Articles

Conformationally Constrained Analogues of Diacylglycerol (DAG). 17.[1] Contrast between *sn*-1 and *sn*-2 DAG Lactones in Binding to Protein Kinase C

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Received December 15, 1999

In previous work, we have obtained potent protein kinase C (PK-C) ligands with low-namomolar binding affinities by constructing diacylglycerol (DAG) mimetics in which the *sn*-2 carbonyl of DAG was constrained into a lactone ring. An additional structural element that helped achieve high binding affinity was the presence of branched acyl or α-alkylidene chains. In the present study, the effects of similarly branched chains on a different lactone system, where the lactone carbonyl is now equivalent to the *sn*-1 carbonyl of DAG, are investigated. In this new lactone template, the two chiral centers must have the *S*-configuration for enzyme recognition. As with the *sn*-2 DAG lactones, the branched chains were designed to optimize van der Waals contacts with a group of conserved hydrophobic amino acids located on the rim of the C1 domain of PK-C. The acyl and α-alkylidene chains were also designed to be lipophilically equivalent (8 carbons each). Eight new compounds (**7**−**14**) representing all possible combinations of linear and branched acyl and α-alkylidene were synthesized and evaluated. The *sn*-1 DAG lactones were less effective as PK-C ligands than the *sn*-2 DAG lactones despite having a similar array of linear or branched acyl and α-alkylidene chains

Introduction

Protein kinase C (PK-C) is a family of at least 10 related serine/threonine kinases with different tissue distributions and cofactor requirements.[2,3] It is now well-established that these PK-C isozymes play a critical role in the regulation of cell growth, differentiation, and apoptosis.[4] With the exception of PK-Cζ and PK-Cλ, all of the isozymes are activated through the binding of diacylglycerol (DAG), which causes translocation of the enzyme(s) to the membrane.[5] DAG functions as a central lipophilic second messenger that is generated in response to the activation of numerous receptors which are coupled through either G-protein or tyrosine kinase mechanisms to activation of phospholipase C hydrolysis of phosphatidylinositol 4,5-bisphosphate.[6] PK-C binds tightly to a series of structurally different and complex natural products such as the phorbol esters,[7] ingenol esters,[8] mezerein,[7] bryostatins,[9] aplysiatoxins,[10] and teleocidins.[11] These ligands can function as powerful structural mimetics of DAG and display binding affinities several orders of magnitude higher than that of DAG.[7−11] The regulatory domain of classical (α, β, and γ) as well as novel (δ, ϵ, η, and θ) PK-C isozymes contains two tandem cysteine-rich structures (C1a and C1b) which can bind independently to phorbol esters and the other ligands with high affinity.[12−14] During the past several years, we have sought to design synthetically accessible PK-C ligands based on the simpler structure of DAG.[15−20] With the combined use of pharmacophore- and receptor-guided approaches, which have been greatly facilitated by the crystal structure of the PK-Cδ−phorbol-13-acetate complex,[21] we have successfully obtained structurally simple and yet powerful PK-C ligands that display binding affinities in the low nanomolar range.[1,20] These molecules have been derived by constraining the glycerol backbone of DAG into a five-membered, 5,5-disubstituted-tetrahydro-2-furanone template (DAG lactone) exemplified in compounds **1**−**5** (Table 1). In the course of these studies, we discovered that the location of the required lipophilic group −which is essential for partitioning and transport between biological membranes− had an important effect in improving affinity.[1,20] As seen in Table 1, the transposition of the large aliphatic chain from the acyl position (*sn*-1) in compound **1** to the α-alkylidene position (*sn*-2) in compound **2** resulted in a 4-fold increase in binding affinity. Through a systematic search that involved modifying the DAG lactone template with a combination of linear or branched acyl and α-alkylidene chains, we were able to optimize hydrophobic contacts with a group of conserved hydrophobic amino acids located on the top half of the C1 domain that resulted in increased binding affinity.[1] The best results were achieved when the lipophilic groups were evenly distributed between the acyl branch and α-alkylidene chain (compounds **3**−**5**, Table 1). These branched α-alkylidene and acyl chains

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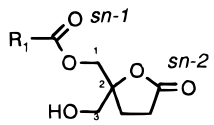
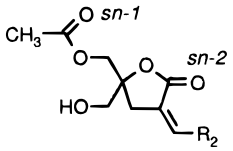
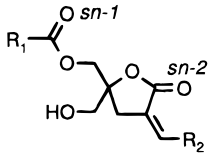
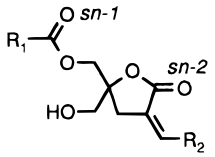
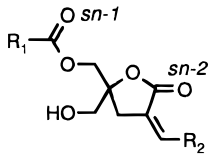
10.1021/jm990613q
Published on Web 08/04/2000

Table 1. PK-Cα Binding Affinity for a Group of Selected *sn*-2 DAG Lactones

DAG-lactone structure	Cpd. #	K_i (nM)
 R_1 = (Z)-$CH_3(CH_2)_7CH{=}CH(CH_2)_7$–	**1**	96±7.5
 R_2 = (Z)-$CH_3(CH_2)_7CH{=}CH(CH_2)_7$–	**2**	24±2.9
 R_1 = (*i*-Pr)$_2$CHCH$_2$– R_2 = $CH_3(CH_2)_8$–	**3**	13±0.4
 R_1 = $CH_3(CH_2)_8$– R_2 = (*i*-Pr)$_2$CHCH$_2$–	**4**	2.3±0.1
 R_1 = R_2 = (*i*-Pr)$_2$CHCH$_2$–	**5**	2.9±0.2

were of critical importance in reaching low-nanomolar binding affinities for PK-C. It is possible that these chains facilitate important van der Waals contacts with hydrophobic segments of the protein as suggested by our modeling studies.[1,20]

Another DAG lactone template that was previously investigated in our laboratory with some success was the 2,3-dideoxy-L-*threo*-hexono-1,4-lactone template, exemplified by compound **6** (Figure 1).[19] The most important structural feature in this template is that the lactone carbonyl is now equivalent to the *sn*-1 carbonyl of DAG, instead of the *sn*-2 carbonyl as in compounds **1**−**5**. In addition, there is an extra chiral center which, as we have previously shown, must have the *S*-configuration.[19] The main part of the glycerol backbone in this template is exocyclic, and the chirality of the *sn*-2 carbon must likewise be in the *S*-configuration, as in DAG, to produce an effective ligand.[19] The original investigation of this template was performed with the myristate ester **6** which displayed modest binding affinity for PK-C (K_i = 1000 nM).[19] In the present work, we investigate the effects of a combination of analogous linear or branched alkyl chains, which were so successful for the *sn*-2 DAG lactone template (Figure 1), on this alternative *sn*-1

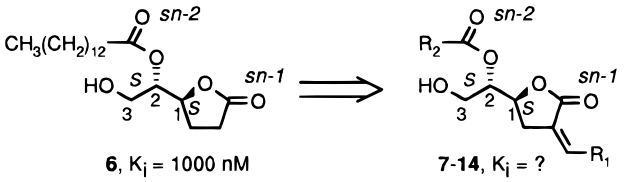
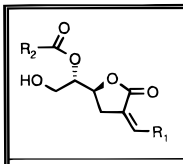


Figure 1. Design strategy for acyl (R_1) and α-alkylidene (R_2) *sn*-1 lactones.

Table 2. PK-Cα Binding Affinity (K_i) and Calculated log *P* for Acyl and α-Alkylidene *sn*-1 DAG Lactones (*Z*- and *E*-isomers)

	Cpd. #	*Z*-isomer K_i (nM)	Cpd. #	*E*-isomer K_i (nM)	Calcd. log P octanol/water
R_1 = R_2 = $CH_3(CH_2)_7$–	**7**	1,758 ±92	**8**	1,202 ±49	6.30
R_1 = $CH_3(CH_2)_7$– R_2 = (*i*-Pr)$_2$CHCH$_2$–	**9**	565 ±52	**10**	579 ±20	6.08
R_1 = (*i*-Pr)$_2$CHCH$_2$– R_2 = $CH_3(CH_2)_7$–	**11**	499 ±16	**12**	1,088 ±22	6.08
R_1 = R_2 = (*i*-Pr)$_2$CHCH$_2$–	**13**	327 ±10	**14**	679 ±21	5.86

DAG lactone template. With the advanced knowledge derived from our extensive investigation on the *sn*-2 DAG lactones, the two lipophilic chains were designed to be nearly equivalent (8 carbons). Thus, a small library of all possible combinations of linear and branched acyl (R_2) and α-alkylidene (R_1) chains (**7**−**14**, Table 2) was synthesized.

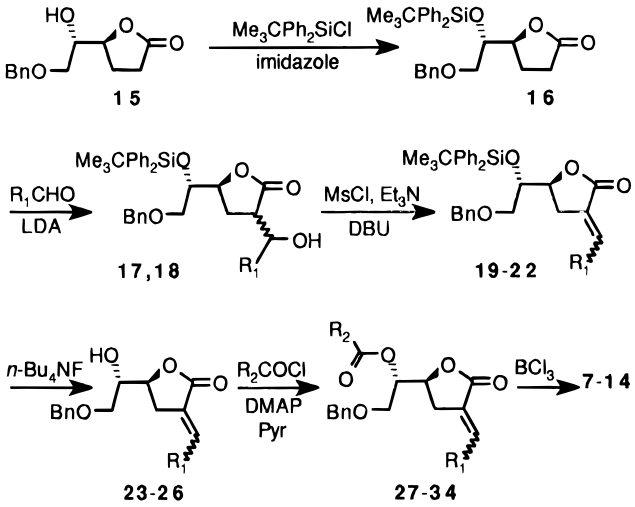
Chemistry

Starting with the known, optically active 6-*O*-benzyl-2,3-dideoxy-L-*threo*-hexono-1,4-lactone (**15**),[19] the enantiopure target compounds were synthesized using the general alkylation and acylation procedures illustrated in Scheme 1. As before, the structural assignment of the different geometrical isomers was determined by ^{1}H NMR spectroscopy where the *β*-vinyl proton of the *E*-isomers appears consistently ca. 0.5 ppm downfield from the corresponding *β*-vinyl proton of the *Z*-isomers.[1,16−18] The most serious challenge with these syntheses is the likelihood of acid-catalyzed acyl migration during the final deprotection step with BCl_3 and even during purification on silica gel column chromatography. Acyl migration is a recognized problem in the preparation of optically active diacylglycerols and related phospholipids.[22,23] We observed that when the acyl chain is branched, acyl migration does not occur, and the final compounds (**9**, **10**, **13**, **14**) could be purified safely by chromatography on silica gel. On the other hand, when the acyl chain is linear, purification of the final compounds was achieved after exhaustive washing with cold hexane or cold petroleum ether. Column chromatography in this instance was to be avoided. Finally, the octanol/water partition coefficients (log *P*) for compound **7**−**14** were calculated according to the fragment-based program KOWWIN 1.63[24] and are listed in Table 2.

Biological Results and Discussion

The interaction of the target *sn*-1 DAG lactones (**7**−**14**) with PK-C was assessed in terms of the ability of

Scheme 1



#	R_1	*Z*/*E*	R_2
17	$CH_3(CH_2)_7$–	—	—
18	$(i\text{-Pr})_2CHCH_2$–	—	—
19	$CH_3(CH_2)_7$–	*Z*	—
20	$CH_3(CH_2)_7$–	*E*	—
21	$(i\text{-Pr})_2CHCH_2$–	*Z*	—
22	$(i\text{-Pr})_2CHCH_2$–	*E*	—
23	$CH_3(CH_2)_7$–	*Z*	—
24	$CH_3(CH_2)_7$–	*E*	—
25	$(i\text{-Pr})_2CHCH_2$–	*Z*	—
26	$(i\text{-Pr})_2CHCH_2$–	*E*	—
27	$CH_3(CH_2)_7$–	*Z*	$CH_3(CH_2)_7$–
28	$CH_3(CH_2)_7$–	*E*	$CH_3(CH_2)_7$–
29	$CH_3(CH_2)_7$–	*Z*	$(i\text{-Pr})_2CHCH_2$–
30	$CH_3(CH_2)_7$–	*E*	$(i\text{-Pr})_2CHCH_2$–
31	$(i\text{-Pr})_2CHCH_2$–	*Z*	$CH_3(CH_2)_7$–
32	$(i\text{-Pr})_2CHCH_2$–	*E*	$CH_3(CH_2)_7$–
33	$(i\text{-Pr})_2CHCH_2$–	*Z*	$(i\text{-Pr})_2CHCH_2$–
34	$(i\text{-Pr})_2CHCH_2$–	*E*	$(i\text{-Pr})_2CHCH_2$–

the ligand to displace bound [20-^{3}H]phorbol 12,13-dibutyrate (PDBU) from a recombinant single isozyme (PK-Cα) in the presence of phosphatidylserine as already described.[15−20] The inhibition curves obtained for all ligands were of the type expected for competitive inhibition, albeit with minor deviations at high concentrations for some compounds, and the ID_{50} values were determined by fit of the data points to the theoretical noncooperative competition curve. The K_i's for inhibition of binding (Table 2) were calculated from the ID_{50} values. The main conclusion from this work is that the *sn*-1-DAG lactones are not efficient PK-C ligands despite having an array of linear or branched acyl (R_2) and α-alkylidene (R_1) chains similar to those of the very potent *sn*-2 DAG lactones (**3**−**5**, Table 1). Furthermore, the importance of balancing the molecules' lipophilic groups between the acyl (R_2) and α-alkylidene (R_1) chains did not have the same beneficial effect that was observed for the *sn*-2 DAG lactones (compare **3**−**5** versus **7**−**14**). Branching of either acyl (R_2) or α-alkylidene (R_1) chains resulted in less than a 2-fold increase in binding affinity (compounds **9**−**12**) relative to **6**, and only the doubly branched *Z*-isomer (**13**) had a K_i value that was 3-fold lower (3-fold more potent) than that of the parent **6**. However, even **13**, with an identical set of substituents as the doubly branched *sn*-2 DAG lactone **5** (*Z*-isomer), was more than 2 orders of magnitude less potent than **5**! This means that *sn*-1 DAG lactones are not as good ligands as the *sn*-2 DAG lactones and that the presence of branched alkyl or acyl chains in the former has a minimal beneficial effect at best. Therefore, lactonization at *sn*-1 is not a productive strategy since these templates probably do not fit adequately into the active site of PK-C, despite having a similar hydrophobic/hydrophilic balance (log *P*) as the *sn*-2 DAG lactones. It is possible that the best *sn*-1 DAG lactones (*Z*-isomers **11** and **13**) are in fact attempting to bind to PK-C as the *sn*-2 DAG lactones. This will happen if the *sn*-1 lactone carbonyl in these compounds is directed into the same binding area as the *sn*-2 lactone carbonyl of DAG lactones **3**−**5**. Indeed, a perfect overlay between the two lactone rings and their corresponding α-alkylidene chains is possible between compounds **13** and **5** (Figure 2, left). However, as in DAG, the two carbonyls are not equivalent and they probably engage in hydrogen-bonding interactions with different parts of the receptor. Therefore, such a binding mode for the *sn*-1 DAG lactones may not be productive. Besides, the remaining critical CH_2OH pharmacophore can orient its OH group into a different domain in each lactone as the C−CH_2-(OH) torsion angle rotates freely. Consequently, the two hydroxyl groups in each molecule are able to overlap only at the tangent of their trajectories (Figure 2, left). The alternative binding mode (Figure 2, right) shows a

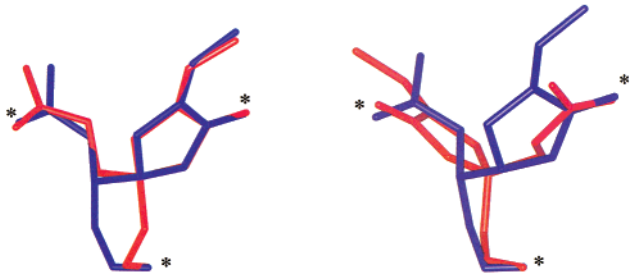


Figure 2. Plot showing two superimpositions of the two DAG lactone templates using the torsional flexible fit method of Quanta 97 (Molecular Simulation Inc.). The *sn*-2 lactone template is depicted in red. The asterisks show the three pharmacophore functional groups that were used for the fit.

better overlap of the polar pharmacophores but a poorer overlap of the important akyl chains. These apparently subtle, albeit important, differences may explain the contrast between otherwise deceptively similar lactone templates which the enzyme is uniquely capable of discriminating.

Experimental Section

General Experimental. All chemical reagents were commercially available. Melting points were determined on a MelTemp II apparatus, Laboratory Devices, and are uncorrected. Silica gel chromatography was performed on silica gel 60, 230−400 mesh (E. Merck). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-250 instrument at 250 and 62.9 MHz, respectively. Spectra were referenced to the solvent in which they were run (7.24 ppm for $CDCl_3$). Infrared spectra were recorded on a Perkin-Elmer 1600 Series FTIR, and specific rotations were measured in a Perkin-Elmer model 241 polarimeter. Positive-ion fast-atom bombardment mass spectra (FABMS) were obtained on a VG 7070E mass spectrometer at an accelerating voltage of 6 kV and a resolution of 2000. Glycerol was used as the sample matrix, and ionization was effected by a beam of xenon atoms. Elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, GA.

5(*S*)-[1(*S*)-(2,2-Dimethyl-1,1-diphenyl-1-silapropoxy)-2-(phenylmethoxy)ethyl]oxolan-2-one (16). *tert*-Butylchlorodiphenylsilane (9.13 mL, 35.1 mmol) was added over a period of 10 min to a chilled (0 °C) solution of **15**[19] (6.38 g, 27.0 mmol) and imidazole (7.36 g, 108 mmol) in DMF (90 mL). The reaction mixture was allowed to reach room temperature, and stirring was continued for a total of 17 h. After the addition of a saturated aqueous solution of ammonium chloride (30 mL), the mixture was extracted with Et_2O (600 mL). The organic extract was washed with water (300 mL), dried over $MgSO_4$, and concentrated. The residue was purified by flash column chromatography over silica gel with mixtures of EtOAc/hexane (1:6) as eluant to give the silylated compound **16** (9.29 g, 19.6 mmol, 73%) as an oil: $[\alpha]^{27}_D$ +47.32° (*c* 3.93, $CHCl_3$); IR ($CHCl_3$) 3042−2863, 1770 (C═O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.76−7.17 (m, 15 H, Ph), 4.81 (ddd, 1 H, *J* = 7.1, 7.1, 2.9 Hz, H-5), 4.37 (AB d, 1 H, *J* = 11.7 Hz, PhC*H*HO), 4.25 (AB d, 1 H, *J* = 11.5 Hz, PhCH*H*O), 3.95 (m, 1 H, C*H*OSi), 3.63 (ABX dd, 1 H, *J* = 9.5, 7.1 Hz, BnOC*H*H), 3.49 (ABX dd, 1 H, *J* = 9.5, 4.9 Hz, BnOCH*H*), 2.75−2.48 (m, 2 H, H-3), 2.27 (d, 1 H, *J* = 8.3 Hz, H-4a), 2.21 (d, 1 H, *J* = 8.3 Hz, H-4b), 1.13 (s, 9 H, *t*-Bu); FAB MS (*m*/*z*, relative intensity) 473 ($MH^+ - H_2$, 1.3), 417 ($MH^+ - C_4H_{10}$, 1.3), 397 (MH^+ − PhH, 3.2), 367 (MH^+ − $PhCH_2OH$, 1.5), 91 ($PhCH_2^+$, 100). Anal. ($C_{29}H_{34}O_4Si$) C, H.

Standard Alkylation Procedure. This procedure was essentially identical to that reported previously.[1] To a solution of lactone **16** in THF (5 mL/mmol) maintained under argon at −78 °C was added dropwise lithium diisopropylamide (1.4 equiv, 2 M solution in heptane/THF/ethylbenzene) and stirred at −78 °C for 2 h. To the formed lithium enolate a solution of the aldehyde (2−4 equiv) in THF (1 mL/mmol) was added dropwise and the stirring continued at −78 °C for 4 h, followed by quenching by the slow addition of a saturated aqueous solution of ammonium chloride (1.25 mL/mmol). The mixture was warmed to room temperature and extracted three times with Et_2O (4.15 mL/mmol). The combined extracts were washed three times with water (2.50 mL/mmol), twice with brine (2.50 mL/mmol), dried ($MgSO_4$), and filtered. Concentration of the filtrate under reduced pressure gave the crude alkylation products which were used directly in the following step without further purification.

Standard Mesylation−Olefination Procedure. This procedure was also based on the same reference. To a stirred solution of the alkylation product in CH_2Cl_2 (10 mL/mmol) were added methanesulfonyl chloride (2 equiv) and triethylamine (4 equiv) at 0 °C. The stirring was continued at 0 °C for 30 min and then at room temperature for 2 h. 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU; 5 equiv) was added while at 0 °C and stirring continued overnight at ambient temperature. The reaction mixture was concentrated and filtered through a pad of silica gel. The filtrate was concentrated and purified by flash column chromatography over silica gel with mixtures of EtOAc/hexane as eluant to give the desired products.

5(*S*)-[1(*S*)-(2,2-Dimethyl-1,1-diphenyl-1-silapropoxy)-2-(phenylmethoxy)ethyl]-3-(hydroxynonyl)oxolan-2-one (17). This compound was obtained as an oil from lactone **16** (0.980 g, 2.07 mmol) and *n*-nonanal (4 equiv). It corresponds to a mixture of diastereoisomers which was used directly in the subsequent step.

5(*S*)-[1(*S*)-(2,2-Dimethyl-1,1-diphenyl-1-silapropoxy)-2-(phenylmethoxy)ethyl]-3-[1-hydroxy-4-methyl-3-(methylethyl)pentyl]oxolan-2-one (18). This compound was obtained as an oil from lactone **16** (1 g, 2.11 mmol) and 4-methyl-3-(methylethyl)pentanal (2 equiv). It corresponds to a mixture of diastereoisomers which was used directly in the subsequent step.

(*Z*)-5(*S*)-[1(*S*)-(2,2-Dimethyl-1,1-diphenyl-1-silapropoxy)-2-(phenylmethoxy)ethyl]-3-nonylideneoxolan-2-one (19) and (*E*)-5(*S*)-[1(*S*)-(2,2-Dimethyl-1,1-diphenyl-1-silapropoxy)-2-(phenylmethoxy)ethyl]-3-nonylideneoxolan-2-one (20). Under standard mesylation−olefination conditions the above mixture of diastereoisomers (**17**) was converted into a separable mixture of olefins. In order of elution, the *Z*-isomer **19** (0.228 g, 0.381 mmol, 19%) was followed by the *E*-isomer **20** (0.493 g, 0.823 mmol, 40%) after silica gel chromatography with EtOAc:hexane (1:19).

Compound 19: oil; $[\alpha]^{27}_D$ +25.59° (*c* 0.94, $CHCl_3$); IR ($CHCl_3$) 3018−2895, 1748 (C═O), 1669 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.74−7.13 (m, 15 H, Ph), 6.19 (m, 1 H, >C═C*H*$(CH_2)_7CH_3$), 4.75 (m, 1 H, H-5), 4.35 (AB d, 1 H, *J* = 11.5 Hz, PhC*H*HO), 4.22 (AB d, 1 H, *J* = 11.7 Hz, PhCH*H*O), 3.90 (m, 1 H, C*H*OSi), 3.67 (ABX dd, 1 H, *J* = 9.3, 7.6 Hz, BnOC*H*H), 3.47 (ABX dd, 1 H, *J* = 9.5, 5.1 Hz, BnOCH*H*), 2.93−2.86 (m, 2 H, H-4), 2.85−2.71 (m, 2 H, >C═CHC*H*$_2$$(CH_2)_6CH_3$), 1.50−1.30 (m, 12 H, >C═CHCH$_2$(C*H*$_2$$)_6CH_3$), 1.08 (s, 9 H, *t*-Bu), 0.96 (br t, 3 H, >C═CHCH$_2$$(CH_2)_6$C*H*$_3$); ^{13}C NMR ($CDCl_3$) δ 169.71, 143.65, 137.65, 135.75, 135.56, 133.64, 132.67, 129.72, 129.56, 128.08, 127.54, 127.49, 127.37, 127.30, 124.15, 75.80, 73.43, 73.09, 70.27, 31.79, 29.64, 29.37, 29.26, 29.17, 29.09, 27.51, 26.75, 22.60, 14.04; FAB MS (*m*/*z*, relative intensity) 597 ($MH^+ - H_2$, 2.7), 541 ($MH^+ - C_4H_{10}$, 4.7), 521 (MH^+ − PhH, 8.8), 491 (MH^+ − $PhCH_2OH$, 3.5), 413 [MH^+ − (PhH + $PhCH_2OH$), 19], 135 ($PhSiOCH_2^+$, 100). Anal. ($C_{38}H_{50}O_4Si$), C, H.

Compound 20: oil; $[\alpha]^{27}_D$ +51.94° (*c* 0.93, $CHCl_3$); IR ($CHCl_3$) 3019−2858, 1749 (C═O), 1679 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.73−7.13 (m, 15 H, Ph), 6.81 (m, 1 H, >C═C*H*$(CH_2)_7CH_3$), 4.84 (m, 1 H, H-5), 4.35 (AB d, 1 H, *J* = 11.5 Hz, PhC*H*HO), 4.22 (AB d, 1 H, *J* = 11.7 Hz, PhCH*H*O), 3.93 (m, 1 H, C*H*OSi), 3.68 (ABX dd, 1 H, *J* = 9.3, 7.6 Hz, BnOC*H*H), 3.48 (ABX dd, 1 H, *J* = 9.3, 5.1 Hz, BnOCH*H*), 2.88−2.82 (m, 2 H, H-4), 2.19 (br q, 2 H, *J* ≈ 7.1 Hz, >C═CHC*H*$_2$$(CH_2)_6CH_3$), 1.58−1.30 (m, 12 H, >C═CHCH$_2$(C*H*$_2$$)_6CH_3$), 1.06 (s, 9 H, *t*-Bu), 0.98 (br t, 3 H, >C═CHCH$_2$$(CH_2)_6$C*H*$_3$); ^{13}C NMR ($CDCl_3$) δ 170.94, 140.12, 137.60, 135.73, 135.55, 133.54, 132.57, 129.77, 129.60, 128.09, 127.60, 127.53, 127.41, 126.13, 76.19, 73.36, 73.12, 70.26, 31.78, 30.18, 29.64, 29.33, 29.14, 28.02, 27.08, 26.72, 22.60, 14.05; FAB MS (*m*/*z*, relative intensity) 597 ($MH^+ - H_2$, 3.3), 541 ($MH^+ - C_4H_{10}$, 2.4), 521 (MH^+ − PhH, 7.0), 491 (MH^+ − $PhCH_2OH$, 7.0), 413 [MH^+ − (PhH + $PhCH_2OH$), 20], 91 ($PhCH_2^+$, 100). Anal. ($C_{38}H_{50}O_4Si$·0.5H_2O) C, H.

(*Z*)-5(*S*)-[1(*S*)-(2,2-Dimethyl-1,1-diphenyl-1-silapropoxy)-2-(phenylmethoxy)ethyl]-3-[4-methyl-3-(methylethyl)-pentylidene]oxolan-2-one (21) and (*E*)-5(*S*)-[1(*S*)-(2,2-Dimethyl-1,1-diphenyl-1-silapropoxy)-2-(phenylmethoxy)-ethyl]-3-[4-methyl-3-(methylethyl)pentylidene]oxolan-2-one (22). Under standard mesylation−olefination conditions the above mixture of diastereoisomers (**18**) was converted into a separable mixture of olefins. In order of elution, the *Z*-isomer **21** (0.402 g, 0.670 mmol, 32%) was followed by the *E*-isomer **22** (0.735 g, 1.23 mmol, 58%) after silica gel chromatography with EtOAc:hexane (1:19).

Compound 21: oil; $[\alpha]^{27}_D$ +22.77° (*c* 2.37, $CHCl_3$); IR

($CHCl_3$) 3071−2861, 1748 (C═O), 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.75−7.14 (m, 15 H, Ph), 6.22 (br t, 1 H, >C═C*H*CH_2CH(*i*-Pr)$_2$), 4.74 (m, 1 H, H-5), 4.36 (AB d, 1 H, J = 11.7 Hz, PhC*H*HO), 4.23 (AB d, 1 H, J = 11.7 Hz, PhCH*H*O), 3.92 (m, 1 H, C*H*OSi), 3.67 (ABX dd, 1 H, J = 9.3, 7.1 Hz, BnOC*H*H), 3.48 (ABX dd, 1 H, J = 9.5, 5.1 Hz, BnOCH*H*), 3.01−2.90 (m, 3 H, H-4$_a$, >C═CHCH_2CH(*i*-Pr)$_2$), 2.72−2.61 (m, 1 H, H-4$_b$), 1.90−1.80 (m, 2 H, 2 × C*H*Me_2), 1.18 (m, 1 H, *H*C(*i*-Pr)$_2$), 1.01 (s, 9 H, *t*-Bu), 0.99 (d, 6 H, J = 6.8 Hz, HC(CH_3)$_2$), 0.96 and 0.94 (doublets, 6 H, J = 2.7 Hz, HC(CH_3)$_2$); ^{13}C NMR ($CDCl_3$) δ 169.70, 145.69, 137.67, 135.78, 135.59, 133.67, 132.68, 129.73, 129.56, 128.08, 127.56, 127.49, 127.38, 123.20, 75.83, 73.33, 73.09, 70.32, 51.10, 30.56, 29.31, 29.17, 26.77, 25.99, 21.62, 21.52, 19.61, 19.34; FAB MS (*m*/*z*, relative intensity) 597 ($MH^+ - H_2$, 2.5), 541 ($MH^+ - C_4H_{10}$, 3.7), 521 (MH^+ − PhH, 7.1), 491 (MH^+ − $PhCH_2OH$, 3.9), 413 [MH^+ − (PhH + $PhCH_2$-OH), 15], 135 ($PhSiOCH_2^+$, 100). Anal. ($C_{38}H_{50}O_4Si$) C, H.

Compound 22: oil; $[\alpha]^{27}_D$ +58.01° (*c* 1.67, $CHCl_3$); IR ($CHCl_3$) 3020−2865, 1748 (C═O), 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.75−7.14 (m, 15 H, Ph), 6.86 (m, 1 H, >C═C*H*CH_2CH(*i*-Pr)$_2$), 4.83 (m, 1 H, H-5), 4.36 (AB d, 1 H, J = 11.5 Hz, PhC*H*HO), 4.23 (AB d, 1 H, J = 11.7 Hz, PhCH*H*O), 3.96 (m, 1 H, C*H*OSi), 3.68 (ABX dd, 1 H, J = 9.3, 7.6 Hz, BnOC*H*H), 3.49 (ABX dd, 1 H, J = 9.5, 5.1 Hz, BnOCH*H*), 2.89−2.83 (m, 2 H, H-4), 2.18−2.08 (m, 2 H, >C═CHCH_2CH(*i*-Pr)$_2$), 1.87 (heptuplet, 2 H, 2 × C*H*Me_2), 1.28 (m, 1 H, *H*C(i-Pr)$_2$), 1.08 (s, 9 H, *t*-Bu), 1.00 and 0.97 (doublets, 6 H, J = 3.0 Hz, HC(CH_3)$_2$), 0.95 and 0.92 (doublets, 3 H, J = 1.7 Hz, HC(CH_3)$_2$); ^{13}C NMR ($CDCl_3$) δ 170.93, 141.87, 137.60, 135.73, 135.56, 133.56, 132.60, 129.77, 129.60, 128.10, 127.61, 127.52, 127.42, 125.31, 76.27, 73.26, 73.12, 70.30, 50.11, 29.19, 29.01, 28.46, 27.18, 26.75, 21.67, 21.39, 19.53, 19.20; FAB MS (*m*/*z*, relative intensity) 597 ($MH^+ - H_2$, 5.8), 541 ($MH^+ - C_4H_{10}$, 6.2), 521 (MH^+ − PhH, 16), 491 (MH^+ − $PhCH_2OH$, 11), 413 [MH^+ − (PhH + $PhCH_2OH$), 27], 57 ($C_4H_9^+$, 100). Anal. ($C_{38}H_{50}O_4Si$·0.2H_2O) C, H.

Standard Desilylation Procedure. A stirred solution of the silylated compound in THF (12 mL/mmol) maintained under argon at 0 °C was treated dropwise with tetrabutylammonium fluoride (1.5 equiv, 2 M solution in THF) and stirred at 0 °C for 40 min. After the solvent was removed, the residue was purified by flash column chromatography on silica gel with mixtures of EtOAc/hexane as eluant to give the deprotected products.

(*Z*)-5(*S*)-[1(*S*)-Hydroxy-2-(phenylmethoxy)ethyl]-3-nonylideneoxolan-2-one (23). Under the standard desilylation conditions, compound **19** (0.540 g, 0.902 mmol) was deblocked. The crude product was purified by column chromatography with different gradients of EtOAc/hexane (1:3 and 3:7) to give **23** (0.309 g, 0.857 mmol, 95%) as a clear oil: $[\alpha]_D^{27}$ +24.57° (*c* 1.05, $CHCl_3$); IR ($CHCl_3$) 3585 (OH), 3021−2856, 1753 (C═O), 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.47−7.34 (m, 5 H, Ph), 6.29 (tt, 1 H, J = 7.7, 2.2 Hz, >C═C*H*(CH_2)$_7$CH_3), 4.66−4.60 (m, 1 H, H-5), 4.65 (s, 2 H, $PhCH_2O$), 3.89 (m, 1 H, C*H*OH), 3.69 (d, 2 H, J = 5.6 Hz, BnOCH_2), 2.96 (m, 2 H, H-4), 2.80−2.72 (m, 2 H, >C═CHCH_2(CH_2)$_6$CH_3), 2.44 (d, 1 H, J = 4.6 Hz, OH), 1.53−1.25 (m, 12 H, >C═CHCH_2(CH_2)$_6$CH_3), 0.96 (br t, 3 H, >C═CH(CH_2)$_7$CH_3); ^{13}C NMR ($CDCl_3$) δ 169.26, 144.52, 137.45, 128.35, 127.78, 127.67, 123.58, 76.36, 73.55, 71.91, 70.49, 31.78, 30.78, 29.33, 29.19, 29.15, 29.03, 27.57, 22.59, 14.05; FAB MS (*m*/*z*, relative intensity) 361 (MH^+, 29), 359 ($MH^+ - H_2$, 19), 91 ($PhCH_2^+$, 100). Anal. ($C_{22}H_{32}O_4$·1.1H_2O) C, H.

(*E*)-5(*S*)-[1(*S*)-Hydroxy-2-(phenylmethoxy)ethyl]-3-nonylideneoxolan-2-one (24). Under the standard desilylation conditions, compound **20** (0.706 g, 1.18 mmol) was deblocked. The crude product was purified by column chromatography with different gradients of EtOAc/hexane (1:3 and 3:7) to give **24** (0.331 g, 0.917 mmol, 78%) as a clear oil: $[\alpha]_D^{27}$ +46.71° (*c* 0.87, $CHCl_3$); IR ($CHCl_3$) 3585 (OH), 3020−2857, 1753 (C═O), 1679 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.51−7.31 (m, 5 H, Ph), 6.80 (tt, 1 H, J = 7.6, 2.9 Hz, >C═C*H*(CH_2)$_7$CH_3), 4.72−4.66 (ddd, 1 H, J = 10.7, 3.7, 3.7 Hz, H-5), 4.64 (s, 2 H, $PhCH_2O$), 3.91−3.87 (m, 1 H, C*H*OH), 3.71 (d, 2 H, J = 5.9 Hz, BnOCH_2), 2.90 (m, 2 H, H-4), 2.70−2.50 (br s, 1 H, OH), 2.24 (br q, 2 H, $J \approx$ 7.3 Hz, >C═CHCH_2(CH_2)$_6$CH_3), 1.59−1.28 (m, 12 H, >C═CHCH_2(CH_2)$_6$CH_3), 0.96 (br t, 3 H, >C═CH(CH_2)$_7$CH_3); ^{13}C NMR ($CDCl_3$) δ 170.63, 140.97, 137.47, 128.34, 127.75, 127.68, 125.56, 76.66, 73.52, 71.86, 70.57, 31.76, 30.18, 29.29, 29.26, 29.12, 28.03, 27.13, 22.57, 14.03; FAB MS (*m*/*z*, relative intensity) 361 (MH^+, 39), 359 ($MH^+ - H_2$, 7.1), 91 ($PhCH_2^+$, 100). Anal. ($C_{22}H_{32}O_4$·0.2H_2O) C, H.

(*Z*)-5(*S*)-[1(*S*)-Hydroxy-2-(phenylmethoxy)ethyl]-3-[4-methyl-3-(methylethyl)pentylidene]oxolan-2-one (25). Under the standard desilylation conditions, compound **21** (0.618 g, 1.03 mmol) was deblocked. The crude product was purified by column chromatography with different gradients of EtOAc/hexane (1:3 and 3:7) to give **25** (0.350 g, 0.972 mmol, 94%) as a clear oil: $[\alpha]^{27}_D$ +28.48° (*c* 1.45, $CHCl_3$); IR ($CHCl_3$) 3583 (OH), 3020−2872, 1752 (C═O), 1666 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.47−7.34 (m, 5 H, Ph), 6.30 (br t, 1 H, $J \approx$ 7.4 Hz, >C═C*H*CH_2CH(*i*-Pr)$_2$), 4.65−4.59 (m, 1 H, H-5), 4.64 (s, 2 H, $PhCH_2O$), 3.88 (dd, 1 H, J = 9.5, 5.4 Hz, C*H*OH), 3.69 (d, 2 H, J = 5.6 Hz, BnOCH_2), 2.96 (m, 2 H, H-4), 2.79 (m, 2 H, >C═CHCH_2CH(*i*-Pr)$_2$), 2.28 (s, 1 H, OH), 1.85 (heptuplet, 2 H, 2 × C*H*Me_2), 1.18 (quintuplet, 1 H, *H*C(*i*-Pr)$_2$), 0.98 (d, 6 H, J = 6.6 Hz, HC(CH_3)$_2$), 0.94 (d, 6 H, J = 6.8 Hz, HC(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 169.33, 146.50, 137.46, 128.35, 127.76, 127.66, 122.58, 76.33, 73.54, 71.91, 70.51, 51.10, 30.95, 29.29, 29.25, 26.14, 21.60, 21.55, 19.41, 19.39; FAB MS (*m*/*z*, relative intensity) 361 (MH^+, 61), 359 ($MH^+ - H_2$, 34), 57 ($C_4H_9^+$, 100). Anal. ($C_{22}H_{32}O_4$·0.2H_2O) C, H.

(*E*)-5(*S*)-[1(*S*)-Hydroxy-2-(phenylmethoxy)ethyl]-3-[4-methyl-3-(methylethyl)pentylidene]oxolan-2-one (26). Under the standard desilylation conditions, compound **22** (1.24 g, 2.07 mmol) was deblocked. The crude product was purified by column chromatography with EtOAc/hexane (1:3) to give **26** (0.684 g, 1.90 mmol, 92%) as a clear oil: $[\alpha]_D^{27}$ +40.91° (*c* 2.08, $CHCl_3$); IR ($CHCl_3$) 3583 (OH), 3020−2873, 1752 (C═O), 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.47−7.34 (m, 5 H, Ph), 6.85 (m, 1 H, >C═C*H*CH_2CH(*i*-Pr)$_2$), 4.70 (ddd, 1 H, J = 7.1, 7.1, 3.4 Hz, H-5), 4.64 (s, 2 H, $PhCH_2O$), 3.91 (m, 1 H, C*H*OH), 3.71 (d, 2 H, J = 5.6 Hz, BnOCH_2), 2.91 (m, 2 H, H-4), 2.65 (s, 1 H, OH), 2.19 (br t, 2 H, >C═CHCH_2CH(*i*-Pr)$_2$), 1.85 (heptuplet, 2 H, C*H*Me_2), 1.28 (quintuplet, 1 H, *H*C(*i*-Pr)$_2$), 0.98 (d, 6 H, J = 6.8 Hz, HC(CH_3)$_2$), 0.93 (d, 6 H, J = 6.8 Hz, HC(CH_3)$_2$); ^{13}C NMR ($CDCl_3$) δ 170.67, 142.74, 137.49, 128.34, 127.75, 127.68, 124.62, 76.65, 73.52, 71.86, 70.58, 50.21, 29.17, 29.12, 28.58, 27.30, 21.57, 21.53, 19.32, 19.30; FAB MS (*m*/*z*, relative intensity) 361 (MH^+, 69), 359 ($MH^+ - H_2$, 11), 91 ($PhCH_2^+$, 100). Anal. ($C_{22}H_{32}O_4$·0.1H_2O) C, H.

Standard Acylation Procedure. A stirred solution of the corresponding alcohol in CH_2Cl_2 (10 mL/mmol) was treated with pyridine (4 equiv), 4-(dimethylamino)pyridine (0.1 equiv) and the corresponding acyl chloride (2−4 equiv). The solution was maitained at room temperature for 3 h, concentrated and purified by flash column chromatography on silica gel with mixtures of EtOAc/hexane as eluant to give the acylated product.

(*Z*)-1(*S*)-[4-Nonylidene-3-oxo(2-oxolan-1(*S*)-yl)]-2-(phenylmethoxy)ethyl Nonanoate (27). By the standard acylation procedure alcohol **23** (0.045 g, 0.125 mmol) was reacted with 4 equiv of nonanoyl chloride to give **27** (0.060 g, 0.120 mmol, 96%) as a clear oil after chromatography with EtOAc/hexane (1:9): $[\alpha]_D^{25}$ +12.08° (*c* 1.57, $CHCl_3$); IR ($CHCl_3$) 3026−2856, 1747 (C═O), 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.47−7.34 (m, 5 H, Ph), 6.24 (m, 1 H, >C═C*H*(CH_2)$_7$CH_3), 5.21 (ddd, 1 H, J = 6.1, 6.1, 3.1 Hz, C*H*OCO(CH_2)$_7$CH_3), 4.86 (heptuplet, 1 H, H-1), 4.65 (AB d, 1 H, J = 11.7 Hz, PhC*H*HO), 4.58 (AB d, 1 H, J = 12.0 Hz, PhCH*H*O), 3.78 (ABX dd, 1 H, J = 10.0, 6.4 Hz, BnOC*H*H), 3.70 (ABX dd, 1 H, J = 10.0, 5.9 Hz, BnOC*H*H), 3.03 (br ddm, 1 H, H-5$_a$), 2.83−2.65 (m, 3 H, H-5$_b$, >C═CHCH_2(CH_2)$_6$CH_3), 2.37 (t, 2 H, J = 7.5 Hz, COCH_2(CH_2)$_6$-CH_3), 1.66 (m, 2 H, COCH$_2$CH_2(CH_2)$_5$CH_3), 1.55−1.25 (m, 22 H, CO(CH_2)$_2$(CH_2)$_5$CH_3, >C═CHCH$_2$(CH_2)$_6$CH_3), 1.01−0.93 (distorted t, 6 H, 2 × CH_3); ^{13}C NMR ($CDCl_3$) δ 173.02, 169.02, 143.97, 137.46, 128.29, 127.68, 127.52, 123.26, 74.18, 73.36, 72.41, 67.85, 34.14, 31.78, 31.73, 30.99, 29.35, 29.24, 29.14,

29.09, 29.05, 27.53, 24.81, 22.59, 22.57, 14.03; FAB MS (*m*/*z*, relative intensity) 501 (MH^+, 16), 393 ($MH^+ - PhCH_2OH$, 13), 91 ($PhCH_2^+$, 100). Anal. ($C_{31}H_{48}O_5 \cdot 0.3H_2O$) C, H.

(*E*)-1(*S*)-[4-Nonylidene-3-oxo(2-oxolan-1(*S*)-yl)]-2-(phenylmethoxy)ethyl Nonanoate (28). By the standard acylation procedure alcohol **24** (0.074 g, 0.206 mmol) was reacted with 4 equiv of nonanoyl chloride to give **28** (0.099 g, 0.197 mmol, 96%) as a clear oil after chromatography with EtOAc/hexane (1:9): $[\alpha]_D^{26}$ +38.23° (*c* 2.13, $CHCl_3$); IR ($CHCl_3$) 3019−2858, 1749 (C=O), 1679 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.47−7.34 (m, 5 H, Ph), 6.79 (tt, 1 H, *J* = 7.5, 2.9 Hz, >C=C*H*(CH_2)$_7CH_3$), 5.23 (ddd, 1 H, *J* = 6.1, 6.1, 3.0 Hz, C*H*OCO(CH_2)$_7CH_3$), 4.94 (heptuplet, 1 H, H-1), 4.66 (AB d, 1 H, *J* = 11.7 Hz, PhC*H*HO), 4.58 (AB d, 1 H, *J* = 12.0 Hz, PhCH*H*O), 3.79 (ABX dd, 1 H, *J* = 9.8, 6.4 Hz, BnOC*H*H), 3.71 (ABX dd, 1 H, *J* = 9.8, 5.9 Hz, BnOCH*H*), 2.97 (ddm, 1 H, H-5_a), 2.66 (dm, 1 H, H-5_b), 2.35 (t, 2 H, *J* = 7.7 Hz, COCH_2(CH_2)$_6CH_3$), 2.20 (br q, 2 H, *J* ≈ 7.3 Hz, >C=CHCH_2(CH_2)$_6CH_3$), 1.64 and 1.52 (multiplets, 4 H, $COCH_2CH_2(CH_2)_5CH_3$, >C=$CHCH_2CH_2(CH_2)_5CH_3$), 1.42−1.25 (m, 20 H, CO(CH_2)$_2$(CH_2)$_5CH_3$, >C=CH(CH_2)$_2$(CH_2)$_5CH_3$), 1.02−0.92 (distorted t, 6 H, 2 × CH_3); ^{13}C NMR ($CDCl_3$) δ 173.02, 170.24, 140.67, 137.44, 128.30, 127.70, 127.55, 125.14, 74.47, 73.40, 72.44, 67.84, 34.09, 31.76, 31.73, 30.15, 29.29, 29.12, 29.03, 28.08, 27.38, 24.80, 22.57, 14.02; FAB MS (*m*/*z*, relative intensity) 501 (MH^+, 20), 393 ($MH^+ - PhCH_2OH$, 16), 361 ($MH^+ - C_7H_{15}CH$=C=O, 3.5), 91 ($PhCH_2^+$, 100). Anal. ($C_{31}H_{48}O_5$) C, H.

(*Z*)-1(*S*)-[4-Nonylidene-3-oxo(2-oxolan-1(*S*)-yl)]-2-(phenylmethoxy)ethyl 4-Methyl-3-(methylethyl)pentanoate (29). By the standard acylation procedure alcohol **23** (0.049 g, 0.136 mmol) was reacted with 2 equiv of 4-methyl-3-(methylethyl)-pentanoyl chloride[1,25] to give **29** (0.044 g, 0.088 mmol, 65%) as a clear oil after chromatography with EtOAc/hexane (1:9): $[\alpha]_D^{26}$ +10.0° (*c* 0.65, $CHCl_3$); IR ($CHCl_3$) 3021−2855, 1748 (C=O), 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.46−7.34 (m, 5 H, Ph), 6.25 (tt, 1 H, *J* = 7.6, 2.0 Hz, >C=C*H*(CH_2)$_7CH_3$), 5.20 (heptuplet, 1 H, C*H*OCOCH_2CH(*i*-Pr)$_2$), 4.88 (heptuplet, 1 H, H-1), 4.64 (AB d, 1 H, *J* = 12.0 Hz, PhC*H*HO), 4.58 (AB d, 1 H, *J* = 12.0 Hz, PhCH*H*O), 3.78 (ABX dd, 1 H, *J* = 9.8, 6.4 Hz, BnOC*H*H), 3.71 (ABX dd, 1 H, *J* = 9.8, 5.9 Hz, BnOCH*H*), 3.03 (br ddm, 1 H, H-5_a), 2.85−2.67 (m, 3 H, H-5_b, >C=CHCH_2(CH_2)$_6CH_3$), 2.25 (d, 2 H, *J* = 5.4 Hz, COCH_2CH(*i*-Pr)$_2$), 1.80 (heptuplet, 2 H, 2 × C*H*(CH_3)$_2$), 1.72−1.63 (m, 1 H, $COCH_2CH$(*i*-Pr)$_2$), 1.52−1.18 (m, 12 H, >C=CHCH_2(CH_2)$_6$-CH_3), 1.00−0.80 (m, 15 H, 2 × HC(CH_3)$_2$, >C=CH(CH_2)$_7$CH_3); ^{13}C NMR ($CDCl_3$) δ 174.08, 169.02, 144.06, 137.47, 128.27, 127.66, 127.52, 123.27, 74.14, 73.36, 72.43, 67.78, 46.58, 32.85, 31.78, 30.88, 29.63, 29.33, 29.24, 29.14, 29.12, 27.53, 22.59, 21.27, 21.24, 18.70, 18.67, 14.03; FAB MS (*m*/*z*, relative intensity) 501 (MH^+, 30), 393 ($MH^+ - PhCH_2OH$, 22), 91 ($PhCH_2^+$, 100). Anal. ($C_{31}H_{48}O_5$) C, H. (Analysis for this compound was off by ≥0.4%.)

(*E*)-1(*S*)-[4-Nonylidene-3-oxo(2-oxolan-1(*S*)-yl)]-2-(phenylmethoxy)ethyl 4-Methyl-3-(methylethyl)pentanoate (30). By the standard acylation procedure alcohol **24** (0.114 g, 0.316 mmol) was reacted with 2 equiv of 4-methyl-3-(methylethyl)-pentanoyl chloride[1,25] to give **30** (0.106 g, 0.212 mmol, 67%) as a clear oil after chromatography with EtOAc/hexane (1:9): $[\alpha]_D^{27}$ +43.6° (*c* 1.00, $CHCl_3$); IR ($CHCl_3$) 3021−2860, 1750 (C=O), 1679 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.46−7.36 (m, 5 H, Ph), 6.81 (tt, 1 H, *J* = 7.6, 2.7 Hz, >C=C*H*(CH_2)$_7CH_3$), 5.22 (ddd, 1 H, *J* = 6.1, 6.1, 2.9 Hz, C*H*OCOCH_2CH(*i*-Pr)$_2$), 4.97 (heptuplet, 1 H, H-1), 4.65 (AB d, 1 H, *J* = 11.2 Hz, PhC*H*HO), 4.58 (AB d, 1 H, *J* = 12.2 Hz, PhCH*H*O), 3.80 (ABX dd, 1 H, *J* = 9.8, 6.6 Hz, BnOC*H*H), 3.73 (ABX dd, 1 H, *J* = 9.8, 5.9 Hz, BnOCH*H*), 2.98 (br dd, 1 H, H-5_a), 2.67 (dm, 1 H, H-5_b), 2.25−2.15 (m, 4 H, COCH_2CH(*i*-Pr)$_2$, >C=CHCH_2(CH_2)$_6CH_3$), 1.87−1.45 (m, 5 H, 2 × C*H*(CH_3)$_2$, >C=$CHCH_2CH_2(CH_2)_5CH_3$, $COCH_2CH$(*i*-Pr)$_2$), 1.42−1.30 (m, 10 H, >C=CH(CH_2)$_2$(CH_2)$_5$-CH_3), 1.00−0.90 (m, 9 H, HC(CH_3)$_2$, >C=CH(CH_2)$_7$CH_3), 0.88−0.83 (d, *J* = 6.2 Hz, 6 H, HC(CH_3)$_2$); ^{13}C NMR ($CDCl_3$) δ 174.10, 170.26, 140.78, 137.44, 128.28, 127.69, 127.56, 125.14, 74.44, 73.41, 72.43, 67.78, 46.61, 32.80, 31.76, 30.17, 29.36, 29.29, 29.10, 28.08, 27.32, 22.57, 21.25, 18.72, 18.61, 14.03; FAB MS (*m*/*z*, relative intensity) 501 (MH^+, 38), 393 ($MH^+ - PhCH_2OH$, 24), 91 ($PhCH_2^+$, 100). Anal. ($C_{31}H_{48}O_5$) C, H.

(*Z*)-1(*S*)-{4-[4-Methyl-3-(methylethyl)pentylidene]-3-oxo(2-oxolan-1(*S*)-yl)}-2-(phenylmethoxy)ethyl Nonanoate (31). By the standard acylation procedure alcohol **25** (0.117 g, 0.323 mmol) was reacted with 4 equiv of nonanoyl chloride to give **31** (0.152 g, 0.304 mmol, 94%) as a clear oil after chromatography with EtOAc/hexane (1:9): $[\alpha]_D^{27}$ +13.25° (*c* 1.54, $CHCl_3$); IR ($CHCl_3$) 3022−2862, 1745 (C=O), 1666 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.46−7.34 (m, 5 H, Ph), 6.26 (br t, 1 H, >C=C*H*CH_2CH(*i*-Pr)$_2$), 5.20 (ddd, 1 H, *J* = 5.9, 5.9, 3.2 Hz, C*H*OCO(CH_2)$_7CH_3$), 4.86 (heptuplet, 1 H, H-1), 4.65 (AB d, 1 H, *J* = 11.7 Hz, PhC*H*HO), 4.58 (AB d, 1 H, *J* = 12.2 Hz, PhCH*H*O), 3.78 (ABX dd, 1 H, *J* = 10.0, 6.3 Hz, BnOC*H*H), 3.70 (ABX dd, 1 H, *J* = 10.0, 5.9 Hz, BnOCH*H*), 3.02 (br dd, 1 H, H-5_a), 2.85−2.65 (m, 3 H, H-5_b, >C=CHCH_2CH(*i*-Pr)$_2$), 2.37 (t, 2 H, *J* = 7.4 Hz, COCH_2(CH_2)$_6CH_3$), 1.92−1.78 (m, 2 H, 2 × C*H*(CH_3)$_2$), 1.75−1.60 (m, 2 H, $COCH_2CH_2(CH_2)_5CH_3$), 1.34 (m, 10 H, CO(CH_2)$_2$(CH_2)$_5CH_3$), 1.17 (quintuplet, 1 H, >C=$CHCH_2CH$(*i*-Pr)$_2$), 1.02−0.90 (m, 15 H, 2 × HC(CH_3)$_2$, CO(CH_2)$_7$CH_3); ^{13}C NMR ($CDCl_3$) δ 173.04, 169.03, 146.14, 137.48, 128.28, 127.67, 127.51, 122.24, 74.09, 73.35, 72.41, 67.86, 51.09, 34.12, 31.73, 30.98, 29.29, 29.22, 29.14, 29.05, 26.08, 24.82, 22.56, 21.59, 21.51, 19.46, 19.37, 14.03; FAB MS (*m*/*z*, relative intensity) 501 (MH^+, 39), 393 ($MH^+ - PhCH_2OH$, 41), 361 ($MH^+ - C_7H_{15}CH$=C=O, 3.3), 91 ($PhCH_2^+$, 100). Anal. ($C_{31}H_{48}O_5$) C, H.

(*E*)-1(*S*)-{4-[4-Methyl-3-(methylethyl)pentylidene]-3-oxo(2-oxolan-1(*S*)-yl)}-2-(phenylmethoxy)ethyl Nonanoate (32). By the standard acylation procedure alcohol **26** (0.097 g, 0.269 mmol) was reacted with 4 equiv of nonanoyl chloride to give **32** (0.098 g, 0.196 mmol, 73%) as a clear oil after chromatography with EtOAc/hexane (1:9): $[\alpha]_D^{26}$ +37.87° (*c* 1.56, $CHCl_3$); IR ($CHCl_3$) 3021−2869, 1747 (C=O), 1676 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.46−7.34 (m, 5 H, Ph), 6.85 (tt, 1 H, *J* = 7.3, 2.9 Hz, >C=C*H*CH_2CH(*i*-Pr)$_2$), 5.24 (ddd, 1 H, *J* = 6.1, 6.1, 2.9 Hz, C*H*OCO(CH_2)$_7CH_3$), 4.95 (heptuplet, 1 H, H-1), 4.66 (AB d, 1 H, *J* = 11.7 Hz, PhC*H*HO), 4.59 (AB d, 1 H, *J* = 12.2 Hz, PhCH*H*O), 3.80 (ABX dd, 1 H, *J* = 9.8, 6.4 Hz, BnOC*H*H), 3.72 (ABX dd, 1 H, *J* = 10.0, 5.9 Hz, BnOCH*H*), 2.97 (br dd, 1 H, H-5_a), 2.66 (dm, 1 H, H-5_b), 2.36 (br t, 2 H, *J* ≈ 7.3 Hz, COCH_2(CH_2)$_6CH_3$), 2.15 (dd, 2 H, *J* = 7.3, 5.9 Hz, >C=CHCH_2CH(*i*-Pr)$_2$), 1.94−1.76 (m, 2 H, 2 × C*H*(CH_3)$_2$), 1.65 (m, 2 H, $COCH_2CH_2(CH_2)_5CH_3$), 1.41−1.22 (m, 11 H, CO(CH_2)$_2$-(CH_2)$_5CH_3$, >C=$CHCH_2CH$(*i*-Pr)$_2$), 1.00−0.88 (m, 15 H, 2 × HC(CH_3)$_2$, CO(CH_2)$_7$CH_3); ^{13}C NMR ($CDCl_3$) δ 173.04, 170.26, 142.66, 137.43, 128.30, 127.71, 127.56, 124.15, 74.43, 73.40, 72.41, 67.85, 50.22, 34.09, 31.73, 29.63, 29.13, 29.03, 28.56, 27.46, 24.80, 22.56, 21.54, 21.48, 19.32, 19.27, 14.03; FAB MS (*m*/*z*, relative intensity) 501 (MH^+, 53), 393 ($MH^+ - PhCH_2OH$, 33), 361 ($MH^+ - C_7H_{15}CH$=C=O, 8.0), 91 ($PhCH_2^+$, 100). Anal. ($C_{31}H_{48}O_5$) C, H.

(*Z*)-1(*S*)-{4-[4-Methyl-3-(methylethyl)pentylidene]-3-oxo(2-oxolan-1(*S*)-yl)}-2-(phenylmethoxy)ethyl 4-Methyl-3-(methylethyl)pentanoate (33). By the standard acylation procedure alcohol **25** (0.138 g, 0.383 mmol) was reacted with 2 equiv of 4-methyl-3-(methylethyl)pentanoyl chloride[1,25] to give **33** (0.179 g, 0.358 mmol, 94%) as a clear oil after chromatography with EtOAc/hexane (1:9): $[\alpha]_D^{27}$ +14.31° (*c* 2.01, $CHCl_3$); IR ($CHCl_3$) 3021−2874, 1746 (C=O), 1666 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.44−7.34 (m, 5 H, Ph), 6.27 (br t, 1 H, >C=C*H*CH_2CH(*i*-Pr)$_2$), 5.18 (ddd, 1 H, *J* = 6.1, 5.9, 3.2 Hz, C*H*OCOCH_2CH(*i*-Pr)$_2$), 4.88 (irregular heptuplet, 1 H, H-1), 4.64 (AB d, 1 H, *J* = 11.7 Hz, PhC*H*HO), 4.58 (AB d, 1 H, *J* = 12.0 Hz, PhCH*H*O), 3.79 (ABX dd, 1 H, *J* = 9.8, 6.3 Hz, BnOC*H*H), 3.71 (ABX dd, 1 H, *J* = 10.0, 5.9 Hz, BnOCH*H*), 3.10−2.65 (m, 4 H, H-5, >C=CHCH_2CH(*i*-Pr)$_2$), 2.25 (d, 2 H, *J* = 5.6 Hz, COCH_2CH(*i*-Pr)$_2$), 1.93−1.75 (m, 4 H, 4 × C*H*(CH_3)$_2$), 1.68 (quintuplet, 1 H, $COCH_2CH$(*i*-Pr)$_2$), 1.17 (quintuplet, 1 H, >C=$CHCH_2CH$(*i*-Pr)$_2$), 1.00−0.85 (m, 24 H, 4 × HC(CH_3)$_2$); ^{13}C NMR ($CDCl_3$) δ 174.11, 169.03, 146.25, 137.49, 128.27, 127.65, 127.52, 122.24, 74.07, 73.36, 72.40, 67.77, 51.10, 46.59, 32.81, 30.88, 29.33, 29.20, 26.08, 21.62, 21.50, 21.29, 21.25, 19.49, 19.33, 18.72, 18.66; FAB MS (*m*/*z*,

relative intensity) 501 (MH^+, 31), 393 ($MH^+ - PhCH_2OH$, 24), 91 ($PhCH_2^+$, 100). Anal. ($C_{31}H_{48}O_5$) C, H.

(*E*)-1(*S*)-{4-[4-Methyl-3-(methylethyl)pentylidene]-3-oxo(2-oxolan-1(*S*)-yl)}-2-(phenylmethoxy)ethyl 4-Methyl-3-(methylethyl)pentanoate (34). By the standard acylation procedure alcohol **26** (0.118 g, 0.327 mmol) was reacted with 2 equiv of 4-methyl-3-(methylethyl)pentanoyl chloride[1,25] to give **34** (0.119 g, 0.238 mmol, 73%) as a clear oil after chromatography with EtOAc/hexane (1:9): $[\alpha]_D^{27}$ +38.58° (*c* 1.13, $CHCl_3$); IR ($CHCl_3$) 30212873, 1750 (C=O), 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.46−7.34 (m, 5 H, Ph), 6.86 (tt, 1 H, J = 7.4, 2.7 Hz, >C=C*H*CH_2CH(*i*-Pr)$_2$), 5.22 (ddd, 1 H, J = 6.1, 6.1, 2.9 Hz, C*H*OCOCH_2CH(*i*-Pr)$_2$), 4.97 (irregular heptuplet, 1 H, H-1), 4.65 (AB d, 1 H, J = 11.7 Hz, PhC*H*HO), 4.59 (AB d, 1 H, J = 12.0 Hz, PhCH*H*O), 3.80 (ABX dd, 1 H, J = 9.8, 6.6 Hz, BnOC*H*H), 3.73 (ABX dd, 1 H, J = 10.0, 5.9 Hz, BnOCH*H*), 2.98 (ddm, 1 H, H-5$_a$), 2.67 (dm, 1H, H-5$_b$), 2.24 (d, 2 H, J = 5.4, COCH_2CH(*i*-Pr)$_2$), 2.15 (dd, 2 H, J = 7.2, 6.0 Hz, >C=CHCH_2CH(*i*-Pr)$_2$), 1.93−1.75 (m, 4 H, 4 × C*H*$(CH_3)_2$), 1.66 (quintuplet, 1 H, COCH$_2$C*H*(*i*-Pr)$_2$), 1.27 (quintuplet, 1 H, >C=CHCH$_2$C*H*(*i*-Pr)$_2$), 1.00−0.85 (m, 24 H, 4 × HC(CH_3)$_2$); ^{13}C NMR (CDCl3) δ 174.11, 170.25, 142.68, 137.44, 128.29, 127.69, 127.57, 124.20, 74.42, 73.41, 72.39, 67.76, 50.21, 46.64, 32.81, 29.31, 29.17, 29.07, 28.55, 27.41, 21.61, 21.44, 21.28, 21.24, 19.38, 19.22, 18.70, 18.67; FAB MS (*m*/*z*, relative intensity) 501 (MH^+, 38), 393 ($MH^+ - PhCH_2OH$, 60), 57 ($C_4H_9^+$, 100). Anal. ($C_{31}H_{48}O_5 \cdot 0.3H_2O$) C, H.

Standard Debenzylation Procedure. A stirred solution of the protected compound in CH_2Cl_2 (17 mL/mmol) was maintained at −78 °C under argon and treated dropwise with BCl_3 (2 equiv, 1 M solution in CH_2Cl_2). The reaction continued for 2 h before it was quenched by the addition of a phosphate buffer (pH 7.2, 3 mL/mmol) while still at −78 °C. The mixture was extracted twice with $CHCl_3$ (30 mL/mmol) and the combined extracts were warmed to room temperature, dried ($MgSO_4$) and filtered.

Method A. The filtrate was concentrated and purified by flash column chromatography on silica gel with mixtures of EtOAc/hexane as eluant to give the final deprotected product.

Method B. The filtrate was concentrated to a solid which was washed exhaustively with cold hexane or cold petroleum ether to give the pure deprotected product.

(*Z*)-2-Hydroxy-1(*S*)-[4-nonylidene-3-oxo(2-oxolan-1(*S*)-yl)]-ethyl Nonanoate (7). By the standard debenzylation procedure (method B) compound 27 (0.060 g, 0.120 mmol) was deprotected. After washing with cold hexane and cold petroleum ether, compound 7 (0.029 g, 0.069 mmol, 58%) was obtained as a solid (−20 °C) which melted at room temperature: $[\alpha]_D^{26}$ +9.71° (*c* 0.35, $CHCl_3$); IR ($CHCl_3$) 3610 (OH), 3020−2857, 1751 (C=O), 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.27 (m, 1 H, >C=C*H*$(CH_2)_7CH_3$), 5.08 (ddd, 1 H, J = 5.6, 5.6, 3.2 Hz, C*H*OCO$(CH_2)_7CH_3$), 4.85 (heptuplet, 1 H, H-1), 3.91 (ABX m, 2 H, CH_2OH), 3.05 (m, 1 H, H-5$_a$), 2.90−2.65 (m, 3 H, H-5$_b$, >C=CHC$H_2(CH_2)_6CH_3$), 2.40 (t, 2 H, $J \approx$ 7.0 Hz, COC$H_2(CH_2)_6$-CH_3), 1.77−1.30 (m, 24 H, COCH$_2$(C$H_2)_6CH_3$, >C=CHCH$_2$-(C$H_2)_6CH_3$), 1.00−0.92 (m, 6 H, >C=CH(CH$_2)_7$CH_3, CO-(CH$_2)_7$CH_3); ^{13}C NMR ($CDCl_3$) δ 173.48, 168.86, 144.33, 123.00, 74.59, 74.28, 61.41 (*C*H$_2$), 34.13 (*C*H$_2$), 31.77 (*C*H$_2$), 31.72 (*C*H$_2$), 31.07 (*C*H$_2$), 29.34 (*C*H$_2$), 29.24 (*C*H$_2$), 29.13 (*C*H$_2$), 29.05 (*C*H$_2$), 28.98 (*C*H$_2$), 27.55 (*C*H$_2$), 24.80 (*C*H$_2$), 22.58 (*C*H$_2$), 22.57 (*C*H$_2$), 14.02; FAB MS (*m*/*z*, relative intensity) 411 (MH^+, 100), 271 ($MH^+ - C_7H_{15}CH$=C=O, 40), 141 ($C_8H_{17}CO^+$, 48), 57 ($C_4H_9^+$, 73). Anal. ($C_{24}H_{42}O_5 \cdot 0.2H_2O$) C, H.

(*E*)-2-Hydroxy-1(*S*)-[4-nonylidene-3-oxo(2-oxolan-1(*S*)-yl)]ethyl Nonanoate (8). By the standard debenzylation procedure (method B) compound **28** (0.069 g, 0.137 mmol) was deprotected. After washing with cold hexane, compound **8** (0.047 g, 0.115 mmol, 84%) was obtained as a solid: mp 79−81 °C; $[\alpha]_D^{26}$ +37.72° (*c* 0.64, $CHCl_3$); IR ($CHCl_3$) 3616 (OH), 3020−2858, 1752 (C=O), 1679 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.81 (tt, 1 H, J = 7.5, 2.7 Hz, >C=C*H*$(CH_2)_7CH_3$), 5.10 (ddd, 1 H, J = 5.6, 5.6, 2.9 Hz, C*H*OCO$(CH_2)_7CH_3$), 4.93 (heptuplet, 1 H, H-1), 3.96 (ABX dd, 1 H, J = 11.0, 5.1 Hz, C*H*HOH), 3.89 (ABX dd, 1 H, J = 11.0, 5.4 Hz, CH*H*OH), 3.03 (br dd, 1 H, H-5$_a$), 2.69 (br dm, 1 H, H-5$_b$), 2.38 (br t, 2 H, $J \approx$ 7.0 Hz, COC$H_2(CH_2)_6CH_3$), 2.22 (br q, 2 H, J = 7.1 Hz, >C=CHC$H_2(CH_2)_6CH_3$), 1.65 and 1.53 (br multiplets, 4 H, COCH$_2$CH_2(CH$_2)_5$CH$_3$, >C=CHCH$_2$CH_2(CH$_2)_5$CH$_3$), 1.45−1.25 (m, 20 H, CO(CH$_2)_2$(C$H_2)_5CH_3$, >C=CH(CH$_2)_2$(C$H_2)_5CH_3$), 1.00−0.90 (distorted triplet, 6 H, CO(CH$_2)_7$CH_3, >C=CH-(CH$_2)_7$CH_3); ^{13}C NMR ($CDCl_3$) δ 173.48, 170.16, 141.04, 124.90, 74.62, 74.59, 61.33 (*C*H$_2$), 34.08 (*C*H$_2$), 31.75 (*C*H$_2$), 31.72 (*C*H$_2$), 30.21 (*C*H$_2$), 29.29 (*C*H$_2$), 29.11 (*C*H$_2$), 29.03 (*C*H$_2$), 28.07 (*C*H$_2$), 27.48 (*C*H$_2$), 24.80 (*C*H$_2$), 22.56 (*C*H$_2$), 14.01; FAB MS (*m*/*z*, relative intensity) 411 (MH^+, 100), 271 ($MH^+ - C_7H_{15}$-CH=C=O, 70), 141 ($C_8H_{17}CO^+$, 43), 57 ($C_4H_9^+$, 77). Anal. ($C_{24}H_{42}O_5$) C, H.

(*Z*)-2-Hydroxy-1(*S*)-[4-nonylidene-3-oxo(2-oxolan-1(*S*)-yl)]ethyl 4-Methyl-3-(methylethyl)pentanoate (9). By the standard debenzylation procedure (method A) compound **29** (0.072 g, 0.144 mmol) was deprotected. After column chromatography with EtOAc/hexane (1:3 and 1:2), compound **9** (0.039 g, 0.094 mmol, 65%) was obtained as an oil: $[\alpha]_D^{26}$ +8.27° (*c* 0.66, $CHCl_3$); IR ($CHCl_3$) 3610 (OH), 3021−2856, 1752 (C=O), 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.28 (br t, 1 H, >C=C*H*$(CH_2)_7CH_3$), 5.06 (ddd, 1 H, J = 5.6, 5.6, 3.4 Hz, C*H*OCOCH$_2$-CH(*i*-Pr)$_2$), 4.87 (heptuplet, 1 H, H-1), 3.90 (ABX br d, 2 H, CH_2OH), 3.08 (m, 1 H, H-5$_a$), 2.87−2.67 (m, 3 H, H-5$_b$, >C=CHC$H_2(CH_2)_6CH_3$), 2.28 (br d, 2 H, $J \approx$ 5.4 Hz, COCH_2CH(*i*-Pr)$_2$), 1.81 (heptuplet, 2 H, 2 × C*H*$(CH_3)_2$), 1.68 (quintuplet, 1 H, COCH$_2$C*H*(*i*-Pr)$_2$), 1.53−1.28 (m, 12 H, >C=CHCH$_2$(C$H_2)_6$-CH_3), 1.00−0.85 (m, 15 H, 2 × HC(CH_3)$_2$, >C=CH(CH$_2)_7CH_3$); ^{13}C NMR ($CHCl_3$) δ 174.60, 168.81, 144.41, 123.00, 74.71, 74.26, 61.41 (*C*H$_2$), 46.71, 32.86 (*C*H$_2$), 31.77 (*C*H$_2$), 30.95 (*C*H$_2$), 29.35, 29.32, 29.23 (*C*H$_2$), 29.13 (*C*H$_2$), 29.09 (*C*H$_2$), 27.55 (*C*H$_2$), 22.57 (*C*H$_2$), 21.28, 21.26, 18.68, 14.02; FAB MS (*m*/*z*, relative intensity) 411 (MH^+, 100), 271 ($MH^+ - (i\text{-Pr})_2$-CHCH=C=O, 18), 141 ((*i*-Pr)$_2$CHCH$_2$CO$^+$, 44), 57 ($C_4H_9^+$, 97). Anal. ($C_{24}H_{42}O_5$) C, H.

(*E*)-2-Hydroxy-1(*S*)-[4-nonylidene-3-oxo(2-oxolan-1(*S*)-yl)]ethyl 4-Methyl-3-(methylethyl)pentanoate (10). By the standard debenzylation procedure (method A) compound **30** (0.092 g, 0.183 mmol) was deprotected. After column chromatography with EtOAc/hexane (1:3 and 1:2), compound **10** (0.058 g, 0.142 mmol, 77%) was obtained as an oil: $[\alpha]_D^{27}$ +46.22° (*c* 1.48, $CHCl_3$); IR ($CHCl_3$) 3594 (OH), 3021−2858, 1753 (C=O), 1679 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.83 (tt, 1 H, J = 7.6, 2.7 Hz, >C=C*H*$(CH_2)_7CH_3$), 5.08 (ddd, 1 H, J = 5.6, 5.6, 3.1 Hz, C*H*OCOCH$_2$CH(*i*-Pr)$_2$), 4.95 (heptuplet, 1 H, H-1), 3.94 (ABX m, 2 H, CH_2OH), 3.03 (br ddm, 1 H, H-5$_a$), 2.72 (br dm, 1 H, H-5$_b$), 2.28−2.17 (m, 4 H, COCH_2CH(*i*-Pr)$_2$, >C=CHC$H_2(CH_2)_6CH_3$), 2.05 (br t, 1 H, OH), 1.80 (septuplets, 2 H, 2 × C*H*$(CH_3)_2$), 1.67 (m, 1 H, COCH$_2$C*H*(*i*-Pr)$_2$), 1.54 (m, 2 H, >C=CHCH$_2$CH_2(CH$_2)_5$CH$_3$), 1.45−1.25 (m, 10 H, >C=CH(CH$_2)_2$(C$H_2)_5CH_3$), 1.02−0.82 (m, 15 H, 2 × HC(CH_3)$_2$, >C=CH(CH$_2)_7$CH_3); ^{13}C NMR ($CDCl_3$) δ 174.63, 170.06, 141.13, 124.86, 74.74, 74.57, 61.44 (*C*H$_2$), 46.73, 32.82 (*C*H$_2$), 31.75 (*C*H$_2$), 30.23 (*C*H$_2$), 29.37 (*C*H$_2$), 29.30, 29.10 (*C*H$_2$), 28.07 (*C*H$_2$), 27.44 (*C*H$_2$), 22.57 (*C*H$_2$), 21.27, 18.71, 18.62, 14.02; FAB MS (*m*/*z*, relative intensity) 411 (MH^+, 50), 271 ($MH^+ - (i\text{-Pr})_2$CHCH=C=O, 26), 141 ((*i*-Pr)$_2$CHCH$_2$CO$^+$, 40), 57 ($C_4H_9^+$, 100). Anal. ($C_{24}H_{42}O_5$) C, H.

(*Z*)-2-Hydroxy-1(*S*)-{4-[4-methyl-3-(methylethyl)pentylidene]-3-oxo(2-oxolan-1(*S*)-yl)}ethyl Nonanoate (11). By the standard debenzylation procedure (method B) compound **31** (0.076 g, 0.152 mmol) was deprotected. After washing with cold hexane, compound **11** (0.053 g, 0.129 mmol, 85%) was obtained as a solid: mp 80−81 °C; $[\alpha]_D^{26}$ +8.26° (*c* 0.96, $CHCl_3$); IR ($CHCl_3$) 3617 (OH), 3021−2871, 1750 (C=O), 1666 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.30 (br t, 1 H, $J \approx$ 7.5 Hz, >C=C*H*CH$_2$CH(*i*-Pr)$_2$), 5.07 (ddd, 1 H, J = 5.6, 5.6, 3.4 Hz, C*H*OCO$(CH_2)_7CH_3$), 4.85 (heptuplet, 1 H, H-1), 3.96 (ABX dd, 1 H, J = 11.5, 5.6 Hz, C*H*HOH), 3.87 (ABX dd, 1 H, J = 11.5, 5.6 Hz, CH*H*OH), 3.08 (m, 1 H, H-5$_a$), 2.95−2.65 (m, 3 H, H-5$_b$, >C=CHCH_2CH(*i*-Pr)$_2$), 2.41 (br t, 2 H, $J \approx$ 7.0 Hz, COC$H_2(CH_2)_6CH_3$), 2.18 (br m, 1 H, OH), 1.93−1.60 (m, 4 H, 2 × C*H*$(CH_3)_2$, COCH$_2$CH_2(CH$_2)_5$CH$_3$), 1.43−1.30 (m, 10 H, CO(CH$_2)_2$(C$H_2)_5CH_3$), 1.18 (quintuplet, 1 H, >C=CHCH$_2$C*H*(*i*-

Pr)$_2$), 1.02−0.90 (m, 15 H, 2 × HC(CH_3)$_2$, CO(CH$_2$)$_7$CH_3); ^{13}C NMR ($CDCl_3$) δ 173.52, 168.91, 146.53, 121.97, 74.61, 74.21, 61.40 (*C*H$_2$), 51.10, 34.11 (*C*H$_2$), 31.71 (*C*H$_2$), 31.05 (*C*H$_2$), 29.29, 29.22, 29.13 (*C*H$_2$), 29.04 (*C*H$_2$), 26.13 (*C*H$_2$), 24.81 (*C*H$_2$), 22.55 (*C*H$_2$), 21.58, 21.50, 19.44, 19.36, 14.01; FAB MS (*m*/*z*, relative intensity) 411 (MH^+, 100), 271 ($MH^+ - C_7H_{15}$-CH=C=O, 41), 141 ($C_8H_{17}CO^+$, 36), 57 ($C_4H_9^+$, 96). Anal. ($C_{24}H_{42}O_5$·0.2H_2O) C, H.

(*E*)-2-Hydroxy-1(*S*)-{4-[4-methyl-3-(methylethyl)pentylidene]-3-oxo(2-oxolan-1(*S*)-yl)}ethyl Nonanoate (12). By the standard debenzylation procedure (method B) compound **32** (0.067 g, 0.134 mmol) was deprotected. After washing with cold petroleum ether, compound **12** (0.032 g, 0.078 mmol, 58%) was obtained as an oil; $[\alpha]^{26}_D$ +43.33 ° (*c* 0.30, $CHCl_3$); IR ($CHCl_3$) 3619 (OH), 3021−2857, 1751 (C=O), 1675 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.88 (tt, 1 H, *J* = 7.3, 2.9 Hz, >C=C*H*CH$_2$-CH(*i*-Pr)$_2$), 5.11 (ddd, 1 H, *J* = 5.6, 5.6, 3.2 Hz, C*H*OCO(CH$_2$)$_7$-CH_3), 4.94 (heptuplet, 1 H, H-1), 3.97 (ABX dd, 1 H, *J* = 11.5, 5.4 Hz, C*H*HOH), 3.91 (ABX dd, 1 H, *J* = 11.2, 5.4 Hz, CH*H*OH), 3.03 (ddm, 1 H, H-5$_a$), 2.70 (dm, 1 H, H-5$_b$), 2.50−2.35 (m, 2 H, COCH_2(CH$_2$)$_6$CH_3), 2.18 (m, 2 H, >C=CHCH_2-CH(*i*-Pr)$_2$), 1.85 (heptuplet, 2 H, 2 × C*H*(CH_3)$_2$), 1.75−1.60 (m, 2 H, COCH$_2$CH_2(CH$_2$)$_5$CH_3), 1.43−1.20 (m, 11 H, CO(CH$_2$)$_2$-(CH_2)$_5$CH_3, >C=CHCH$_2$C*H*(*i*-Pr)$_2$), 1.02−0.90 (m, 15 H, 2 × HC(CH_3)$_2$, CO(CH$_2$)$_7$CH_3); ^{13}C NMR ($CDCl_3$) δ 173.50, 170.09, 143.00, 123.89, 74.63, 74.54, 61.46 (*C*H$_2$), 50.24, 34.08 (*C*H$_2$), 31.71 (*C*H$_2$), 29.63 (*C*H$_2$), 29.12, 29.03 (*C*H$_2$), 28.61 (*C*H$_2$), 27.57 (*C*H$_2$), 24.80 (*C*H$_2$), 22.55 (*C*H$_2$), 21.55, 21.49, 19.31, 19.28, 14.02; FAB MS (*m*/*z*, relative intensity) 411 (MH^+, 100), 271 ($MH^+ - C_7H_{15}CH$=C=O, 63), 141 ($C_8H_{17}CO^+$, 21), 57 ($C_4H_9^+$, 49). Anal. ($C_{24}H_{42}O_5$) C, H.

(*Z*)-2-Hydroxy-1(*S*)-{4-[4-methyl-3-(methylethyl)pentylidene]-3-oxo(2-oxolan-1(*S*)-yl)}ethyl 4-Methyl-3-(methylethyl)pentanoate (13). By the standard debenzylation procedure (method A) compound **33** (0.159 g, 0.317 mmol) was deprotected. After column chromatography with EtOAc/hexane (1:3 and 1:2), compound **13** (0.051 g, 0.124 mmol, 39%) was obtained as a solid: mp 88 °C; $[\alpha]^{26}_D$ +7.02° (*c* 0.57, $CHCl_3$); IR ($CHCl_3$) 3618 (OH), 3020−2874, 1751 (C=O), 1665 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.31 (br t, 1 H, >C=C*H*CH$_2$CH(*i*-Pr)$_2$), 5.05 (ddd, 1 H, *J* = 5.4, 5.4, 3.4 Hz, C*H*OCOCH$_2$CH(*i*-Pr)$_2$), 4.87 (heptuplet, 1 H, H-1), 3.96 (ABX dd, 1 H, *J* = 11.2, 5.2 Hz, C*H*HOH), 3.90 (ABX dd, 1 H, *J* = 11.0, 5.5 Hz, CH*H*OH), 3.15−2.67 (m, 4 H, H-5, >C=CHCH_2CH(*i*-Pr)$_2$), 2.29 (d, 2 H, *J* = 5.4 Hz, COCH_2CH(*i*-Pr)$_2$), 1.92−1.75 (m, 4 H, 4 × C*H*-(CH_3)$_2$), 1.69 (quintuplet, 1 H, COCH$_2$C*H*(*i*-Pr)$_2$), 1.18 (quintuplet, 1 H, >C=CHCH$_2$CH(*i*-Pr)$_2$), 1.02−0.87 (m, 24 H, 4 × HC(CH_3)$_2$); ^{13}C NMR ($CDCl_3$) δ 174.65, 168.81, 146.64, 121.94, 74.71, 74.23, 61.51 (*C*H$_2$), 51.12, 46.71, 32.82 (*C*H$_2$), 30.97 (*C*H$_2$), 29.34, 29.22, 26.13 (*C*H$_2$), 21.62, 21.51, 21.30, 21.27, 19.47, 19.34, 18.70, 18.67; FAB MS (*m*/*z*, relative intensity) 411 (MH^+, 69), 271 (MH^+ − (*i*-Pr)$_2$CHCH=C=O, 30), 141 ((*i*-Pr)$_2$CHCH$_2$CO$^+$, 47), 57 ($C_4H_9^+$, 100). Anal. ($C_{24}H_{42}O_5$) C, H.

(*E*)-2-Hydroxy-1(*S*)-{4-[4-methyl-3-(methylethyl)pentylidene]-3-oxo(2-oxolan-1(*S*)-yl)}ethyl 4-Methyl-3-(methylethyl)pentanoate (14). By the standard debenzylation procedure (method A) compound **34** (0.080 g, 0.160 mmol) was deprotected. After column chromatography with EtOAc/hexane (1:3 and 1:2), compound **14** (0.029 g, 0.069 mmol, 43%) was obtained as a solid: mp 68 °C; $[\alpha]^{25}_D$ +45.91° (*c* 0.44, $CHCl_3$); IR ($CHCl_3$) 3495 (OH), 3021−2874, 1751 (C=O), 1675 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.89 (tt, 1 H, *J* = 7.3, 2.7 Hz >C=C*H*CH$_2$-CH(*i*-Pr)$_2$), 5.08 (ddd, 1 H, *J* = 5.6, 5.6, 2.9 Hz, C*H*OCOCH$_2$-CH(*i*-Pr)$_2$), 4.96 (heptuplet, 1 H, H-1), 3.98 (ABX dd, 1 H, *J* = 12.9, 5.6 Hz, C*H*HOH), 3.92 (ABX dd, 1 H, *J* = 11.7, 5.6 Hz, CH*H*OH), 3.05 (ddm, 1 H, H-5$_a$), 2.72 (dm, 1 H, H-5$_b$), 2.27 (d, 2 H, *J* = 5.4 Hz, COCH_2CH(*i*-Pr)$_2$), 2.18 (m, 2 H, >C=CHCH_2-CH(*i*-Pr)$_2$), 1.94−1.73 (m, 4 H, 4 × C*H*(CH_3)$_2$), 1.66 (quintuplet, 1 H, COCH$_2$C*H*(*i*-Pr)$_2$), 1.28 (quintuplet, 1 H, >C=CHCH$_2$C*H*(*i*-Pr)$_2$), 1.02−0.84 (m, 24 H, 4 × HC(CH_3)$_2$); ^{13}C NMR ($CDCl_3$) δ 174.65, 170.07, 143.04, 123.92, 74.74, 74.55, 61.45 (*C*H$_2$), 50.23, 46.75, 32.82 (*C*H$_2$), 29.34, 29.18, 29.09, 28.61 (*C*H$_2$), 27.53 (*C*H$_2$), 21.61, 21.46, 21.29, 21.27, 19.37, 19.24, 18.68; FAB MS (*m*/*z*, relative intensity) 411 (MH^+, 83), 271 (MH^+ − (*i*-Pr)$_2$-CHCH=C=O, 45), 141 ((*i*-Pr)$_2$CHCH$_2$CO$^+$, 38), 57 ($C_4H_9^+$, 100). Anal. ($C_{24}H_{42}O_5$) C, H.

Acknowledgment. The authors thank Dr. James A. Kelley from this laboratory for mass spectral analysis and interpretation.

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JM990613Q