-(5,6-Dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-3-[(thexyldimethylsilyl)oxy]-4,6-octadienes. Method A. A solution of 1-(5,6-dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-3-[(thexyldimethylsilyl)oxy]-4,6-octadienes (0.38 g, 1 mmol) and hydroquinone (0.002 g, 0.03 mmol) in toluene (16 mL) was heated at 180 °C overnight. Removal of the solvent followed by flash chromatography (10% ethyl acetate in hexane[27]) furnished the pure naphthopyrans.

[3a*S*-3aα,4α,6aα,7β,8β,9aα,9bα]-3a,4,6a,7,8,9,9a,9b-Octahydro-4,8-dimethyl-7-[(thexyldimethylsilyl)oxy]naphtho[1,8-*bc*]pyran-3(2*H*,3a*H*)-one (17a): oil; 0.075 g (20%); $[\alpha]^{20}_D$ −40° (*c* 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.066 (s, 3 H, CH_3Si), 0.082 (s, 3 H, CH_3Si), 0.83 (s, 3 H, CH_3C), 0.84 (s, 3 H, CH_3C), 0.88 (d, 6 H, *J* = 7 Hz, CH_3CH), 0.90 (d, 3 H, *J* = 7.3 Hz, H-8'), 1.06 (d, 3 H, *J* = 7.3 Hz, H-4'), 1.50 (ddd, 1 H, *J* = 2.9, 3.2, and 13.8 Hz, H-9), 1.62 (q, 1 H, *J* = 7 Hz, $CHCH_3$), 1.72 (ddd, 1 H, *J* = 2.9, 12.6, and 13.8 Hz, H-9), 1.98 (dddq, 1 H, *J* = 2, 3.2, 7.3, and 12.6 Hz, H-8), 2.30 (dddd, 1 H, *J* = 2.5, 2.9, 3.5, and 6.7 Hz, H-6a), 2.39 (dddq, 1 H, *J* = 2.5, 3.3, 7.3, and 7.3 Hz, H-4), 2.62 (ddd, 1 H, *J* = 2.9, 6.7, and 10.3 Hz, H-9b), 2.84 (ddd, 1 H, *J* = 2.3, 7.3, and 10.3 Hz, H-3a), 3.63 (ddd, 1 H, *J* = 2.9, 2.9, and 2.9 Hz, H-9a), 3.73 (d, 1 H, *J* = 17.6 Hz, H-2), 3.90 (dd, 1 H, *J* = 2.05 and 2.9 Hz, H-7), 3.98 (dd, 1 H, *J* = 2.3 and 17.6 Hz, H-2), 5.63 (ddd, 1 H, *J* = 2.5, 3.3, and 9.1 Hz, H-5), 5.92 (ddd, 1 H, *J* = 2.3, 3.5, and 9.1 Hz, H-6); ^{13}C NMR ($CDCl_3$) δ −2.87 (q, CH_3Si), −2.40 (q, CH_3Si), 17.30 (q, C-4'), 18.64 (q, C-8' + CH_3 thexyl), 20.40 (q, CH_3 thexyl), 25.01 (s, C thexyl), 26.59 (d, C-8), 31.95 (d, C-4), 32.39 (t, C-9), 34.21 (d, CH thexyl), 34.90 (d, C-9b), 41.18 (d, C-6a), 52.24 (d, C-3a), 73.80 (d, C-9a), 74.04 (d, C-7), 74.04 (t, C-2), 131.45 (d, C-5), 133.42 (d, C-6), 211.98 (s, C-3). Anal. Calcd for $C_{22}H_{38}O_3Si$: C, 69.79; H, 10.12. Found: C, 69.75; H, 10.10.

[3a*S*-3aα,4α,6aα,7α,8β,9aα,9bα]-3a,4,6a,7,8,9,9a,9b-Octahydro-4,8-dimethyl-7-[(thexyldimethylsilyl)oxy]naphtho[1,8-*bc*]pyran-3(2*H*,3a*H*)-one (17b): oil; 0.15 g (39.5%); $[\alpha]^{20}_D$ −35° (*c* 0.42 $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.039 (s, 3 H, CH_3Si), 0.089 (s, 3 H, CH_3Si), 0.86 (s, 3 H, CH_3C), 0.88 (s, 3 H, CH_3C), 0.91 (d, 6 H, *J* = 6.99 Hz, CH_3CH), 0.93 (d, 3 H, *J* = 6.7 Hz, H-8'), 1.00 (d, 3 H, *J* = 7.3 Hz, H-4'), 1.29 (ddd, 1 H, *J* = 2.9, 12.6, and 13.7 Hz, H-9), 1.66 (q, 1 H, *J* = 7 Hz, $CHCH_3$), 1.81 (ddd, 1 H, *J* = 3, 3.53, and 13.7 Hz, H-9), 1.92 (dddq, 1 H, *J* = 3.5, 6.7, 10.5, and 12.6 Hz, H-8), 2.47 (dddq, 1 H, *J* = 2.9, 3.7, 7.3, and 7.3 Hz, H-4), 2.58 (ddd, 1 H, *J* = 3.1, 6.5, and 10.1 Hz, H-9b), 2.61 (dddd, 1 H, *J* = 3.4, 3.7, 4.77, and 6.5 Hz, H-6a), 2.83 (ddd, 1 H, *J* = 2.2, 7.3, and 10.1 Hz, H-3a), 3.52 (dd, 1 H, *J* = 4.8 and 10.4 Hz, H-7), 3.58 (ddd, 1 H, *J* = 2.9, 3, and 3.1 Hz, H-9a), 3.69 (d, 1 H, *J* = 17.8 Hz, H-2), 3.84 (dd, 1 H, *J* = 2.2 and 17.8 Hz, H-2), 5.62 (ddd, 1 H, *J* = 3.4, 3.7, and 9.2 Hz, H-5), 6.30 (ddd, 1 H, *J* = 2.9, 3.7, and 9.2 Hz, H-6); ^{13}C NMR −2.84 (q, CH_3Si), −2.07 (q, CH_3Si), 17.32 (q, C-4'), 18.63 (q, CH_3 thexyl), 18.63 (q, C-8'), 20.37 (q, CH_3 thexyl), 24.96 (s, C thexyl), 29.51 (d, C-8), 31.81 (d, C-4), 37.66 (t, C-9), 34.18 (d, CH thexyl), 40.12 (d, C-9b), 40.65 (d, C-6a), 53.18 (d, C-3a), 72.64 (d, C-9a), 74.02 (t, C-2), 76.04 (d, C-7), 132.72 (d, C-6), 130.32 (d, C-5), 206.53 (s, C-3). Anal. Calcd for $C_{22}H_{38}O_3Si$: C, 69.79; H, 10.12. Found: C, 69.56; H, 10.17.

[3a*S*-3aα,4β,6aβ,7β,8α,9aα,9bα]-3a,4,6a,7,8,9,9a,9b-Octahydro-4,8-dimethyl-7-[(thexyldimethylsilyl)oxy]naphthol[1,8-*bc*]pyran-3(2*H*,3a*H*)-one (17c): needles 0.25 g (56%); mp 70–72 °C; $[\alpha]^{20}_D$ + 92° (*c* 0.1 $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.065 (s, 6 H, CH_3Si), 0.81 (s, 3 H, CH_3C), 0.82 (s, 3 H, CH_3C), 0.88 (d, 6 H, *J* = 6.75 Hz, CH_3CH), 0.99 (d, 3 H, *J* = 7.3 Hz, H-4'), 1.10 (d, 3 H, *J* = 7.3 Hz, H-8'), 1.61 (q, 1 H, *J* = 6.7 Hz, $CHCH_3$), 1.68 (dddd, 1 H, *J* = 1.2, 1.3, 2.6, and 14.7 Hz, H-9), 1.86 (dddq, 1 H, *J* = 1.3, 2.3, 6.2, and 7.3 Hz, H-8), 2.11 (ddd, 1 H, *J* = 3.2, 6.16, and 14.7 Hz, H-9), 2.45 (dddd, 1 H, *J* = 1.2, 1.8, 2.64, and 11.4 Hz, H-6a), 2.50 (ddd, 1 H, *J* = 0.9, 0.9, and 5 Hz, H-3a), 2.64 (ddd, 1 H, *J* = 1.8, 5, and 11.4 Hz, H-9b), 2.97 (ddq, 1 H, *J* = 1.8, 4.1, and 7.3 Hz, H-4), 3.68 (ddd, 1 H, *J* = 1.2, 1.2, and 2.3 Hz, H-7), 3.89 (dd, 1 H, *J* = 0.9 and 14.1 Hz, H-2), 4.03 (d, 1 H, *J* = 14.1 Hz, H-2), 4.1 (ddd, 1 H, *J* = 1.8, 2.6, and 3.2 Hz, H-9a), 5.35 (ddd, 1 H, *J* = 1.7, 1.8, and 10 Hz, H-6), 5.54 (dddd, 1 H, *J* = 0.9, 2.6, and 4.1, 10 Hz, H-5); ^{13}C NMR ($CDCl_3$) −2.81 (q, CH_3Si), −2.58 (q, CH_3Si), 18.60 and 20.33 (q, C-4', C-8', CH_3 thexyl), 24.60 (s, C thexyl), 35.78 (d, C-8), 26.03 (d, C-4), 31.54 (d, C-6a), 31.99 (t, C-9), 34.02 (d, CH thexyl), 34.20 (d, C-9b), 53.22 (d, C-3a), 76.50 (d, C-9a), 75.88 (d, C-7), 73.82 (t, C-2), 128.53 (d, C-6), 131.1 (d, C-5), 207.57 (s, C-3). Anal. Calcd for $C_{22}H_{38}O_3Si$: C, 69.79; H, 10.12. Found: C, 69.31; H, 10.29.

[3a*S*-3aα,4β,6aβ,7α,8α,9aα,9bα]-3a,4,6a,7,8,9,9a,9b-Octahydro-4,8-dimethyl-7-[(thexyldimethylsilyl)oxy]naphtho[1,8-*bc*]pyran-3(2*H*,3a*H*)-one (17e): oil; 0.059 g (15%); $[\alpha]^{20}_D$ 0° (*c* 0.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.045 (s, 3 H, CH_3Si), 0.056 (s, 3 H, CH_3Si), 0.82 (s, 3 H, CH_3C), 0.83 (s, 3 H, CH_3C), 0.86 (d, 6 H, *J* = 6.75 Hz, CH_3CH), 0.98 (d, 3 H, *J* = 7.3 Hz, H-4'), 1.08 (d, 3 H, *J* = 7.3 Hz, H-8'), 1.62 (q, 1 H, *J* = 6.7 Hz, $CHCH_3$), 1.62 (overlap, 1 H, H-9), 1.80 (ddd, 1 H, *J* = 3.5, 5.5, and 14.7 Hz, H-9), 1.92 (ddd, 1 H, *J* = 2, 5.5, and 11.4 Hz, H-9b), 2.03 (dddq, 1 H, *J* = 2, 5.3, 5.5, and 7.3 Hz, H-8) 2.32 (dddd, 1 H, *J* = 2.6, 2.6, 10, and 11.4 Hz, H-6a), 2.47 (ddd, 1 H, *J* = 0.9, 0.9, and 5.6 Hz, H-3a), 2.96 (ddq, 1 H, *J* = 1.8, 3.8, and 7.3 Hz, H-4), 3.38 (dd, 1 H, *J* = 5.2 and 10 Hz, H-7), 3.85 (dd, 1 H, *J* = 0.9 and 14.4 Hz, H-2), 4.00 (d, 1 H, *J* = 14.4 Hz, H-2), 4.01 (ddd, 1 H, *J* = 2, 2.05, and 3.5 Hz, H-9a), 5.51 (ddd, 1 H, *J* = 2.6, 3.8, and 10.3 Hz, H-5), 5.78 (ddd, 1 H, *J* = 0.9, 1.8, 1.8, and 10.3 Hz, H-6); ^{13}C NMR ($CDCl_3$) δ −2.92 (q, CH_3Si), −1.99 (q, CH_3Si), 14.81 (q, C-8'), 18.58 (q, CH_3 thexyl), 20.35 (q, CH_3 thexyl), 21.34 (q, C-4'), 25.02 (s, C thexyl) 25.75 (d, C-4), 32.78 (d, C-6a), 34.03 (d, CH thexyl), 34.9 (d, C-8), 35.20 (t, C-9), 40.37 (d, C-9b), 53.37 (d, C-3a), 73.58 (d, C-9a), 75.45 (t, C-2), 75.99 (d, C-7), 125.71 (d, C-6), 130.68 (d, C-5), 206.53 (s, C-3). Anal. Calcd for $C_{22}H_{38}O_3Si$: C, 69.79; H, 10.12. Found: C, 69.61; H, 10.17.

Method B. 1-(5,6-Dihydro-5-oxo-2*H*-pyran-2-yl)-2-methyl-3-[(thexyldimethylsilyl)oxy]-4,6-octadiene (**10a**) (0.1 g, 0.295 mmol) and (menthyloxy)aluminum dichloride (2.27 mL, 0.44 M in dichloromethane, 1.34 mmol) were stirred at room temperature under nitrogen for 0.5 h. Then the reaction mixture was quenched with $NaHSO_4$ (2.5 mL). Extraction with diethyl ether (3 × 2.5 mL), followed by washing of the combined organic layers with saturated aqueous sodium hydrogenocarbonate (5 mL), drying ($MgSO_4$), concentration, and flash chromatography (10% ethyl acetate in hexane[27]) furnished **17a** (19 mg, 19%) and **17b** (41 mg 41%). In the same fashion **10b** afforded **17c** (0.055 g, 55%) and **17e** (13 mg, 13%).

Method C. 1-[5,6-Dihydro-5-oxo-2*H*-pyran-2-yl]-2-methyl-3-[(thexyldimethylsilyl)oxy]-4,6-octadienes (neat, 0.1 g, 1 mmol) and some crystal of hydroquinone were heated at 100 °C for 24 h in an ultrasonic cleaner. Flash chromatography (10% ethyl acetate in hexane[27]) furnished the pure naphthopyran in the same yields as those observed for the thermal reaction.

Method D. Silica gel (0.15 g, flash chromatography grade) was calcined at 1000 °C (Bunsen burner) under nitrogen. Then the silica gel was added at room temperature to a toluene (0.6

(27) The solvents were carefully degassed by bubbling argon under ultrasound, and nitrogen was used as gas carrier.

mL) solution of **10b** (0.10 g, 0.295 mmol). The suspension was heated at 100 °C for 2 h. The silica gel was filtrated then washed with diethyl ether. Removal of the solvents followed by flash chromatography (10% ethyl acetate in hexane[27]) furnished 0.016 g (16%) of **17c**, 0.049 g (49%) of **17d**, and 0.009 g (9%) of **17e**.

[3a*S*-3aα,4β,6aβ,7α,8β,9aβ,9bβ]-3a,4,6a,7,8,9,9a,9b-Octahydro-4,8-dimethyl-7-[(thexyldimethylsilyl)oxy]naphtho[1,8-*bc*]pyran-3(2*H*,3a*H*)-one (17d): oil; $[\alpha]^{20}_D$ +37.2° (*c* 1 $CHCl_3$); ^{1}H-NMR (CD_3COCD_3) δ 0.035 (s, 3 H, CH_3Si), 0.056 (s, 3 H, CH_3Si), 0.84 (s, 6 H, CH_3C), 0.88 (d, 6 H, J = 6, 75 Hz, CH_3CH), 1.01 (d, 3 H, J = 6.4 Hz, H-4′), 1.11 (d, 3 H, J = 6.4 Hz, H-8′), 1.63 (overlap, 1 H, H-8), 1.63 (q, 1 H, J = 6.7 Hz, $CHCH_3$), 1.92 (ddd, 1 H, J = 12.3, 12.6, and 12.6 Hz, H-9), 2.06 (ddd, 1 H, J = 4.1, 6.5, and 12.3 Hz, H-9), 2.13 (dddd, 1 H, J = 1, 5, 5.6, and 10 Hz, H-6a), 2.33 (dd, 1 H, J = 8.8 and 13.5 Hz, H-3a), 2.44 (ddd, 1 H, J = 5, 5.2, and 13.5 Hz, H-9b), 2.58 (dddq, 1 H, J = 2, 2.3, 6.5, and 8.8 Hz, H-4), 3.18 (dd, 1 H, J = 9.68 and 10 Hz, H-7), 3.85 (d, 1 H, J = 14.7 Hz, H-2), 4.06 (ddd, 1 H, J = 4.1, 5.2, and 12.6 Hz, H-9a), 4.08 (d 1 H, J = 14.7 Hz, H-2), 5.52 (ddd, 1 H, J = 1, 2.3, and 10.3 Hz, H-6), 5.84 (ddd, 1 H, J = 2, 5.6, and 10.3 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ −1.12 (q, CH_3Si), −1.36 (q, CH_3Si), 18.58 (q, CH_3 thexyl), 18.67 (q, C-8′), 20.54 (q, CH_3 thexyl), 21.83 (q, C-4′), 24.60 (s, C thexyl), 29.64 (d, C-4), 32.11 (t, C-9), 34.04 (d, CH thexyl), 38.02 (d, C-8), 42.08 (d, C-9b), 42.77 (d, C-6a), 47.80 (d, C-3a), 69.21 (t, C-2), 72.75 (d, C-9a), 78.85 (d, C-7), 128.28 (d, C-6), 132.52 (d, C-5), 208.03 (s, C-3). Anal. Calcd for $C_{22}H_{38}O_3Si$: C, 69.79; H, 10.12. Found: C, 70.05; H, 10.15.

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Supplementary Material Available: Experimental procedures and Scheme III (11 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.