Conformationally Constrained Analogues of Diacylglycerol. 26. Exploring the Chemical Space Surrounding the C1 Domain of Protein Kinase C with DAG-Lactones Containing Aryl Groups at the *sn*-1 and *sn*-2 Positions

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Diacylglycerol lactones (DAG-lactones) are known to operate as effective agonists of protein kinase C (PKC), surpassing in potency the activity of natural diacylglycerol (DAG). Localization of activated PKC isozymes in the cell is determined in part by the different cellular scaffolds, the lipid composition of the specific membranes, and the targeting information intrinsic to the individual isoforms bound to DAG. This multifaceted control of diversity suggests that, to develop effective DAG-lactones capable of honing in on a specific cellular target, we need to gain a better understanding of the chemical space surrounding its binding site. Seeking to augment the chemical repertoire of DAG-lactone side chains that could steer the translocation of PKC to specific cellular domains, we report herein the effects of incorporating simple or substituted phenyl residues. A combined series of *n*-alkyl and phenyl substitutions were used to explore the optimal location of the phenyl group on the side chains. The substantial differences in binding affinity between DAG-lactones with identical functionalized phenyl groups at either the *sn*-1 or *sn*-2 position are consistent with the proposed binding model in which the DAG-lactone binds to the C1 domain of PKC with the acyl chain oriented toward the interior of the membrane and the α-alkylidene or α-arylalkylidene chains directed to the surface of the C1 domain adjacent to the lipid interface. We conclude that DAG-lactones containing α-phenylalkylidene side chains at the *sn*-2 position represent excellent scaffolds upon which to explore further chemical diversity.

Introduction

Diacylglycerol (DAG) is the principal physiological activator for the majority of protein kinase C (PKC) isozymes.[1−4] As such, it is an important second messenger involved in the regulation of cellular proliferation, survival, and differentiation. Adding to this complex set of responses, oftentimes redundant and even antagonistic, are some additional DAG responsive targets that do not belong to the PKC family. These include PKDs, RasGRP, chimaerins, Munc-13, and DAG kinases, whose activation increases the level of complexity and multiplicity of responses from DAG.[5−7] Gaining knowledge about how the regulation of PKC isozymes, PKD, and the non-kinase protein targets control important intracellular events represents an important field of study, particularly considering the high degree of cross-talk between these differently DAG activated pathways and their implications on cancer, immune responses, and neurobiology.[8,9]

Activation of conventional (cPKC = α, *β*I, *β*II, and *γ*) and novel (nPKC = *δ*, *ϵ*, *η*, and *θ*) isoforms typically involves recruitment of the enzyme to the membrane via an allosteric interaction with DAG.[10,11] Although there are many distinct species of DAG, the DAG that activates these isozymes is proposed to be a polyunsaturated form generated in response to PLC-mediated hydrolysis of inositol lipids, such as phosphatidylinositol (4,5)-biphosphate.[2] PKC action can be localized to multiple compartments, which aside from the plasma membrane include the endoplasmic reticulum, the Golgi apparatus, and the nucleus.[12] Localization is determined in part by the different cellular scaffolds, the lipid composition of the specific membranes,[13] and the targeting information intrinsic to the individual isoform bound to DAG.[14] This multifaceted control of diversity suggests that, to improve the likelihood of developing DAG-like molecules capable of translocating PKCs to specific cellular targets, we need to gain a better understanding of the chemical space surrounding the DAG binding site.

Previously, we have discovered potent DAG-like molecules, referred to as DAG-lactones, that strongly activate PKC isozymes.[15] Diverse alkyl chains incorporated on these templates at both their acyl and α-alkylidene positions have helped us explore the surrounding binding sites of various isozymes with some degree of success in achieving selective translocation of some isozymes to specific cellular sites.[15] In a recent paper describing a solid-phase method for the synthesis of DAG-lactones, we briefly described a few compounds containing aryl moieties which showed potentially interesting properties.[16] However, no attempt was made to find the optimal location of the aryl group at either the acyl or α-alkylidene positions. Since aryl groups provide the opportunity to add additional diversity through the various substitution patterns on the aromatic moieties, allowing us to probe further into the surrounding chemical space of the binding sites, we set out to investigate in a systematic fashion the effects of incorporating aryl residues

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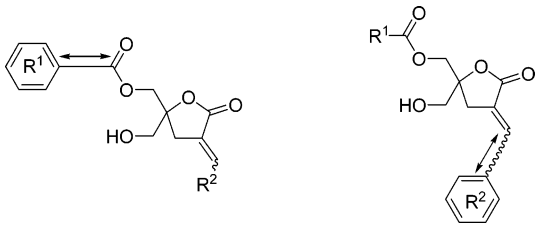


Figure 1. Design of aryl-substituted DAG-lactones to locate the optimal location of the phenyl ring.

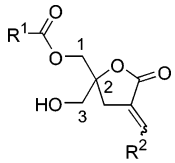


Figure 2. Generic structure of a DAG-lactone (the numbers correspond to the glycerol backbone).

Table 1. Determination of the Optimal Location of the Phenyl Ring on the R_1 Arm[a]

	R^1	R^2	log *P*	K_i(*E*-isomer) (nM)	K_i(*Z*-isomer) (nM)
1	$Ph(CH_2)_3$	*n*-C_6H_{13}	4.13	27 ± 3	17 ± 1
2	$Ph(CH_2)_2$	*n*-C_7H_{15}	4.13	18 ± <1	14 ± 1
3	$PhCH_2$	*n*-C_8H_{17}	4.13	44 ± 2	45 ± 3
4	Ph	*n*-C_9H_{19}	4.13	14 ± 1	9 ± 1
5	cyclohexyl	*n*-C_9H_{19}	4.86	9 ± 1	5 ± <1
6	Ph	(*i*-Pr)$_2$CHCH$_2$	3.76	28 ± 3	16 ± 1
7	cyclohexyl	(*i*-Pr)$_2$CHCH$_2$	4.03	10 ± <1	8 ± 1

[a] See the general structure in Figure 2.

on DAG-lactones. From the data presented herein, we conclude that aryl substituents represent useful scaffolds upon which to explore chemical diversity on the DAG-lactones.

DAG-Lactone Design and PKC Binding Affinity

In previous studies with DAG and DAG-lactones having different arrays of branched alkyl chains at the acyl and the α-alkylidene positions, we have identified compounds that display high binding affinity with reduced lipophilicity (log *P*). Among DAG analogues, we identified a compound with a 40 nM binding affinity and a log *P* of 3.8,[17] whereas for DAG-lactones the log *P* could be as low as 3.2 for a compound displaying a 30 nM binding affinity.[18] Even with potent PKC ligands, such as phorbol 12,13-dibutyrate (PDBU) and prostratin, the log *P* values could be as low as 3.4 and 1.9, respectively.[17] Therefore, the same principle of achieving the lowest possible log *P* value to minimize nonselective lipid binding was also applied once the optimal location of the aromatic ring on the side chains of the DAG-lactones was identified. For the initial phase of this investigation, a simple phenyl ring (Ph) was used as a probe along both the *sn*-1 (acyl) and *sn*-2 (α-alkylidene) chains as illustrated in Figure 1, and on the basis of the work cited above and other studies,[18,19] an initial target value of log *P* around 4 was selected.

We started by investigating the optimal location for the phenyl ring on the *sn*-1 acyl chain (R^1) using a combination of variable-length *n*-alkyl chains at the α-alkylidene position (R^2) to maintain a constant calculated log *P*[20] of 4.13 (Figure 2, Table 1, compounds **1**−**4**). For these studies PKC-α was used as the target enzyme. The binding affinities of the DAG-lactones, as reflected by their K_i values, were measured using a competition assay with phorbol 12,13-dibutyrate. The assay has been described in detail previously.[21] Because the phospholipid bilayer contributes to the binding interaction, along with the C1 domain of the kinase, the assays are routinely conducted in the presence of 100 μg/mL phosphatidylserine (PS), which fulfills this phospholipid requirement. Analysis of binding to the intact PKC has the advantage that it is most appropriate for evaluating ligand interactions with PKC as a therapeutic target. Among PKC isoforms, we examined PKC-α for comparison with our extensive knowledge of structure−activity relationships for other DAG-lactones with this isoform[15] and because of its important role as a therapeutic target in cancer.[22,23] Because multiple structural elements within PKC contribute to membrane interactions, e.g., the calcium responsive C2 domain in PKC-α, and because the ligand−membrane−PKC interactions are coupled to PKC activation,[11,14] in select cases for which we wished most closely to understand the mechanistic basis underlying differences in measured binding affinities, we have also extended our analysis to the individual C1 domain (vide infra). For these latter studies, we used the C1b domain of PKC-δ both because of the availability for this domain of the X-ray structure of its interaction with a ligand[24] and for the technical considerations of stability and solubility.

Table 2. Functionalization of the Phenyl Ring at the Optimal Position on the R^1 Arm[a]

	R^1	R^2	log *P*	K_i(*E*-isomer) (nM)	K_i(*Z*-isomer) (nM)
8	(2-OMe)Ph	(*i*-Pr)$_2$CHCH$_2$	3.77	73 ± 2	23 ± 1
9	(3-OMe)Ph	(*i*-Pr)$_2$CHCH$_2$	3.77	39 ± 2	24 ± 1
10	(4-OMe)Ph	(*i*-Pr)$_2$CHCH$_2$	3.77	36 ± 2	18 ± 1
11	(2-OH)Ph	(*i*-Pr)$_2$CHCH$_2$	3.47	67 ± 3	30 ± 4
12	(3-OH)Ph	(*i*-Pr)$_2$CHCH$_2$	3.47	670 ± 15	406 ± 11
13	(4-OH)Ph	(*i*-Pr)$_2$CHCH$_2$	3.47	2400 ± 530	983 ± 88

[a] See the general structure in Figure 2.

Guided by the K_i values of the typically more potent *Z*-isomers, the most favorable location for the phenyl ring was found to be closest to the *sn*-1-carbonyl (compound **4**, Table 1). We then compared the effects of exchanging the phenyl ring of **4** for a cyclohexane ring (compound **5**). We found that even though the K_i value was 1.78-fold lower (higher affinity) the log *P* value was 0.73 log unit higher, thus resulting in no significant net gain. Because branched α-alkylidene chains lower the log *P* value relative to that of their comparable linear counterparts and also have been shown to be more effective in selectively translocating PKC isozymes α and δ to different cellular sites,[25,26] compound **6** was synthesized. In relation to **4**, this compound showed a slight 1.76-fold increase in K_i (lower affinity), perhaps due to its 0.36 unit drop in log *P* value. Although this reduction in binding affinity was recovered in compound **7**, which combines a cyclohexylacyl group with the same branched α-alkylidene chain, compound **6** was still considered to be the best candidate for further studies not only because it had the lowest log *P* value (3.76), but also because of the ease with which the phenyl ring could be further functionalized without generating new asymmetric centers.

Starting with the selected parent compound **6** (Table 1), we then studied the effects of adding polar methoxy (**8**−**10**) and hydroxyl (**11**−**13**) groups at various positions on the phenyl ring (Table 2). Relative to **6**, the addition of a methoxy group did not seem to have a significant effect on the calculated log *P* value. Therefore, because compounds **8**−**10** have the same capacity as **6** to partition into a lipid environment, they were expected to provide information about the possible presence of polar binding sites in their vicinity. Surprisingly, the methoxy groups induced only a minimal effect on PKC binding, showing a slight decrease in affinity relative to that of **6**.

In contrast, the hydroxyl group, which caused a small reduction in the log *P* value, had a significant negative effect

Table 3. Optimal Location of the Phenyl Ring on the R^2 Arm[a]

	R^1	R^2	log *P*	K_i(*E*-isomer) (nM)
14	$(i\text{-Pr})_2CHCH_2$	Ph	3.61	12 ± 3
15	$(i\text{-Pr})_2CHCH_2$	$PhCH_2$	3.69	14 ± 2
16	$(i\text{-Pr})_2CHCH_2$	$Ph(CH_2)_2$	4.09	9 ± <1

[a] See the general structure in Figure 2.

Table 4. Functionalization of the Phenyl Ring at the Optimal Position on the R^2 Arm[a]

	R^1	R^2	log *P*	K_i(*E*-isomer) (nM)
17	$(i\text{-Pr})_2CHCH_2$	(2-OMe)Ph	3.62	16 ± 2
18	$(i\text{-Pr})_2CHCH_2$	(3-OMe)Ph	3.62	12 ± 1
19	$(i\text{-Pr})_2CHCH_2$	(4-OMe)Ph	3.62	7 ± <1
20	$(i\text{-Pr})_2CHCH_2$	(2-OH)Ph	3.32	22 ± 1
21	$(i\text{-Pr})_2CHCH_2$	(3-OH)Ph	3.32	17 ± <1
22	$(i\text{-Pr})_2CHCH_2$	(4-OH)Ph	3.32	19 ± 3

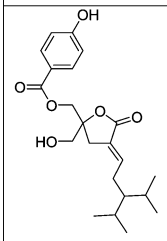
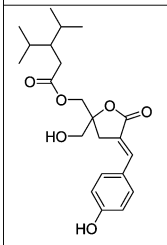
[a] See the general structure in Figure 2.

on both *E*- and *Z*-isomers as the binding affinity plummeted ca. 25-fold and ca. 70-fold, respectively, for the *meta*- and *para*-isomers (compounds **12** and **13**, Table 2). Remarkably, the decrease in binding affinity for the *ortho*-isomer (**11**) in relation to **6** (Table 1) was only ca. 2-fold for both *E*- and *Z*-isomers. These combined results agree with a binding model in which the acyl aryl ring is projected outside the C1 domain and into the lipid milieu where a substantial desolvation penalty is incurred for the free hydroxyl group. In compound **11**, the intramolecular H-bonding of the *o*-hydroxyl and the acyl carbonyl forms a stable six-membered cyclic structure, thus explaining why this *ortho*-isomer pays a lesser penalty of dehydration.

The results from Table 2 prompted us to search for specific interactions with the phenyl ring located at the alternative, α-alkylidene position. As before, this also required determining the best position for the phenyl ring on the α-alkylidene chain. To rationally evaluate the two possible alternative locations of the phenyl ring, the reverse isomer of compound **6** (Table 3, compound **14**) was synthesized along with two elongated analogues containing one (**15**) and two (**16**) additional methylene groups to increase the separation between the double bond and the phenyl ring (Table 3). As can be appreciated, **14** (the reverse isomer of **6**), of which only the *E*-isomer was isolated, as explained in Chemistry, had a slightly better binding affinity than **6** and a similar calculated log *P* value. While distancing the phenyl moiety from the double bond produced essentially no change in binding affinity, the log *P* value increased steadily. Therefore, compound **14** was selected for further studies.

Compounds **17**−**22** (Table 4) were synthesized with the intention of probing for complementary H-bond donors or acceptors around the C1 domain. In contrast to those of compounds **8**−**13** (Table 2), where the functionalized phenyl ring was part of the acyl moiety and large differences were observed between the methoxy- and hydroxy-substituted compounds, the differences in K_i values between the methoxy and hydroxyl groups for compounds **17**−**22** were found to be smaller, suggesting that these groups are indeed able to find H-bonding partners. Although the increases in binding affinity are modest relative to that of the parent compound **14**, they reach a value of 7 nM for the *p*-methoxy isomer, showing that affinity increases in the order *ortho* < *meta* < *para*. Remarkably, the presence of a hydroxyl group does not lead to great loss in binding affinity as with the reverse isomers (Table 2), and only small changes of <2.5-fold are seen. The slightly better performance of the methoxy isomers points to the presence of accessible H-bond donors at the active site that can bind effectively. The hydroxyl groups probably bind in a similar fashion albeit a little less effectively.

Table 5. Comparison of *p*-Hydroxyl Ligands in Binding to PKC-δ-C1b in the Presence or Absence of PS

	PKC-δ-C1b w/PS	PKC-δ-C1b w/o PS	$K_{w/o\ PS}/K_{w/PS}$
 **13-*E***	980 ± 220 nM	16900 ± 1600 nM	17
 **22-*E***	1.40 ± < 1 nM	170 ± 13 nM	121
$K_{13\text{-}E}/K_{22\text{-}E}$	700	99	

Taken together, the combined results from Tables 2−4 point to the existence of important differences between compounds with identically functionalized phenyl groups at both ends of the DAG-lactone. These results are consistent with the proposed binding model in which the DAG-lactone binds to the C1 domain with the acyl chain oriented toward the lipid and its α-alkylidene chain possibly interacting with the surrounding space on the surface of the C1 domain. This binding model is further supported by the observed 128-fold difference between isomers (*E*)-**13** (K_i = 2400 nM) and **(***E***)-22** (K_i = 19 nM).

To study in more detail the contrast between **(***E***)-13** and **(***E***)-22** in a simpler system than the intact PKC-α isozyme, we decided to compare their binding affinities for the isolated δ-C1b domain (Table 5). This specific C1 domain was chosen both because the X-ray structure of its interaction with a ligand is known[24] and for technical considerations of stability and solubility. Using the C1 domain, we have a strong basis for relating our experimental K_i values to insights generated from computer modeling.[17,18] For the full PKC molecule, other structural features contributing to membrane interaction, e.g., the pseudosubstrate domain or the C2 domain, the presence of two functional C1 domains with distinct behavior, and the coupling of ligand binding and membrane interaction to a conformational change in the enzyme, with a resultant effect of this conformational change on the energetics of binding, all complicate interpretation.

Using the C1b domain, we further analyzed K_i for ligand binding both under normal conditions, in which anionic phospholipid (PS) is present to fulfill the complementary binding half-site along with the C1 domain, and in the absence of phospholipid. This latter condition, although nonphysiological, helps dissect the contributions to the binding complex of the C1 domain and of the lipid bilayer. This is important, because the only crystal structure available is that of the binary complex of the ligand and C1 domain,[24] whereas the experimental measurements under standard conditions represent the binding

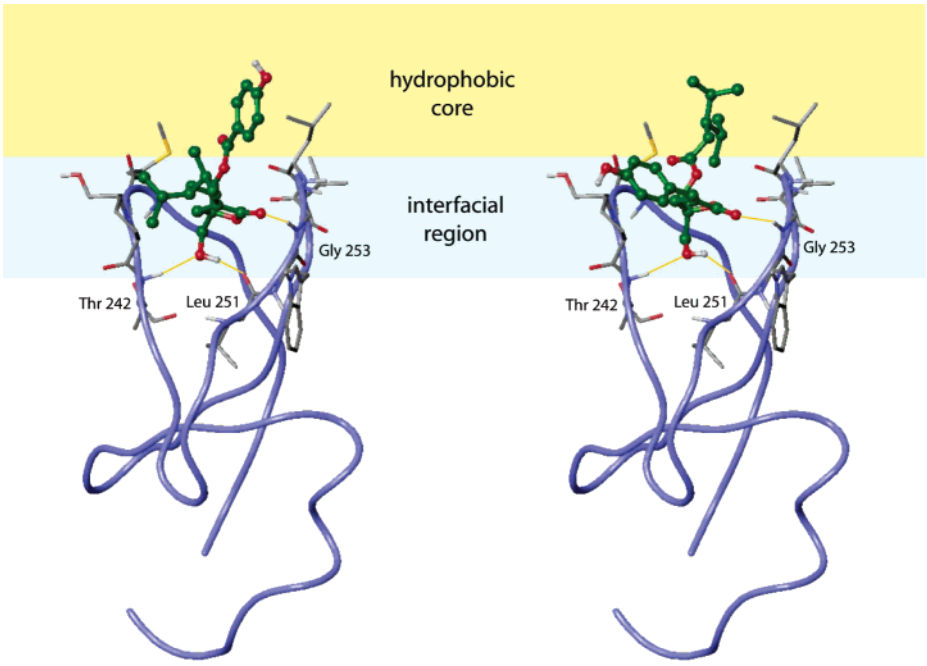
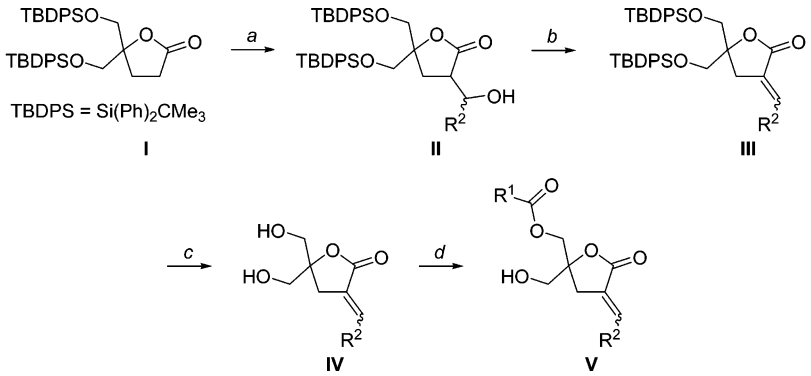


Figure 3. Model of the PKC-δ-C1b domain with bound DAG-lactones displaying the same hydrogen-bonding pattern as observed in the crystal structure of the same domain bound to phorbol (yellow lines). Although the exact depth of penetration and orientation of the PKC-δ-C1b domain relative to that of the membrane bilayer is not known experimentally, we can develop a reasonable estimate based on the location of hydrophobic residues in the binding site loops. The bilayer interfacial region, which consists of the lipid headgroups and ordered water, is colored pale blue, and the hydrophobic core of the lipid acyl chains is colored yellow. The left-hand structure shows the docked configuration of compound (*E*)-**13**, with the polar hydroxyl group on the acyl side chain projected into the hydrophobic core of the bilayer. The right-hand structure shows the docked configuration of compound (*E*)-**22**, with the α-phenylalkylidene side chain projected parallel to the membrane surface in the interfacial region, where the hydroxyl group could form hydrogen bonds to water or lipid headgroups.

Scheme 1[a]



[a] Conditions and reagents: (a) LDA, $ZnCl_2$, R^2CHO, THF, −78 °C; (b) Et_3N, MsCl, DBU, CH_2Cl_2, 0 °C → rt; (c) 70% HF/pyridine, pyridine, 0 °C → rt, or $Et_3N{\cdot}3HF$, CH_3CN, Δ; (d) Bu_2SnO, 4 Å molecular sieves, PhMe, Δ, then R^1COCl, 0 °C.

affinity for the ternary complex of ligand−C1 domain−phospholipid. The details of the assays were as described previously.[27,28]

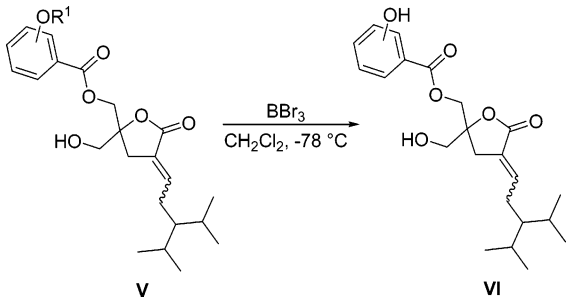
The 128-fold difference in favor of **(***E***)-22** over its isomer **(***E***)-13** with PKC-α (Tables 2 and 4) was magnified to 700-fold when we switched to the isolated PKC-δ-C1b domain in the presence of PS (Table 5). In the absence of PS, on the other hand, this difference dropped to only 99-fold. Because the lipophilicities of both isomers **(***E***)-13** and **(***E***)-22** are the same, and the expected desolvation penalties when PS is present should also be similar, removal of the lipid will impact more significantly the isomer where the OH is engaged in polar interactions with the charged PS headgroups. Hence, in the absence of PS, **(***E***)-13** experienced only a 17-fold drop in binding affinity, whereas the stronger ligand **(***E***)-22** experienced a 121-fold drop.

As before, these data further support the model already proposed, where the DAG-lactone binds to the C1 domain with the *sn*-1 acyl group oriented toward the hydrophobic lipid domain and the α-phenylalkylidene side chain projected parallel to the membrane surface in the interfacial region (Figure 3).

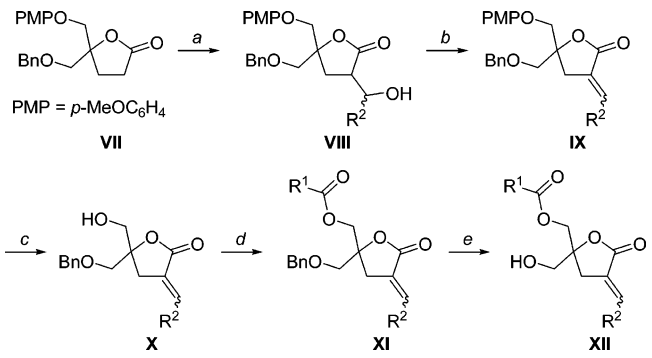
Chemistry

The DAG-lactones **1**−**10** (*E* and *Z*), (*E*)-**11**, (*E*)-**12**, (*E*)-**14**, and (*E*)-**15** were synthesized as racemates according to published methodology established in our laboratories as exemplified in Scheme 1.[25] Treatment of the previously reported protected lactone **I**[25] with LDA and $ZnCl_2$ followed by aldehyde gave the aldol adduct **II**. Subsequent mesylation followed by elimination with diazabicyclo[5.4.0]undec-7-ene (DBU) gave the α-alkylidene DAG-lactone **III** as a mixture of *E*- and *Z*-isomers, which were separated by silica gel chromatography. Consistent with previously synthesized DAG-lactones, the vinyl proton of the *Z*-isomer displayed a characteristic multiplet at $\delta = 6.12-6.18$ in its ^1H NMR spectrum, while the corresponding signal

Scheme 2



Scheme 3[a]



[a] Conditions and reagents: (a) LiHMDS, R^2CHO, THF, −78 °C; (b) Et_3N, MsCl, DBU, CH_2Cl_2, 0 °C → rt; (c) CAN, CH_3CN, 0 °C; (d) Et_3N, DMAP, R^1COCl; (e) BCl_3, CH_2Cl_2, −78 °C.

of the *E*-isomer appeared more downfield at $\delta = 6.72-6.77$. Deprotection of **III** was accomplished using either HF/pyridine or $Et_3N{\cdot}3HF$. Monoacylation of the resulting diol was accomplished using Bu_2SnO[29] and acyl chloride to give the *E*- and *Z*-isomers of DAG-lactones **1**−**10** and **14**−**15**. The *o*- and *m*-methoxy groups of DAG-lactones (*E*)-**8** and (*E*)-**9 (V)** were successfully removed with BBr_3 to give (*E*)-**11** and (*E*)-**12 (VI)**, respectively (Scheme 2). However, under the same reaction conditions, the corresponding *Z*-isomers of **8** and **9** gave inseparable *E*/*Z*-mixtures of **11** and **12**, while the *para*-isomer was completely cleaved to give diol **IV** ($R^2 = CH_2CH(i\text{-}Pr)_2$) instead of **13**. In this case, cleavage of the O−B bond occurred preferentially via formation of *p*-quinone rather than by simple aqueous hydrolysis during workup. These compounds ((*Z*)-**11**, (*Z*)-**12**, (*E*)-**13**, and (*Z*)-**13**) were obtained by an alternative route (vide infra).

An alternative strategy, which takes advantage of the lability of the benzyl protecting group, was employed for the phenol-substituted DAG-lactones ((*Z*)-**11**, (*Z*)-**12**, (*E*)-**13**, (*Z*)-**13**, and (*E*)-**20**−(*E*)-**22**) (Scheme 3). This improved method was then adapted as a general method for the synthesis of the remaining DAG-lactones (**16**−**22**) selected for this study. Starting from the previously reported asymmetrically protected DAG-lactone **VII**,[30,31] treatment with lithium bis(trimethylsilyl)amide (LHMDS) followed by the designated aldehyde gave the aldol adduct **VIII**. In a manner similar to the method described above, subsequent mesylation followed by elimination with DBU gave the diprotected α-alkylidene DAG-lactones **IX** as mixtures of *E*- and *Z*-isomers, except for the precursors of compounds **17**−**22** (Table 4), which gave exclusively the *E*-isomer. Selective deprotection of **IX** to remove the PMP group was accomplished using ceric ammonium nitrate (CAN) in acetonitrile to give **X**. Acylation with the selected acyl chloride, followed by debenzylation, gave the desired DAG-lactones **XII**. For DAG-lactones (*E*)-**17**−(*E*)-**19** and (*E*)-**20**−(*E*)-**22**, commercially available anisaldehyde and (benzyloxy)benzaldehyde isomers were used, respectively, for the aldol condensation step. For DAG-lactones (*Z*)-**11**, (*Z*)-**12**, (*E*)-**13**, and (*Z*)-**13**, the requisite isomeric (benzyloxy)benzoic acid chlorides were synthesized from the corresponding commercially available aldehydes according to published methods (see the Experimental Section). Unlike the method in Scheme 1, (*Z*)-**11**, (*Z*)-**12**, (*E*)-**13**, and (*Z*)-**13** were easily obtained by this approach without any evidence of *E*/*Z*-isomerization. Using the benzyl-protected aromatic aldehyde, or acid chloride, also offered the advantage of avoiding the hydrolysis challenges that were encountered with the method used in Scheme 2 and simplicity in simultaneously cleaving both benzyl protecting groups in the last step.

Discussion

As a starting point, the phenyl ring was selected as the simplest aryl group. To find the optimal placement of the phenyl ring at the acyl position, several analogues were constructed with the phenyl ring tethered to an alkyl chain at a predetermined distance away from the lactone moiety and successively brought closer until it was directly bonded to the carbonyl, giving the benzoate ester. Methylene bridges from 3 down to 0 units were employed, and for each methylene unit that was removed to bring the phenyl ring closer to the lactone ring, one was added to the α-alkylidene position to maintain a constant, optimal calculated log *P* value of approximately 4 (Table 1, compounds **1**−**4**). All of the compounds were separated into their geometric isomers, and typically the more effective *Z*-isomers were about 1.2−1.5-fold more potent than the *E*-isomers. The combination of the benzoate ester with a previously discovered highly effective branched α-alkylidene moiety[25] gave a set of compounds ((*E*)-**6** and (*Z*)-**6**) with a log *P* value below 4 and with just a slight 1.7-fold drop in binding affinity relative to that of compounds (*E*)-**4** and (*Z*)-**4** (Table 1). Two cyclohexyl variants of **4** and **6** were synthesized to investigate the changes resulting from the removal of the π-system (Table 1, compounds **5** and **7**). However, the meager increase in affinity accrued at the expense of a higher log *P* value and the expected difficulty in obtaining simple substituted analogues on the cyclohexyl ring convinced us that compound **6** provided the best combination of substituents. This compound allowed us to explore the effects of *ortho*-, *meta*- and *para*-substitutions on the phenyl ring (Table 2, compounds **8**−**13**). In keeping with the notion that the benzoate ester moiety at *sn*-1 appears to be projected into the lipid environment of the membrane, no advantage was derived by adding a methoxy group on the phenyl ring at various positions, as demonstrated by compounds **8**−**10**. In a similar manner, the conversion of methoxy groups into phenols (**11**−**13**) carried the corresponding penalty of having these hydrophilic groups projected into a hydrophobic lipid milieu. It is interesting that the *ortho*-substituted compounds (*E*)-**11** and (*Z*)-**11** were 10−15 times more potent than the corresponding *m*-isomers (*E*)-**12** and (*Z*)-**12** and ca. 35 times more potent than the *p*-isomers (*E*)-**13** and (*Z*)-**13**). This is probably due to the lower desolvation penalty of compound **11** when moving into the lipid medium due to the intramolecular hydrogen bonding of the phenol with the *sn*-1-carbonyl of the lactone.

Moving the aromatic moiety to an α-phenylalkylidene position while maintaining the esterase stable [$COCH_2CH(i\text{-}Pr)_2$] acyl group was also explored, commencing at the position closest to the lactone and increasing the distance of the phenyl ring by one or two methylene units (Table 3, compounds **14**−**16**). In the case of **14**, only the more thermodynamically stable *E*-isomer was obtained. Since the K_i values for these compounds were all in the same range, the compound with the

phenyl ring closest to the lactone ((*E*)-**14**) was selected because it had the lowest calculated log *P* value. This compound is the reverse isomer of **6**, and with a comparable calculated log *P* value it showed better binding affinity than either (*E*)-**6** or (*Z*)-**6**.

In contrast to the case in which the functionalized phenyl ring was part of the acyl moiety, the comparable K_i values observed for both sets of methoxy- and hydroxyphenyl-substituted compounds in Table 4 ((*E*)-**17**−(*E*)-**22**) suggest that these groups are able to find H-bonding partners. Remarkably, the presence of the OH in (*E*)-**20**−(*E*)-**22** does not lead to a significant loss in binding affinity as with the reverse isomers in Table 2. Since only *E*-isomers were obtained in this series, we cannot determine whether the same trend of "*Z* better than *E*" observed for the α-alkylidene isomers will hold.

The contrasting results in Tables 2−4 point to the existence of notable differences between compounds with identical functionalized phenyl groups at both ends of the DAG-lactone. These results are consistent with a model in which the DAG-lactone occupies the C1 domain with its acyl chain oriented toward the inner lipid core and where the polar groups on the α-phenylalkylidene chain could bind beyond the C1 domain at the lipid interface (Figure 3). The observed 128- and 700-fold differences in binding affinities between isomers (*E*)-**13** and (*E*)-**22** for PKC-α and the isolated δ-C1b domain support this binding model. Because molecular docking of these isomers into the empty δ-C1b domain did not reveal any critical H-bonding contacts with amino acids on the surface of the C1 domain, we consider it likely that the contrasting behaviors displayed by these isomers point to important polar interactions at the lipid interface in the ternary complex (Figure 3).

We conclude from the present study that both DAG templates containing the aryl ring closest to the lactone represent useful scaffolds upon which to explore future chemical diversity. In the case of the benzoate ester **4**, compounds bearing additional alkyl groups (Me, Et, *i*-Pr, and *t*-Bu) designed to seek additional interactions with the membrane will be investigated. In the case of the α-phenylalkylidene analogues, where the substituents are expected to engage in polar interactions, additional polar groups will be used to explore chemical diversity. We anticipate that a combination of substituents balancing the properties of lipophilicity at the *sn*-1 position and chemical specificity at the *sn*-2 position of DAG-lactones will provide efficient tools with which to explore specific translocation patterns of PKC to subcellular spaces.

Experimental Section

Biological Activity. Enzyme−ligand interactions were assessed in terms of the ability of the ligand to displace bound [20-^{3}H]phorbol 12,13-dibutyrate (PDBU) from a recombinant single isozyme (PKC-α) in the presence of phosphatidylserine.[21,32−35] The partition coefficients (log *P*) were calculated according to the atom-based program MOE SLog P.[20]

General Procedures. All chemical reagents were commercially available. Melting points were determined on a MelTemp II apparatus, Laboratory Devices, and are uncorrected. Column chromatography was performed on silica gel 60, 230−400 mesh (E. Merck or Bodman Industries), and analytical TLC was performed on Analtech Uniplates silica gel GF. ^{1}H and ^{13}C NMR spectra were recorded either on a Bruker AC-250 instrument at 250 and 62.9 MHz, respectively; or on a Varian Unity Inova instrument at 400 and 100 MHz, respectively. Spectra are referenced to the solvent in which they were run (7.26 ppm for $CDCl_3$). Positive ion fast atom bombardment mass spectra (FABMS) were obtained on a VG 7070E-HF double-focusing mass spectrometer operated at an accelerating voltage of 6 kV under the control of a MASPEC-II data system for Windows (Mass Spectrometry Services, Ltd.). Either glycerol or 3-nitrobenzyl alcohol was used as the sample matrix, and ionization was effected by a beam of xenon atoms generated in a saddle-field ion gun at 8.0 ± 0.5 kV. Nominal mass spectra were obtained at a resolution of 1200, and matrix-derived ions were background subtracted during data system processing. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA.

Molecular Modeling. Structures for compounds (*E*)-**13** and (*E*)-**22** were built in Sybyl[36] and minimized with the MMFF94 force field and partial charges.[37] These compounds were then docked into the crystal structure of the C1b domain of PKC-δ,[24] using the program GOLD 2.2.[38] We used standard default genetic algorithm settings, with the binding site defined by atoms within a 10.0 Å radius of the Nϵ atom of residue Q257. The stochastic nature of the GOLD docking algorithm gives a mixture of two binding modes. We know, however, from detailed energetic analysis that the *sn*-2 binding mode is preferred for the lactone template,[18] and we therefore included H-bonding constraints to bias the docking toward this mode. This allowed us to focus on exploring the conformational space available to the aryl side chains.

(Benzyloxy)benzoic Acids and (Benzyloxy)benzoyl Chlorides. 4-(Benzyloxy)benzoic acid is commercially available. The other isomers were obtained according to the method of Heaney and Newbold[39] from the corresponding aldehydes.[40,41] The acid chlorides were obtained after treatment with neat thionyl chloride at 50 °C. Azeotropic removal of the excess reagent with benzene afforded the crude acid chlorides, which were used immediately.

General Procedure for the Synthesis of II. Procedure A. According to a literature procedure,[32] a solution of **I** (1 equiv) in THF (7 mL/mmol) at −78 °C was treated dropwise with LDA (2.5 equiv) and stirred at the same temperature for 1 h. $ZnCl_2$ (1.1 equiv) was added followed by dropwise addition of R^1CHO (1.5 equiv), and the reaction was stirred at −78 °C for 1 h and then −40 °C for 1 h. The reaction mixture was then quenched with a saturated aqueous solution of NH_4Cl and allowed to warm to room temperature. The layers were separated, and the aqueous layer was extracted with Et_2O (3×). The combined organics were washed with H_2O (1×) and brine (1×), dried over $MgSO_4$, and concentrated in vacuo. Purification by silica gel flash column chromatography gave **II** as an oil which was used directly without further purification.

Procedure B. According to the literature procedure,[32] a solution of **I** (1 equiv) in THF (5 mL/mmol) at −78 °C was treated dropwise with LDA (1.5 equiv) and stirred at the same temperature for 2 h. A solution of R^1CHO (2 equiv) was added dropwise, and the reaction was stirred at −78 °C overnight. The reaction mixture was then quenched with a saturated aqueous solution of NH_4Cl and allowed to warm to room temperature. The layers were separated, and the aqueous layer was extracted with Et_2O (3×). The combined organics were washed with H_2O (2×) and brine (1×), dried over $MgSO_4$, and concentrated in vacuo. Purification by silica gel flash column chromatography gave **II** as a mixture of diastereomers which were used directly in the next step.

5,5-Bis[(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]-3-(hydroxyheptyl)-3,4,5-trihydrofuran-2-one (II, $R^2 = C_6H_{13}$). According to general procedure A, **I** and heptyl aldehyde (1.14 g, 10.0 mmol) were reacted to give **II** ($R^2 = C_6H_{13}$; 5.15 g, 100% yield).

5,5-Bis[(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]-3-(hydroxyoctyl)-3,4,5-trihydrofuran-2-one (II, $R^2 = C_7H_{15}$). According to general procedure A, **I** and octyl aldehyde (1.31 g, 10.2 mmol) were reacted to give **II** ($R^2 = C_7H_{15}$; 4.04 g, 78% yield).

5,5-Bis[(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]-3-(hydroxynonyl)-3,4,5-trihydrofuran-2-one (II, $R^2 = C_8H_{17}$). According to general procedure A, **I** and nonyl aldehyde (1.16 g, 8.14 mmol) were reacted to give **II** ($R^2 = C_8H_{17}$; 3.47 g, 66% yield).

5,5-Bis[(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]-3-(hydroxydecyl)-3,4,5-trihydrofuran-2-one (II, $R^2 = C_9H_{19}$). According to general procedure A, **I** and decyl aldehyde (3.82 g,

24.4 mmol) were reacted to give **II** ($R^2 = C_9H_{19}$; 13.63 g, 100% yield).

5,5-Bis[(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]-3-[1-hydroxy-4-methyl-3-(methylethyl)pentyl]-3,4,5-trihydrofuran-2-one (II, $R^2 = CH_2CH(i\text{-}Pr)_2$). This compound was prepared as previously reported.[25]

5,5-Bis[(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]-3-(hydroxyphenylmethyl)-3,4,5-trihydrofuran-2-one (II, $R^2 = Ph$). According to general procedure B, **I** and benzaldehyde (2.09 g, 19.7 mmol) were reacted to give **II** (R^2 = Ph; 6.32 g, 90% yield).

5,5-Bis[(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]-3-(1-hydroxy-2-phenylethyl)-3,4,5-trihydrofuran-2-one (II, $R^2 = CH_2Ph$). According to general procedure B, **I** and phenylacetaldehyde (2.26 g, 18.8 mmol) were reacted to give **II** ($R^2 = CH_2Ph$; 6.32 g, 90% yield).

General Procedure for the Synthesis of III. Procedure C. According to the literature procedure,[32] a solution of **II** (1 equiv) and triethylamine (4 equiv) in CH_2Cl_2 (10 mL/mmol) was treated dropwise with MsCl (2 equiv) at 0 °C and then stirred at room temperature for 1 h. The reaction mixture was then cooled again to 0 °C, DBU (5 equiv) was added dropwise at 0 °C, and the reaction mixture was allowed to reach room temperature overnight. The volatiles were removed in vacuo, and the residue was treated with EtOAc followed by 1 N HCl. The layers were separated, and the aqueous layer was extracted with EtOAc (1×). The combined organics were washed with H_2O (2×) and brine (1×), dried over $MgSO_4$, and concentrated in vacuo. Purification by silica gel flash column chromatography gave **III** as a mixture of *E*- and *Z*-isomers.

5,5-Bis[(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]-3-heptylidene-4,5-dihydrofuran-2-one (III, $R^2 = C_6H_{13}$). According to the general procedure C, **II** ($R^2 = C_6H_{13}$; 4.39 g, 5.95 mmol) was reacted to give (*E*)-**III** ($R^2 = C_6H_{13}$; 2.26 g, 53% yield) and (*Z*)-**III** ($R^2 = C_6H_{13}$; 941 mg, 22% yield).

Data for (*E*)-III ($R^2 = C_6H_{13}$): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.87 (app t, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_3$C*H*$_3$), 0.97 (s, 18 H, CCH$_2$OSiPh$_2$C(C*H*$_3$)$_3$), 1.20−1.35 (m, 6 H, C=CHCH$_2$CH$_2$(C*H*$_2$)$_3$CH$_3$), 1.35−1.50 (m, 2 H, C=CHCH$_2$C*H*$_2$(CH$_2$)$_3$CH$_3$), 2.13−2.20 (m, 2 H, C=CHC*H*$_2$CH$_2$(CH$_2$)$_4$CH$_3$), 2.70−2.75 (m, 2 H, H-4$_{ab}$), 3.68 (AB q, J = 10.8 Hz, 4 H, CC*H*$_2$OSiPh$_2$C(CH$_3$)$_3$), 6.68 (tt, J = 7.5, 2.9 Hz, 1 H, C=C*H*CH$_2$CH$_2$(CH$_2$)$_3$CH$_3$), 7.29−7.60 (m, 20 H, CCH$_2$OSi*Ph*$_2$C(CH$_3$)$_3$). Anal. ($C_{45}H_{58}O_4Si_2 \cdot 0.5H_2O$) C, H.

Data for (*Z*)-III ($R^2 = C_6H_{13}$): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.86 (app t, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_3$C*H*$_3$), 0.98 (s, 18 H, CCH$_2$OSiPh$_2$C(C*H*$_3$)$_3$), 1.20−1.43 (m, 8 H, C=CHCH$_2$C*H*$_2$(C*H*$_2$)$_3$CH$_3$), 2.60−2.75 (m, 2 H, C=CHC*H*$_2$CH$_2$(CH$_2$)$_3$CH$_3$), 2.80 (br d, J = 2.1 Hz, 2 H, H-4$_{ab}$), 3.66 (AB q, J = 10.7 Hz, 4 H, CC*H*$_2$OSiPh$_2$C(CH$_3$)$_3$), 6.09 (tt, J = 7.6, 2.1 Hz, 1 H, C=C*H*CH$_2$CH$_2$(CH$_2$)$_3$CH$_3$), 7.32−7.61 (m, 20 H, CCH$_2$OSi*Ph*$_2$C(CH$_3$)$_3$). Anal. ($C_{46}H_{60}O_4Si_2$) C, H.

5,5-Bis[(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]-3-octylidene-4,5-dihydrofuran-2-one (III, $R^2 = C_7H_{15}$). According to general procedure C, **II** ($R^2 = C_7H_{15}$; 3.71 g, 4.94 mmol) was reacted to give (*E*)-**III** ($R^2 = C_7H_{15}$; 1.85 g, 51% yield) and (*Z*)-**III** ($R^2 = C_7H_{15}$; 782 mg, 22% yield).

Data for (*E*)-III ($R^2 = C_7H_{15}$): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.86 (app t, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_4$C*H*$_3$), 0.97 (s, 18 H, CCH$_2$OSiPh$_2$C(C*H*$_3$)$_3$), 1.15−1.35 (m, 8 H, C=CHCH$_2$CH$_2$(C*H*$_2$)$_4$CH$_3$), 1.35−1.51 (m, 2 H, C=CHCH$_2$C*H*$_2$(CH$_2$)$_4$CH$_3$), 2.10−2.20 (m, 2 H, C=CHC*H*$_2$CH$_2$(CH$_2$)$_4$CH$_3$), 2.80 (br d, J = 2.0 Hz, 2 H, H-4$_{ab}$), 3.68 (AB q, J = 10.7 Hz, 4 H, CC*H*$_2$OSiPh$_2$C(CH$_3$)$_3$), 6.68 (tt, J = 7.5, 2.9 Hz, 1 H, C=C*H*CH$_2$CH$_2$(CH$_2$)$_4$CH$_3$), 7.32−7.60 (m, 20 H, CCH$_2$OSi*Ph*$_2$C(CH$_3$)$_3$). Anal. ($C_{46}H_{60}O_4Si_2$) C, H.

Data for (*Z*)-III ($R^2 = C_7H_{15}$): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.86 (app t, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_4$C*H*$_3$), 0.98 (s, 18 H, CCH$_2$OSiPh$_2$C(C*H*$_3$)$_3$), 1.20−1.48 (m, 10 H, C=CHCH$_2$C*H*$_2$(C*H*$_2$)$_4$CH$_3$), 2.62−2.74 (m, 2 H, C=CHC*H*$_2$CH$_2$(CH$_2$)$_4$CH$_3$), 2.80 (br d, 2 H, H-4$_{ab}$), 3.66 (AB q, J = 10.7 Hz, 4 H, CC*H*$_2$OSiPh$_2$C(CH$_3$)$_3$), 6.09 (tt, J = 7.6, 2.1 Hz, 1 H, C=C*H*CH$_2$CH$_2$(CH$_2$)$_4$CH$_3$), 7.32−7.60 (m, 20 H, (CH$_3$)$_3$CSi*Ph*$_2$OCH$_2$C). Anal. ($C_{46}H_{60}O_4Si_2$) C, H.

5,5-Bis[(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]-3-nonylidene-4,5-dihydrofuran-2-one (III, $R^2 = C_8H_{17}$). According to general procedure C, **II** ($R^2 = C_8H_{17}$; 5.39 g, 7.04 mmol) was reacted to give (*E*)-**III** ($R^2 = C_8H_{17}$; 3.80 g, 72% yield) and (*Z*)-**III** ($R^2 = C_8H_{17}$; 542 mg, 10% yield).

Data for (*E*)-III ($R^2 = C_8H_{17}$): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.86 (app t, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_5$C*H*$_3$), 0.97 (s, 18 H, CCH$_2$OSiPh$_2$C(C*H*$_3$)$_3$), 1.25−1.40 (m, 10 H, C=CHCH$_2$CH$_2$(C*H*$_2$)$_5$CH$_3$), 1.40−1.55 (m, 2 H, C=CHCH$_2$C*H*$_2$(CH$_2$)$_5$CH$_3$), 2.10−2.18 (m, 2 H, C=CHC*H*$_2$CH$_2$(CH$_2$)$_5$CH$_3$), 2.72 (br s, 2 H, H-4$_{ab}$), 3.68 (AB q, J = 10.7 Hz, 4 H, CC*H*$_2$OSiPh$_2$C(CH$_3$)$_3$), 6.60−6.73 (m, 1 H, C=C*H*CH$_2$CH$_2$(CH$_2$)$_5$CH$_3$), 7.30−7.45 and 7.58−7.65 (m, 20 H, CCH$_2$OSi*Ph*$_2$C(CH$_3$)$_3$). Anal. ($C_{47}H_{62}O_4Si_2$) C, H.

Data for (*Z*)-III ($R^2 = C_8H_{17}$): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.86 (app t, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_5$C*H*$_3$), 0.96 (s, 18 H, CCH$_2$OSiPh$_2$C(C*H*$_3$)$_3$), 1.25−1.48 (m, 12 H, C=CHCH$_2$C*H*$_2$(C*H*$_2$)$_5$CH$_3$), 2.60−2.76 (m, 2 H, C=CHC*H*$_2$CH$_2$(CH$_2$)$_5$CH$_3$), 2.88 (br d, J = 2.0 Hz, 2 H, H-4$_{ab}$), 3.66 (AB q, J = 10.7 Hz, 4 H, CC*H*$_2$OSiPh$_2$C(CH$_3$)$_3$), 6.05−6.15 (m, 1 H, C=C*H*CH$_2$CH$_2$(CH$_2$)$_5$CH$_3$), 7.23−7.45 and 7.56−7.60 (m, 20 H, CCH$_2$OSi*Ph*$_2$C(CH$_3$)$_3$). Anal. ($C_{47}H_{62}O_4Si_2$) C, H.

5,5-Bis[(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]-3-decylidene-4,5-dihydrofuran-2-one (III, $R^2 = C_9H_{19}$). According to general procedure C, **II** ($R^2 = C_9H_{19}$; 12.51 g, 16.05 mmol) was reacted to give (*E*)-**III** ($R^2 = C_9H_{19}$; 7.67 g, 63% yield) and (*Z*)-**III** ($R^2 = C_9H_{19}$; 2.57 g, 21% yield).

Data for (*E*)-III ($R^2 = C_9H_{19}$): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.97 (app t, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_6$C*H*$_3$), 1.08 (s, 18 H, CCH$_2$OSiPh$_2$C(C*H*$_3$)$_3$), 1.35 (s, 12 H, C=CHCH$_2$CH$_2$(C*H*$_2$)$_6$CH$_3$), 1.49−1.52 (m, 2 H, C=CHCH$_2$C*H*$_2$(CH$_2$)$_6$CH$_3$), 2.19−2.27 (q, J = 7. 1 Hz, 2 H, C=CHC*H*$_2$CH$_2$(CH$_2$)$_6$CH$_3$), 2.83 (s, 2 H, H-4$_{ab}$), 3.79 (AB q, J = 10.7 Hz, 4 H, CC*H*$_2$OSiPh$_2$C(CH$_3$)$_3$), 6.74−6.85 (m, 1 H, C=C*H*CH$_2$CH$_2$(CH$_2$)$_6$CH$_3$), 7.41−7.51 and 7.68−7.71 (m, 20 H, CCH$_2$OSi*Ph*$_2$C(CH$_3$)$_3$). Anal. ($C_{48}H_{64}O_4Si_2$).

Data for (*Z*)-III ($R^2 = C_9H_{19}$): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.97 (app t, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_6$C*H*$_3$), 1.09 (s, 18 H, CCH$_2$OSiPh$_2$C(C*H*$_3$)$_3$), 1.35−1.55 (m, 14 H, C=CHCH$_2$C*H*$_2$(C*H*$_2$)$_6$CH$_3$), 2.74−2.85 (m, 2 H, C=CHC*H*$_2$CH$_2$(CH$_2$)$_6$CH$_3$), 2.91 (d, J = 1.7 Hz, 2 H, H-4$_{ab}$), 3.78 (AB q, J = 10.7 Hz, 4 H, CC*H*$_2$OSiPh$_2$C(CH$_3$)$_3$), 6.20 (t, J = 7.6 Hz, 1 H, C=C*H*CH$_2$CH$_2$(CH$_2$)$_6$CH$_3$), 7.41−7.51 and 7.68−7.71 (m, 20 H, CCH$_2$OSi*Ph*$_2$C(CH$_3$)$_3$). Anal. ($C_{48}H_{64}O_4Si_2$) C, H.

(*E*)-5,5-Bis[(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]-3-[4-methyl-3 -(methylethyl)pentylidene]-4,5-dihydrofuran-2-one (III, $R^2 = CH_2CH(i\text{-}Pr)_2$) and (*Z*)-5,5-Bis[(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]-3-[4-methyl-3-(methylethyl)-pentylidene]-4,5-dihydrofuran-2-one (III, $R^2 = CH_2CH(i\text{-}Pr)_2$). These compounds are known and were prepared as previously reported.[25]

5,5-Bis[(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]-3-(phenylmethylene)-4,5-dihydrofuran-2-one (III, $R^2 = Ph$). According to general procedure C, **II** (R^2 = Ph; 6.27 g, 8.60 mmol) was reacted to give (*E*)-**III** (R^2 = Ph; 5.11 g, 84% yield) as the major product and (*Z*)-**III** (R^2 = Ph; 218 mg, 3% yield), which was only isolated as a crude oil.

Data for (*E*)-III ($R^2 = Ph$): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.06 (s, 18 H, CCH$_2$OSiPh$_2$C(C*H*$_3$)$_3$), 3.15 (d, J = 2.7 Hz, 2 H, H-4$_{ab}$), 3.85 (AB q, J = 10.9 Hz, 4 H, CC*H*$_2$OSiPh$_2$C(CH$_3$)$_3$), 7.35−7.53 and 7.60−7.68 (m, 26 H, CCH$_2$OSi*Ph*$_2$C(CH$_3$)$_3$ and C=C*H*Ph). Anal. ($C_{45}H_{50}O_4Si_2$) C, H.

(*Z*)-III ($R^2 = Ph$). Although this product was only obtained as a crude oil, it helped establish the stereochemistry of the double bond, relative to that of the major isomer (*E*)-**III**, on the basis of the chemical shift of the C=C*H*Ph signal: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.08 (s, 18 H, CCH$_2$OSiPh$_2$C(C*H*$_3$)$_3$), 3.14 (d, J = 2.2 Hz, 2 H, H-4$_{ab}$), 3.83 (AB q, J = 10.5 Hz, 4 H, CC*H*$_2$OSiPh$_2$C(CH$_3$)$_3$), 6.98 (br s, 1 H, C=C*H*Ph), 7.38−7.50, 7.69−7.72, and 7.88−7.91 (m, 25 H, CCH$_2$OSi*Ph*$_2$C(CH$_3$)$_3$ and C=CH*Ph*).

(*E*)-5,5-Bis[(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]-3-(2-phenylethylidene)-4,5-dihydrofuran-2-one (III, $R^2 = CH_2Ph$). According to general procedure C, **II** ($R^2 = CH_2Ph$; 5.60 g, 7.54

mmol) was reacted to give (*E*)-**III** ($R^2 = CH_2Ph$; 2.85 g, 52% yield) and a mixture of byproducts. A characteristic pattern consisting of NMR signals at δ 6.56 (d, $J = 16$ Hz, 1 H) and δ 6.28 (dd, $J = 16$, 6.8 Hz, 1 H) confirmed that the double bond in the byproducts had rearranged and that it was no longer conjugated to the lactone carbonyl.

Data for II ($R^2 = CH_2Ph$): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.08 (s, 18 H, $CCH_2OSiPh_2C(CH_3)_3$), 2.88 (s, 2 H, H-4_{ab}), 3.58 (d, $J = 7.3$ Hz, 2 H, C=CHCH_2Ph), 3.79 (AB q, $J = 10.8$ Hz, 4 H, $CCH_2OSiPh_2C(CH_3)_3$), 6.94−7.02 (m, 1 H, C=CHCH$_2$Ph), 7.22−7.51 and 7.67−7.70 (m, 25 H, $CCH_2OSiPh_2C(CH_3)_3$ and C=CHCH$_2$*Ph*). Anal. ($C_{46}H_{52}O_4Si_2 \cdot 0.25H_2O$) C, H.

General Procedure for the Synthesis of IV. Procedure D. A solution of **III** (1 equiv) in pyridine (7 mL/mmol) was treated dropwise with HF/pyridine (70%, 5 equiv) at 0 °C and allowed to reach room temperature overnight. The reaction mixture was then quenched with solid $NaHCO_3$ and filtered. The filtrate was concentrated in vacuo and azeotroped with toluene and chloroform. Purification by silica gel flash column chromatography gave **IV**.

Procedure E. According to the literature procedure,[42] a suspension of **III** (1 equiv) in CH_3CN (29 mL/mmol) was treated with $Et_3N \cdot 3HF$ (6 equiv) and heated to reflux for 5 h. The reaction mixture was then cooled to room temperature, pH 7.0 potassium phosphate buffer (1 mL/mL CH_3CN) was added, and the mixture was stirred for 30 min. The reaction mixture was then diluted with EtOAc, the layers were separated, and the aqueous layer was extracted with EtOAc (2×). The combined organic layers were washed with brine (1×), dried over $MgSO_4$, and concentrated in vacuo. Purification by silica gel flash column chromatography gave **IV**.

(*E*)-5,5-Bis(hydroxymethyl)-3-heptylidene-4,5-dihydrofuran-2-one (IV, $R^2 = C_6H_{13}$). According to general procedure E, (*E*)-**III** ($R^2 = C_6H_{13}$; 820 mg, 1.14 mmol) was reacted to give (*E*)-**IV** ($R^2 = C_6H_{13}$; 206 mg, 75% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.97 (app t, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_3$CH_3), 1.37 (br s, 6 H, C=CHCH$_2$CH$_2$(CH_2)$_3$CH$_3$), 1.50−1.65 (m, 2 H, C=CHCH$_2$CH_2(CH$_2$)$_3$CH$_3$), 2.22−2.30 (m, 2 H, C=CHCH_2-CH$_2$(CH$_2$)$_3$CH$_3$), 2.42 (t, $J = 5.9$ Hz, 2 H, CCH$_2$OH), 2.81 (br s, 2 H, H-4_{ab}), 3.74−3.91 (overlapping AB quartets, 4 H, CCH_2OH), 6.80−6.88 (m, 1 H, C=CHCH$_2$CH$_2$(CH$_2$)$_3$CH$_3$); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.08, 22.57, 28.04, 29.03, 29.39, 30.32, 31.59, 65.17, 85.09, 126.12, 142.19, 170.47; FAB-MS (*m*/*z*, relative intensity) 243 (MH^+, 100). Anal. ($C_{13}H_{22}O_4$).

(*Z*)-5,5-Bis(hydroxymethyl)-3-heptylidene-4,5-dihydrofuran-2-one (IV, $R^2 = C_6H_{13}$). According to general procedure D, (*Z*)-**III** ($R^2 = C_6H_{13}$; 976 mg, 1.36 mmol) was reacted to give (*Z*)-**IV** ($R^2 = C_6H_{13}$; 257 mg, 78% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.96 (app t, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_3$CH_3), 1.36−1.53 (m, 8 H, C=CHCH$_2$CH_2(CH_2)$_3$CH$_3$), 2.46 (br s, 2 H, CCH$_2$OH), 2.74−2.81 (m, 2 H, C=CHCH_2CH$_2$(CH$_2$)$_3$CH$_3$), 2.86 (br d, $J = 2.2$ Hz, 2 H, H-4_{ab}), 3.81 (AB q, $J = 12.0$ Hz, 4 H, CCH_2OH), 6.33 (tt, $J = 7.7$, 2.2 Hz, 1 H, C=CHCH$_2$CH$_2$(CH$_2$)$_3$CH$_3$); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.00, 22.50, 27.71, 28.86, 28.94, 31.55, 32.59, 64.98, 84.18, 123.92, 145.70, 169.14; FAB-MS (*m*/*z*, relative intensity) 243 (MH^+, 100). Anal. ($C_{13}H_{22}O_4 \cdot 0.2H_2O$) C, H.

(*E*)-5,5-Bis(hydroxymethyl)-3-octylidene-4,5-dihydrofuran-2-one (IV, $R^2 = C_7H_{15}$). According to general procedure E, (*E*)-**III** ($R^2 = C_7H_{15}$; 3.71 g, 4.94 mmol) was reacted to give (*E*)-**IV** ($R^2 = C_7H_{15}$; 227 mg, 80% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.83−0.89 (m, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_4$CH_3), 1.26 (s, 8 H, C=CHCH$_2$CH$_2$(CH_2)$_4$CH$_3$), 1.43−1.48 (m, 2 H, C=CHCH$_2$CH_2-(CH$_2$)$_4$CH$_3$), 2.02 (br s, 2 H, CCH$_2$OH), 2.11−2.20 (m, 2 H, C=CHCH_2CH$_2$(CH$_2$)$_4$CH$_3$), 2.71 (m, 2 H, H-4_{ab}), 3.73 (AB q, $J = 12.0$ Hz, 4 H, CCH_2OH), 6.74 (tt, $J = 7.6$, 2.9 Hz, 1 H, C=CHCH$_2$CH$_2$(CH$_2$)$_4$CH$_3$); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.04, 22.58, 28.03, 29.01, 29.27, 29.34, 30.27, 31.69, 65.20, 84.96, 126.11, 142.26, 170.41; FAB-MS (*m*/*z*, relative intensity) 257 (MH^+, 100). Anal. ($C_{14}H_{24}O_4$) C, H.

(*Z*)-5,5-Bis(hydroxymethyl)-3-octylidene-4,5-dihydrofuran-2-one (IV, $R^2 = C_7H_{15}$). According to general procedure D, (*Z*)-**III** ($R^2 = C_7H_{15}$; 1.08 g, 1.47 mmol) was reacted to give (*Z*)-**IV** ($R^2 = C_7H_{15}$; 317 mg, 84% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.93−0.96 (m, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_4$CH_3), 1.33 (s, 8 H, C=CHCH$_2$CH$_2$(CH_2)$_4$CH$_3$), 1.45−1.53 (m, 2 H, C=CHCH$_2$CH_2-(CH$_2$)$_4$CH$_3$), 2.33 (br s, 2 H, CCH$_2$OH), 2.73−2.82 (m, 2 H, C=CHCH_2CH$_2$(CH$_2$)$_4$CH$_3$), 2.87 (d, $J = 2.0$ Hz, 2 H, H-4_{ab}), 3.81 (distorted AB q, $J = 12.1$ Hz, 4 H, CCH_2OH), 6.32 (tt, $J = 7.7$, 2.2 Hz, 1 H, C=CHCH$_2$CH$_2$(CH$_2$)$_4$CH$_3$); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.02, 22.56, 27.71, 28.98, 29.03, 29.17, 31.69, 32.62, 64.69, 84.57, 124.07, 145.58, 169.62; FAB-MS (*m*/*z*, relative intensity) 257 (MH^+, 100). Anal. ($C_{14}H_{24}O_4$) C, H.

(*E*)-5,5-Bis(hydroxymethyl)-3-nonylidene-4,5-dihydrofuran-2-one (IV, $R^2 = C_8H_{17}$). According to general procedure E, (*E*)-**III** ($R^2 = C_8H_{17}$; 760 mg, 1.02 mmol) was reacted to give (*E*)-**IV** ($R^2 = C_8H_{17}$; 255 mg, 92% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.86 (app t, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_5$CH_3), 1.5 (s, 10 H, C=CHCH$_2$CH$_2$(CH_2)$_5$CH$_3$), 1.43−1.48 (m, 2 H, C=CHCH$_2$CH_2-(CH$_2$)$_5$CH$_3$), 1.97 (br s, 2 H, CCH$_2$OH), 2.12−2.20 (m, 2 H, C=CHCH_2CH$_2$(CH$_2$)$_5$CH$_3$), 2.70−2.72 (m, 2 H, H-4_{ab}), 3.73 (AB q, $J = 12.0$ Hz, 4 H, CCH_2OH), 6.74 (tt, $J = 7.6$ 2.9 Hz, 1 H, C=CHCH$_2$CH$_2$(CH$_2$)$_5$CH$_3$); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.05, 22.62, 28.03, 29.15, 29.31, 30.27, 31.79, 65.21, 84.90, 126.10, 142.26, 170.33; FAB-MS (*m*/*z*, relative intensity) 271 (MH^+, 100). Anal. ($C_{15}H_{26}O_4$).

(*Z*)-5,5-Bis(hydroxymethyl)-3-nonylidene-4,5-dihydrofuran-2-one (IV, $R^2 = C_8H_{17}$). According to general procedure E, (*Z*)-**III** ($R^2 = C_8H_{17}$; 390 mg, 0.52 mmol) was reacted to give (*Z*)-**IV** ($R^2 = C_8H_{17}$; 130 mg, 93% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.83−0.88 (m, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_5$CH_3), 1.24−1.40 (m, 12 H, C=CHCH$_2$CH_2(CH_2)$_5$CH$_3$), 2.06 (br s, 2 H, CCH$_2$OH), 2.66−2.69 (m, 2 H, C=CHCH_2CH$_2$(CH$_2$)$_5$CH$_3$), 2.75−2.78 (m, 2 H, H-4_{ab}), 3.71 (AB q, $J = 12.0$ Hz, 4 H, CCH_2OH), 6.23 (tt, $J = 7.7$, 2.3 Hz, 1 H, C=CHCH$_2$CH$_2$(CH$_2$)$_5$CH$_3$); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.07, 22.63, 27.75, 29.03, 29.19, 29.24, 29.36, 31.82, 32.63, 65.11, 84.07, 124.41, 145.86, 169.13; FAB-MS (*m*/*z*, relative intensity) 271 (MH^+, 100). Anal. ($C_{15}H_{26}O_4$).

(*E*)-5,5-Bis(hydroxymethyl)-3-decylidene-4,5-dihydrofuran-2-one (IV, $R^2 = C_9H_{19}$). According to general procedure E, (*E*)-**III** ($R^2 = C_9H_{19}$; 790 mg, 1.04 mmol) was reacted to give (*E*)-**IV** ($R^2 = C_9H_{19}$; 271 mg, 92% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.81−0.91 (m, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_6$CH_3), 1.25 (s, 12 H, C=CHCH$_2$CH$_2$(CH_2)$_6$CH$_3$), 1.38−1.54 (m, 2H, C=CHCH$_2$CH_2(CH$_2$)$_6$CH$_3$), 1.97 (br s, 2 H, CCH$_2$OH), 2.08−2.24 (m, 2 H, C=CHCH_2CH$_2$(CH$_2$)$_6$CH$_3$), 2.65−2.75 (m, 2 H, H-4_{ab}), 3.73 (AB q, $J = 12.1$ Hz, 4 H, CCH_2OH), 6.74 (tt, $J = 7.6$, 2.8 Hz, 1 H, C=CHCH$_2$CH$_2$(CH$_2$)$_6$CH$_3$); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.06, 22.64, 28.03, 29.24, 29.34, 29.45, 30.27, 31.82, 65.22, 84.85, 126.11, 142.26, 170.34; FAB-MS (*m*/*z*, relative intensity) 285 (MH^+, 100). Anal. ($C_{16}H_{28}O_4$) C, H.

(*Z*)-5,5-Bis(hydroxymethyl)-3-decylidene-4,5-dihydrofuran-2-one (IV, $R^2 = C_9H_{19}$). According to general procedure D, (*Z*)-**III** ($R^2 = C_9H_{19}$; 997 mg, 1.31 mmol) was reacted to give (*Z*)-**IV** ($R^2 = C_9H_{19}$; 334 mg, 90% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.93−0.96 (m, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_6$CH_3), 1.34−1.70 (m, 14 H, C=CHCH$_2$CH_2(CH_2)$_6$CH$_3$), 2.12 (t, $J = 6.4$ Hz, 2 H, CCH$_2$OH), 2.74−2.87 (m, 2 H, C=CHCH_2CH$_2$(CH$_2$)$_6$CH$_3$), 2.88 (d, $J = 2.2$ Hz, 2 H, H-4_{ab}), 3.74−3.90 (overlapping AB quartets, 4 H, CCH_2OH), 6.33 (tt, $J = 7.7$, 2.2 Hz, 1 H, C=CHCH$_2$CH$_2$(CH$_2$)$_6$-CH$_3$); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.05, 22.61, 27.72, 28.99, 29.22, 29.38, 29.45, 29.63, 31.81, 32.60, 64.96, 84.22, 123.89, 145.86, 169.20; FAB-MS (*m*/*z*, relative intensity) 285 (MH^+, 100). Anal. ($C_{16}H_{28}O_4$) C, H.

(*E*)-5,5-Bis(hydroxymethyl)-3-[4-methyl-3-(methylethyl)pentylidene]-4,5-dihydrofuran-2-one (IV, $R^2 = CH_2CH(i\text{-}Pr)_2$). This compound is known and was prepared as previously reported.[25]

(*Z*)-5,5-Bis(hydroxymethyl)-3-[4-methyl-3-(methylethyl)pentylidene]-4,5-dihydrofuran-2-one (IV, $R^2 = CH_2CH(i\text{-}Pr)_2$). This compound is known and was prepared as previously reported.[25]

(*E*)-5,5-Bis(hydroxymethyl)-3-(phenylmethylene)-4,5-dihydrofuran-2-one (IV, R^2 = Ph). According to general procedure D, (*E*)-**III** (R^2 = Ph; 2.08 g, 2.92 mmol) was reacted to give (*E*)-**IV** (R^2 = Ph; 672 mg, 98% yield): ^{1}H NMR (250 MHz, d_4-MeOH) δ 3.22 (d, $J = 2.7$ Hz, 2 H, H-4_{ab}), 3.74 (AB q, $J = 12.1$ Hz, 4 H,

CC*H*$_2$OH), 7.47−7.68 (m, 6 H C=C*HPh*); ^{13}C NMR (62.9 MHz, d_4-MeOH) δ 32.61, 65.29, 87.91, 127.79, 130.04, 130.92, 131.26, 136.24, 136.78, 174.04; FAB-MS (*m*/*z*, relative intensity) 235 (MH^+, 100). Anal. ($C_{13}H_{14}O_4$) C, H.

(*E*)-5,5-Bis(hydroxymethyl)-3-(2-phenylethylidene)-4,5-dihydrofuran-2-one (IV, R^2 = CH$_2$Ph). According to general procedure D, (*E*)-**III** (R^2 = CH$_2$Ph; 1.36 g, 1.87 mmol) was reacted to give (*E*)-**IV** (R^2 = CH$_2$Ph; 411 mg, 88% yield): ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.70 (s, 2 H, H-4$_{ab}$), 2.88 (s, 2 H, C=CHC*H*$_2$Ph), 3.60 (d, J = 1.5 Hz, 2 H, CCH$_2$O*H*), 3.82 (AB q, J = 12.1 Hz, 4 H, CC*H*$_2$OH), 6.98 (tt, J = 7.6, 2.7 Hz, 1 H, C=C*H*CH$_2$Ph), 7.27−7.42 (m, 5 H C=CHCH$_2$*Ph*); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 29.37, 36.21, 64.90, 85.6, 126.65, 127.23, 128.31, 128.67, 137.33, 139.25, 170.5; FAB-MS (*m*/*z*, relative intensity) 249 (MH^+, 100). Anal. ($C_{14}H_{16}O_4 \cdot 0.25H_2O$) C, H.

General Procedure for the Synthesis of V. Procedure F. According to the literature procedure,[43] a mixture of **IV** (1 equiv), 4 Å molecular sieves (800 mg/mmol), and Bu_2SnO (1.5 equiv) in anhydrous toluene (14 mL/mmol) was heated to reflux for 2.5 h. The reaction mixture was then cooled to 0 °C, treated dropwise with the corresponding acid chloride (1.1 equiv), and stirred at 0 °C for 1 h. The reaction mixture was then quenched with pH 7.0 potassium phosphate buffer (1 mL/mL of toluene) and filtered through a pad of Celite. The filtrate was then extracted with $CHCl_3$ (1×), and the organic layer was dried over $MgSO_4$ and concentrated in vacuo. Purification by silica gel flash column chromatography gave **V** and variable amounts of the diacylated product, which was not characterized.

Procedure G. A solution of **IV** (1 equiv) in CH_2Cl_2 (16 mL/mmol) was treated with anhydrous pyridine (2 equiv) at room temperature and stirred for 2 h. The reaction temperature was then lowered to 0 °C, and the acid chloride (1.5 equiv) was added dropwise. The resulting solution was stirred at 0 °C for 30 min to 1 h and then at room temperature until the reaction was considered complete as determined by TLC. The crude solution was then concentrated in vacuo and the residue purified by silica gel flash column chromatography to give **V** and variable amounts of the diacylated product, which was not characterized.

(*E*)-[4-Heptylidene-2-(hydroxymethyl)-5-oxo-2,3-dihydrofur-2-yl]methyl 4-Phenylbutanoate ((*E*)-1, (*E*)-V, R^1 = Ph(CH$_2$)$_3$, R^2 = C$_6$H$_{13}$). According to general procedure F, (*E*)-**IV** (R^2 = C_6H_{13}; 160 mg, 0.66 mmol) and Ph(CH$_2$)$_3$COCl (132 mg, 0.72 mmol) were reacted to give (*E*)-**1** ((*E*)-**V**, R^1 = Ph(CH$_2$)$_3$, R^2 = C_6H_{13}; 196 mg, 76% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.94−0.99 (m, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_3$C*H*$_3$), 1.36 (br s, 6 H, C=CHCH$_2$CH$_2$(C*H*$_2$)$_3$CH$_3$), 1.48−1.57 (m, 2 H, C=CHCH$_2$C*H*$_2$-(CH$_2$)$_3$CH$_3$), 1.97−2.09 (m, 2 H, CCH$_2$OC(O)CH$_2$C*H*$_2$CH$_2$Ph), 2.19−2.27 (m, 2 H, C=CHC*H*$_2$CH$_2$(CH$_2$)$_3$CH$_3$), 2.44 (t, J = 7.6 Hz, 2 H, CCH$_2$OC(O)C*H*$_2$CH$_2$CH$_2$Ph), 2.70−2.94 (m, 4 H, H-3$_{a,b}$ and CC*H*$_2$OC(O)CH$_2$CH$_2$CH$_2$Ph), 3.68−3.83 (m, 2 H, HOC*H*$_2$C), 4.31 (AB q, J = 11.8 Hz, 2 H, CC*H*$_2$OC(O)CH$_2$CH$_2$CH$_2$Ph), 6.80−6.89 (m, 1 H, C=C*H*CH$_2$CH$_2$(CH$_2$)$_3$CH$_3$), 7.23−7.40 (m, 5 H, CCH$_2$OC(O)CH$_2$CH$_2$CH$_2$*Ph*); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.10, 22.59, 26.34, 28.05, 29.04, 29.88, 30.34, 31.60, 33.35, 35.08, 64.78, 65.35, 82.88, 125.57, 126.05, 128.41, 140.98, 142.21, 169.71, 173.15; FAB-MS (*m*/*z*, relative intensity) 389 (MH^+, 92), 147 (100). Anal. ($C_{23}H_{32}O_5$).

(*Z*)-[4-Heptylidene-2-(hydroxymethyl)-5-oxo-2,3-dihydrofur-2-yl]methyl 4-Phenylbutanoate ((*Z*)-1, (*Z*)-V, R^1 = Ph(CH$_2$)$_3$, R^2 = C$_6$H$_{13}$). According to general procedure F, (*Z*)-**IV** (R^2 = C_6H_{13}; 103 mg, 0.42 mmol) and Ph(CH$_2$)$_3$COCl (84.4 mg, 0.46 mmol) were reacted to give (*Z*)-**1** ((*Z*)-**V**, R^1 = Ph(CH$_2$)$_3$, R^2 = C_6H_{13}; 74 mg, 45% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.94−0.96 (m, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_3$C*H*$_3$), 1.34−1.52 (m, 8 H, C=CHCH$_2$C*H*$_2$(C*H*$_2$)$_3$CH$_3$), 1.97−2.09 (m, 3 H, CCH$_2$O*H* and CCH$_2$OC(O)CH$_2$C*H*$_2$CH$_2$Ph), 2.44 (t, J = 7.4 Hz, 2 H, CCH$_2$OC-(O)C*H*$_2$CH$_2$CH$_2$Ph), 2.70−3.00 (m, 6 H, C=CHC*H*$_2$CH$_2$(CH$_2$)$_3$-CH$_3$, CCH$_2$OC(O)CH$_2$CH$_2$C*H*$_2$Ph, and H-3$_{ab}$), 3.73 (AB q, J = 12.2 Hz, 2 H, CC*H*$_2$OH), 4.29 (AB q, J = 12.0 Hz, 2 H, CC*H*$_2$OC(O)-CH$_2$CH$_2$CH$_2$Ph), 6.31 (m, 1 H, C=C*H*CH$_2$CH$_2$(CH$_2$)$_3$CH$_3$), 7.23−7.40 (m, 5 H, CCH$_2$OC(O)CH$_2$CH$_2$CH$_2$*Ph*); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.01, 22.50, 26.23, 27.68, 28.87, 28.96, 31.55, 33.01, 33.25, 34.97, 64.51, 65.10, 82.12, 123.43, 125.93, 128.29, 128.30, 140.88, 145.64, 168.41, 173.08; FAB-MS (*m*/*z*, relative intensity) 389 (MH^+, 23), 147 (100). Anal. ($C_{23}H_{32}O_5 \cdot 0.5H_2O$) C, H.

(*E*)-[2-(Hydroxymethyl)-4-octylidene-5-oxo-2,3-dihydrofur-2-yl]methyl 3-Phenylpropanoate ((*E*)-2, (*E*)-V, R^1 = Ph(CH$_2$)$_2$, R^2 = C$_7$H$_{15}$). According to general procedure F, (*E*)-**IV** (R^2 = C_7H_{15}; 170 mg, 0.66 mmol) and Ph(CH$_2$)$_2$COCl (122.6 mg, 0.73 mmol) were reacted to give (*E*)-**2** ((*E*)-**V**, R^1 = Ph(CH$_2$)$_2$, R^2 = C_7H_{15}, 203 mg, 79% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.94−0.99 (m, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_4$C*H*$_3$), 1.36 (br s, 8 H, C=CHCH$_2$CH$_2$(C*H*$_2$)$_4$CH$_3$), 1.52−1.58 (m, 2 H, C=CHCH$_2$C*H*$_2$-(CH$_2$)$_4$CH$_3$), 2.14−2.28 (m, 3 H, C=CHC*H*$_2$CH$_2$(CH$_2$)$_4$CH$_3$ and CCH$_2$O*H*), 2.59−2.88 (m 4 H, H-3$_{ab}$ and CCH$_2$OC(O)-C*H*$_2$CH$_2$Ph), 3.03 (t, J = 7.6 Hz, 2 H, CCH$_2$OC(O)CH$_2$C*H*$_2$Ph), 3.59−3.76 (m, 2 H, CC*H*$_2$OH), 4.30 (AB q, J = 12.0 Hz, 2 H, CC*H*$_2$OC(O)CH$_2$CH$_2$Ph), 6.80−6.89 (m, 1 H, C=C*H*CH$_2$CH$_2$(CH$_2$)$_4$-CH$_3$), 7.25−7.41 (m, 5 H, CCH$_2$OC(O)CH$_2$CH$_2$*Ph*); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 13.52, 22.06, 27.51, 28.48, 28.74, 29.23, 29.74, 30.21, 31.15, 34.97, 64.05, 64.76, 82.17, 124.90, 125.79, 127.58, 127.93, 139.35, 141.65, 169.09, 171.95; FAB-MS (*m*/*z*, relative intensity) 389 (MH^+, 100). Anal. ($C_{23}H_{32}O_5$).

(*Z*)-[2-(Hydroxymethyl)-4-octylidene-5-oxo-2,3-dihydrofur-2-yl]methyl 3-Phenylpropanoate ((*Z*)-2, (*Z*)-V, R^1 = Ph(CH$_2$)$_2$, R^2 = C$_7$H$_{15}$). According to general procedure F, (*Z*)-**IV** (R^2 = C_7H_{15}; 159 mg, 0.62 mmol) and Ph(CH$_2$)$_2$COCl (114.9 mg, 0.68 mmol) were reacted to give (*Z*)-**2** ((*E*)-**V**, R^1 = Ph(CH$_2$)$_2$, R^2 = C_7H_{15}; 188 mg, 78% yield): oil, ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.93−0.98 (m, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_4$C*H*$_3$), 1.35−1.52 (m, 10 H, C=CHCH$_2$C*H*$_2$(C*H*$_2$)$_4$CH$_3$), 2.63−2.93 (m, 6 H, C=CHC*H*$_2$CH$_2$(CH$_2$)$_4$CH$_3$, CCH$_2$OC(O)C*H*$_2$CH$_2$Ph, and H-3$_{ab}$), 3.03 (t, J = 7.7 Hz, 2 H, CCH$_2$OC(O)CH$_2$C*H*$_2$Ph), 3.65 (AB q, J = 12.2 Hz, 2 H, HOC*H*$_2$C), 4.28 (AB q, J = 11.7 Hz, 2 H, CC*H*$_2$OC(O)CH$_2$CH$_2$Ph), 6.29 (tt, J = 7.7, 2.1 Hz, 1 H, C=C*H*CH$_2$CH$_2$(CH$_2$)$_4$CH$_3$), 7.25−7.41 (m, 5 H, CCH$_2$OC(O)-CH$_2$CH$_2$*Ph*); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.03, 22.57, 27.69, 29.01, 29.17, 30.74, 31.68, 32.94, 35.51, 64.39, 65.13, 82.02, 123.38, 126.27, 128.10, 128.42, 139.87, 145.67, 168.36, 172.47; FAB-MS (*m*/*z*, relative intensity) 389 (MH^+, 100). Anal. ($C_{23}H_{32}O_5$) C, H.

(*E*)-[2-(Hydroxymethyl)-4-nonylidene-5-oxo-2,3-dihydrofur-2-yl]methyl 2-Phenylacetate ((*E*)-3, (*E*)-V, R^1 = PhCH$_2$, R^2 = C$_8$H$_{17}$). According to general procedure F, (*E*)-**IV** (R^2 = C_8H_{17}; 133 mg, 0.49 mmol) and PhCH$_2$COCl (83 mg, 0.54 mmol) were reacted to give (*E*)-**3** ((*E*)-**V**, R^1 = PhCH$_2$, R^2 = C_8H_{17}; 119 mg, 63% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.94−0.99 (m, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_5$C*H*$_3$), 1.36 (br s, 10 H, C=CHCH$_2$CH$_2$-(C*H*$_2$)$_5$CH$_3$), 1.51−1.57 (m, 2 H, C=CHCH$_2$C*H*$_2$(CH$_2$)$_5$CH$_3$), 2.12−2.24 (m, 3 H, C=CHC*H*$_2$CH$_2$(CH$_2$)$_5$CH$_3$ and *H*OCH$_2$C), 2.63 (dt, 1 H, J = 17.1, 1.2 Hz, H-3$_a$), 2.81 (dt, 1 H, J = 17.1, 1.2 Hz, H-3$_b$), 3.62−3.78 (m, 2 H, HOC*H*$_2$C), 3.73 (s, 2 H, PhC*H*$_2$C(O)-OCH$_2$C), 4.33 (AB q, J = 11.8 Hz, 2 H, PhCH$_2$C(O)OC*H*$_2$C), 6.78−6.86 (m, 1 H, C=C*H*CH$_2$CH$_2$(CH$_2$)$_5$CH$_3$), 7.31−7.41 (m, 5 H, *Ph*CH$_2$C(O)OCH$_2$C); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 13.54, 22.08, 27.49, 28.62, 28.78, 28.80, 29.12, 29.71, 31.26, 40.58, 64.22, 65.07, 82.20, 124.85, 126.69, 128.05, 128.56, 132.69, 141.65, 169.04, 170.60; FAB-MS (*m*/*z*, relative intensity) 389 (MH^+, 88), 91 (100). Anal. ($C_{23}H_{32}O_5$) C, H.

(*Z*)-[2-(Hydroxymethyl)-4-nonylidene-5-oxo-2,3-dihydrofur-2-yl]methyl 2-Phenylacetate ((*Z*)-3, (*Z*)-V-*Z*, R^1 = PhCH$_2$, R^2 = C$_8$H$_{17}$). According to general procedure F, (*Z*)-**IV** (R^2 = C_8H_{17}; 101 mg, 0.37 mmol) and PhCH$_2$COCl (63.1 mg, 0.41 mmol) were reacted to give (*Z*)-**3** ((*Z*)-**V**, R^1 = PhCH$_2$, R^2 = C_8H_{17}; 117 mg, 82% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.93−0.98 (m, 3 H, C=CHCH$_2$CH$_2$(CH$_2$)$_5$C*H*$_3$), 1.35−1.61 (m, 12 H, C=CHCH$_2$C*H*$_2$-(C*H*$_2$)$_5$CH$_3$), 2.15 (br s, 1 H, CCH$_2$O*H*), 2.66−2.93 (m, 4 H, C=CHC*H*$_2$CH$_2$(CH$_2$)$_5$CH$_3$ and H-3$_{ab}$), 3.61−3.68 (m, 2 H, CC*H*$_2$-OH), 3.73 (s, 2 H, CCH$_2$OC(O)C*H*$_2$Ph), 4.31 (AB q, J = 11.8 Hz, 2 H, CC*H*$_2$OC(O)CH$_2$Ph), 6.26−6.32 (m, 1 H, C=C*H*CH$_2$-CH$_2$(CH$_2$)$_5$CH$_3$), 7.32−7.44 (m, 5 H, CCH$_2$OC(O)CH$_2$*Ph*); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 13.55, 22.09, 27.22, 28.51, 28.66,

28.73, 28.83, 31.28, 32.37, 40.57, 64.04, 64.93, 81.56, 122.82, 126.69, 128.03, 128.56, 132.71, 145.23, 167.84, 170.65; FAB-MS (*m*/*z*, relative intensity) 389 (MH^+, 22), 91 (100). Anal. ($C_{23}H_{32}O_5 \cdot 0.25H_2O$) C, H.

(*E*)-[4-Decylidene-2-(hydroxymethyl)-5-oxo-2,3-dihydrofur-2-yl]methyl Benzoate ((*E*)-4, (*E*)-V, R¹ = Ph, R² = C_9H_{19}). According to general procedure F, (*E*)-**IV** ($R^2 = C_9H_{19}$; 168 mg, 0.59 mmol) and benzoyl chloride (90.8 mg, 0.65 mmol) were reacted to give (*E*)-**4** ((*E*)-**V**, R^1 = Ph, $R^2 = C_9H_{19}$; 215 mg, 94% yield): ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.93−0.99 (m, 3 H, C═CHCH$_2$CH$_2$(CH$_2$)$_6$C*H*$_3$), 1.32 (br s, 12 H, C═CHCH$_2$CH$_2$-(C*H*$_2$)$_6$CH$_3$), 1.48−1.53 (m, 2 H, C═CHCH$_2$C*H*$_2$(CH$_2$)$_6$CH$_3$), 2.24 (q, *J* = 7.40 Hz, C═CHC*H*$_2$CH$_2$(CH$_2$)$_6$CH$_3$), 2.34 (br s, 1 H, *H*OCH$_2$C), 2.85 (dm, *J* = 17 Hz, 1 H, H-3$_a$), 2.98 (dm, *J* = 17 Hz, 1 H, H-3$_a$), 3.86 (br AB q, *J* = 12.0 Hz, 2 H, HOC*H*$_2$C), 4.57 (AB q, *J* = 11.8 Hz, 2 H, PhC(O)OC*H*$_2$C), 6.33 (m, 1 H, C═C*H*CH$_2$-CH$_2$(CH$_2$)$_6$CH$_3$), 7.49−7.55 (m 2 H, *Ph*C(O)OCH$_2$C), 7.67 (t, *J* = 7.3 Hz, 1 H, *Ph*C(O)OCH$_2$C), 8.07 (d, *J* = 7.1 Hz, 2 H, *Ph*C(O)-OCH$_2$C); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 13.55, 22.09, 27.47, 28.70, 28.74, 28.80, 28.86, 29.39, 29.74, 31.27, 64.24, 65.49, 82.62, 125.10, 127.87, 128.45, 129.14, 132.88, 141.57, 165.62, 169.22; FAB-MS (*m*/*z*, relative intensity) 389 (MH^+, 65), 105 (100). Anal. ($C_{23}H_{32}O_5$).

(*Z*)-[4-Decylidene-2-(hydroxymethyl)-5-oxo-2,3-dihydrofur-2-yl]methyl Benzoate ((*Z*)-4, (*Z*)-V, R¹ = Ph, R² = C_9H_{19}). According to general procedure F, (*Z*)-**IV** ($R^2 = C_9H_{19}$; 161 mg, 0.57 mmol) and benzoyl chloride (88.4 mg, 0.63 mmol) were reacted to give (*Z*)-**4** ((*Z*)-**V**, R^1 = Ph, $R^2 = C_9H_{19}$; 197 mg, 89% yield): white solid; mp 58−60 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.94−0.99 (m, 3 H, C═CHCH$_2$CH$_2$(CH$_2$)$_6$C*H*$_3$), 1.34−1.46 (m, 14 H, C═CHCH$_2$C*H*$_2$(C*H*$_2$)$_6$CH$_3$), 2.31 (br s, 1 H, *H*OCH$_2$C), 2.74−2.85 (m, 2 H, C═CHC*H*$_2$CH$_2$(CH$_2$)$_6$CH$_3$), 2.90 (dm, *J* = 17 Hz, 1 H, H-3$_a$), 3.07 (dm, *J* = 17 Hz, 1 H, H-3$_b$), 3.84 (AB q, *J* = 12.1 Hz, 2 H, HOC*H*$_2$C), 4.56 (AB q, *J* = 11.7 Hz, 2 H, PhC(O)OC*H*$_2$C), 6.33 (tt, *J* = 7.7, 2.1 Hz, 1 H, C═C*H*CH$_2$CH$_2$(CH$_2$)$_6$CH$_3$), 7.49−7.55, 7.64−7.70, and 8.06−8.10 (m, 5 H, *Ph*C(O)OCH$_2$C); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 13.56, 22.11, 27.23, 28.47, 28.73, 28.80, 28.86, 28.94, 31.32, 32.67, 64.12, 65.38, 81.97, 123.05, 127.86, 128.52, 129.15, 132.85, 145.06, 165.62, 168.00; FAB-MS (*m*/*z*, relative intensity) 389 (MH^+, 22), 105 (100). Anal. ($C_{23}H_{32}O_5$) C, H.

(*E*)-[4-Decylidene-2-(hydroxymethyl)-5-oxo-2,3-dihydrofur-2-yl]methyl Cyclohexanecarboxylate ((*E*)-5, (*E*)-V, R¹ = Cyclohexyl, R² = C_9H_{19}). According to general procedure F, (*E*)-**IV** ((*E*)-**V**, $R^2 = C_9H_{19}$; 80 mg, 0.28 mmol) and cyclohexanecarbonyl chloride (44.9 mg, 0.31 mmol) were reacted to give (*E*)-**5** (R^1 = cyclohexyl, $R^2 = C_9H_{19}$; 99.8 mg, 90% yield): ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.94−0.99 (m, 3 H, C═CHCH$_2$CH$_2$(CH$_2$)$_6$C*H*$_3$), 1.25−1.45 (br s, 14 H, C═CHCH$_2$C*H*$_2$(C*H*$_2$)$_6$CH$_3$), 1.45−2.05 (m, 10 H, *c*-*Hex*C(O)OCH$_2$C), 2.21−2.30 (m, 2 H, C═CHC*H*$_2$CH$_2$(CH$_2$)$_6$-CH$_3$), 2.41 (tt, *J* = 11.0, 3.5 Hz, 1 H, *c*-*Hex*C(O)OCH$_2$C), 2.72 (br d, *J* = 17.3 Hz, 1 H, H-3$_a$), 2.90 (br d, *J* = 17.1 Hz, 1 H, H-3$_b$), 3.75 (AB q, *J* = 17.2 Hz, 2 H, HOC*H*$_2$C), 4.31 (AB q, *J* = 11.8 Hz, 2 H, c-HexC(O)OC*H*$_2$C), 6.81−6.90 (m, 1 H, C═C*H*CH$_2$-CH$_2$(CH$_2$)$_6$CH$_3$); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.04, 22.59, 25.25, 25.57, 28.00, 28.83, 29.21, 29.28, 29.33, 29.40, 29.74, 30.24, 31.78, 42.93, 64.66, 65.10, 82.98, 125.62, 141.96, 169.69, 175.63; FAB-MS (*m*/*z*, relative intensity) 395 (MH^+, 64), 83 (100). Anal. ($C_{23}H_{38}O_5$) C, H.

(*Z*)-[4-Decylidene-2-(hydroxymethyl)-5-oxo-2,3-dihydrofur-2-yl]methyl Cyclohexanecarboxylate ((*Z*)-5, (*Z*)-V, R¹ = Cyclohexyl, R² = C_9H_{19}). According to general procedure G, (*Z*)-**IV** ((*Z*)-**V**, $R^2 = C_9H_{19}$; 128 mg, 0.45 mmol) and cyclohexanecarbonyl chloride (65.8 mg, 0.45 mmol) were reacted to give (*Z*)-**5** ((*Z*)-**V**, R^1 = cyclohexyl, $R^2 = C_9H_{19}$; 90 mg, 50% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.93−0.99 (m, 3 H, C═CHCH$_2$CH$_2$-(CH$_2$)$_6$C*H*$_3$), 1.34−1.52 and 1.73−1.99 (m's, 24 H, C═CHCH$_2$C*H*$_2$-(C*H*$_2$)$_6$CH$_3$) and *c*-*Hex*C(O)OCH$_2$C), 2.25 (br s, 1 H, *H*OCH$_2$C), 2.41 (tt, *J* = 10.9, 3.5 Hz, 1 H, *c*-*Hex*C(O)OCH$_2$C), 2.74−3.01 (m, 4 H, H-3$_{ab}$ and C═CHC*H*$_2$CH$_2$(CH$_2$)$_6$CH$_3$), 3.73 (AB q, *J* = 12.1 Hz, 2 H, HOC*H*$_2$C), 4.29 (AB q, *J* = 12.0 Hz, 2 H, c-HexC-(O)OC*H*$_2$C), 6.30−6.36 (m, 1 H, C═C*H*CH$_2$CH$_2$(CH$_2$)$_6$CH$_3$); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.05, 22.60, 25.28, 27.71, 28.84, 29.01, 29.12, 29.23, 29.38, 29.43, 31.81, 33.03, 42.96, 64.53, 64.97, 82.24, 123.54, 145.50, 168.41, 175.64; FAB-MS (*m*/*z*, relative intensity) 395 (MH^+, 51), 83 (100). Anal. ($C_{23}H_{38}O_5$) C, H.

(*E*)-{2-(Hydroxymethyl)-4-[4-methyl-3-(methylethyl)pentylidene]-5-oxo-2,3-dihydrofur-2-yl}methyl Benzoate ((*E*)-6, (*E*)-V, R¹ = Ph, R² = CH$_2$CH(*i*-Pr)$_2$). According to general procedure F, (*E*)-**IV** ($R^2 = CH_2CH(i\text{-}Pr)_2$; 110 mg, 0.41 mmol) and benzoyl chloride (63.0 mg, 0.45 mmol) were reacted to give (*E*)-**6** ((*E*)-**V**, R^1 = Ph, $R^2 = CH_2CH(i\text{-}Pr)_2$; 129 mg, 84% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.85−0.98 (m, 12 H, C═CHCH$_2$CH(CH-(C*H*$_3$)$_2$)$_2$), 1.21−1.30 (m, 1 H, C═CHCH$_2$C*H*(CH(CH$_3$)$_2$)$_2$), 1.75−1.91 (m, 2 H, C═CHCH$_2$CH(C*H*(CH$_3$)$_2$)$_2$), 2.11−2.26 (m, 3 H, C═CHC*H*$_2$CH(CH(CH$_3$)$_2$)$_2$ and *H*OCH$_2$C), 2.85 (dd, *J* = 17.1, 2.2 Hz, 1 H, H-3$_a$), 2.95−3.03 (m, 1 H, H-3$_b$), 3.87 (AB q, *J* = 12.0 Hz, 2 H, HOC*H*$_2$C), 4.58 (AB q, *J* = 12.0 Hz, 2 H, PhC(O)OC*H*$_2$C), 6.88−6.97 (m, 1 H, C═C*H*CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 7.49−7.55, 7.64−7.69, 8.05−8.08 (m, 5 H, *Ph*C(O)OCH$_2$C); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.26, 21.38, 29.06, 29.14, 50.20, 64.81, 66.00, 83.11, 124.69, 128.37, 128.96, 129.63, 133.36, 143.92, 166.11, 169.76; FAB-MS (*m*/*z*, relative intensity) 375 (MH^+, 83), 105 (100). Anal. ($C_{22}H_{30}O_5$) C, H.

(*Z*)-{2-(Hydroxymethyl)-4-[4-methyl-3-(methylethyl)pentylidene]-5-oxo-2,3-dihydrofur-2-yl}methyl Benzoate ((*E*)-6, (*Z*)-V, R¹ = Ph, R² = CH$_2$CH(*i*-Pr)$_2$). According to general procedure G, (*Z*)-**IV** ($R^2 = CH_2CH(i\text{-}Pr)_2$; 75 mg, 0.28 mmol) and benzoyl chloride (47.2 mg, 0.33 mmol) were reacted to give (*Z*)-**6** ((*Z*)-**V**, R^1 = Ph, $R^2 = CH_2CH(i\text{-}Pr)_2$; 60 mg, 57% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.91−1.00 (m, 12 H, C═CHCH$_2$CH-(CH(C*H*$_3$)$_2$)$_2$), 1.13−1.22 (m, 1 H, C═CHCH$_2$C*H*(CH(CH$_3$)$_2$)$_2$), 1.65 (br s, 1 H, *H*OCH$_2$C), 1.76−1.92 (m, 2 H, C═CHCH$_2$CH-(C*H*(CH$_3$)$_2$)$_2$), 2.71−2.85 (m, 2 H, C═CHC*H*$_2$CH(CH(CH$_3$)$_2$)$_2$), 2.89 (dd, *J* = 16.6, 2.2 Hz, 1 H, H-3$_a$), 3.09 (dd, *J* = 16.4, 2.7 Hz, 1 H, H-3$_b$), 3.83 (AB q, 2 H, HOC*H*$_2$C), 4.56 (AB q, 2 H, PhC-(O)OC*H*$_2$C), 6.32−6.38 (m, 1 H, C═C*H*CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 7.50−7.53, 7.64−7.70, 8.07−8.11 (m, 5 H, *Ph*C(O)OCH$_2$C); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.19, 21.41, 26.29, 29.24, 29.32, 51.08, 64.65, 65.74, 82.31, 122.41, 128.36, 129.02, 129.65, 133.35, 147.79, 165.10, 168.35; FAB-MS (*m*/*z*, relative intensity) 375 (MH^+, 47), 105 (100). Anal. ($C_{22}H_{30}O_5$).

(*E*)-{2-(Hydroxymethyl)-4-[4-methyl-3-(methylethyl)pentylidene]-5-oxo-2,3-dihydrofur-2-yl}methyl Cyclohexanecarboxylate ((*E*)-7, (*E*)-V, R¹ = Cyclohexyl, R² = CH$_2$CH(*i*-Pr)$_2$). According to general procedure F, (*E*)-**IV** ($R^2 = CH_2CH(i\text{-}Pr)_2$; 100 mg, 0.37 mmol) and cyclohexanecarbonyl chloride (65.8 mg, 0.45 mmol) were reacted to give (*E*)-**7** ((*E*)-**V**, R^1 = cyclohexyl, $R^2 = CH_2CH(i\text{-}Pr)_2$; 112 mg, 79% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.94 and 0.99 (br d, *J* ≈ 7 Hz, 12 H, C═CHCH$_2$CH-(CH(C*H*$_3$)$_2$)$_2$), 1.25−1.52 and 1.71−1.98 (m, 10 H, *c*-*Hex*C(O)-OCH$_2$C, *H*OCH$_2$C, and C═CHCH$_2$C*H*(C*H*(CH$_3$)$_2$)$_2$), 2.18−2.23 (m, 2 H, C═CHC*H*$_2$CH(CH(CH$_3$)$_2$)$_2$), 2.35−2.45 (m, 1 H, *c*-*Hex*C-(O)OCH$_2$C), 2.74 (dd, *J* = 17.3, 2.2 Hz, 1 H, H-3$_a$), 2.91 (dd, *J* = 17.1, 2.4 Hz, 1 H, H-3$_b$), 3.76 (AB q, *J* = 12.0 Hz, 2 H, HOC*H*$_2$C), 4.31 (AB q, *J* = 12.0 Hz, 2 H, c-HexC(O)C*H*$_2$C), 6.87−6.95 (m, 1 H, C═C*H*CH$_2$CH(CH(CH$_3$)$_2$)$_2$); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.29, 21.54, 25.56, 28.65, 28.84, 28.96, 29.14, 29.17, 29.91, 42.93, 50.24, 64.74, 65.08, 82.89, 124.64, 143.84, 169.67, 175.62; FAB-MS (*m*/*z*, relative intensity) 381 (MH^+, 91), 83 (100). Anal. ($C_{22}H_{36}O_5$) C, H.

(*Z*)-{2-(Hydroxymethyl)-4-[4-methyl-3-(methylethyl)pentylidene]-5-oxo-2,3-dihydrofur-2-yl}methyl Cyclohexanecarboxylate ((*Z*)-7, (*Z*)-V, R¹ = Cyclohexyl, R² = CH$_2$CH(*i*-Pr)$_2$). According to general procedure G, (*Z*)-**IV** ($R^2 = CH_2CH(i\text{-}Pr)_2$; 94 mg, 0.35 mmol) and cyclohexanecarbonyl chloride (61.4 mg, 0.42 mmol) were reacted to give (*Z*)-**7** ((*Z*)-**V**, R^1 = cyclohexyl, $R^2 = CH_2CH(i\text{-}Pr)_2$; 78 mg, 58% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.94 and 0.99 (br d, *J* ≈ 7 Hz, 12 H, C═CHCH$_2$CH-(CH(C*H*$_3$)$_2$)$_2$), 1.15−2.10 (m, 13 H, *c*-*Hex*C(O)OCH$_2$C and C═CHCH$_2$C*H*(C*H*(CH$_3$)$_2$)$_2$), 2.36−2.46 (m, 1 H, *c*-*Hex*C(O)-OCH$_2$C), 2.74−2.81 (m, 3 H, C═CHC*H*$_2$CH(CH(CH$_3$)$_2$)$_2$ and

H-3$_a$), 2.92−2.99 (m, 1 H, *H*-3$_b$), 3.72 (AB q, J = 12.2 Hz, 2 H, HOCH_2C), 4.29 (AB q, J = 11.8 Hz, 2 H, c-HexC(O)CH_2C), 6.31−6.38 (m, 1 H, C=C*H*CH$_2$CH(CH(CH$_3$)$_2$)$_2$); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 25.28, 26.28, 28.85, 28.88, 29.29, 29.32, 33.13, 42.93, 51.12, 64.58, 64.91, 82.17, 122.47, 147.69, 168.48, 175.69; FAB-MS (*m*/*z*, relative intensity) 381 (MH$^+$, 61), 83 (100). Anal. ($C_{22}H_{36}O_5$) C, H.

(*E*)-[{2-(Hydroxymethyl)-4-[4-methyl-3-(methylethyl)pentylidene]-5-oxo-2,3 −dihydrofur-2-yl}methyl 2-Methoxybenzoate ((*E*)-8, (*E*)-V, R^1 = 2-(OMe)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$). According to general procedure G, (*E*)-**IV** (R^2 = CH$_2$CH(*i*-Pr)$_2$; 213 mg, 0.79 mmol) and 2-methoxybenzoyl chloride (201.7 mg, 1.18 mmol) were reacted to give (*E*)-**8** ((*E*)-**V**, R^1 = 2-(OMe)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$; 182 mg, 57% yield) as an oily paste: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.85−0.98 (m, 12 H, C=CHCH$_2$CH(CH(C*H*$_3$)$_2$)$_2$), 1.22−1.33 (m, 1 H, C=CHCH$_2$C*H*(CH(CH$_3$)$_2$)$_2$), 1.75−1.88 (m, 2 H, C=CHCH$_2$CH(C*H*(CH$_3$)$_2$)$_2$), 2.16−2.22 (m, 2 H, C=CHC*H*$_2$CH(CH(CH$_3$)$_2$)$_2$), 2.85 (dd, J = 17.3, 2.2 Hz, 1 H, H-3$_a$), 2.96 (dd, J = 16.8, 2.2 Hz, 1 H, H-3$_b$), 3.86 (AB q, $J \approx$ 12 Hz, 2 H, HOC*H*$_2$C), 3.97 (s, 3 H, C*H*$_3$OC$_6$H$_4$C(CO)CH$_2$C), 4.53 (AB q, J = 12.0 Hz, 2 H, CH$_3$OC$_6$H$_4$C(CO)C*H*$_2$C), 6.87−6.94 (m, 1 H, C=C*H*CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 7.03−7.09 and 7.55−7.62 (m, 3 H, CH$_3$OC$_6$*H*$_4$C(CO)CH$_2$C), 7.88 (dd, J = 7.8, 1.7 Hz, 1 H, CH$_3$OC$_6$*H*$_4$C(CO)CH$_2$C); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.26, 21.57, 28.65, 29.07, 29.14, 30.15, 50.20, 55.77, 65.18, 66.05, 82.85, 111.85, 118.52, 120.11, 124.72, 132.03, 134.12, 143.83, 159.28, 165.75, 169.77; FAB-MS (*m*/*z*, relative intensity) 405 (MH$^+$, 14), 135 (100). Anal. ($C_{23}H_{32}O_6$·0.3H_2O) C, H.

(*Z*)-[{2-(Hydroxymethyl)-4-[4-methyl-3-(methylethyl)pentylidene]-5-oxo-2,3 −dihydrofur-2-yl}methyl 2-Methoxybenzoate ((*Z*)-8, (*Z*)-V, R^1 = 2-(OMe)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$). According to general procedure G, (*Z*)-**IV** (R^2 = CH$_2$CH(*i*-Pr)$_2$; 196 mg, 0.72 mmol) and 2-methoxybenzoyl chloride (149 mg, 0.87 mmol) were reacted to give (*Z*)-**8** ((*Z*)-**V**, R^1 = 2-(OMe)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$; 143 mg, 49% yield) as a white solid: mp 96.4−97.5 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.90−0.99 (m, 12 H, C=CHCH$_2$CH(CH(C*H*$_3$)$_2$)$_2$), 1.13−1.22 (m, 1 H, C=CHCH$_2$C*H*(CH(CH$_3$)$_2$)$_2$), 1.75−1.91 (m, 2 H, C=CHCH$_2$CH(C*H*(CH$_3$)$_2$)$_2$), 2.65−3.10 (m, 4 H, H-3$_{ab}$ and C=CHC*H*$_2$CH(CH(CH$_3$)$_2$)$_2$), 3.84 (s, 2 H, HOC*H*$_2$C), 3.98 (s, 3 H, C*H*$_3$OC$_6$H$_4$C(CO)CH$_2$C), 4.51 (AB q, $J \approx$ 12 Hz, 2 H, CH$_3$OC$_6$H$_4$C(CO)C*H*$_2$C), 6.31−6.38 (m, 1 H, C=C*H*CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 70.4−7.09 and 7.55−7.62 (m, 3 H, CH$_3$OC$_6$*H*$_4$C(CO)CH$_2$C), 7.89 (dd, J = 7.8, 1.7 Hz, 1 H, CH$_3$OC$_6$*H*$_4$C(CO)CH$_2$C); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.30, 19.41, 21.53, 21.60, 26.27, 29.24, 29.31, 33.44, 51.07, 55.84, 65.05, 65.86, 82.09, 111.88, 118.63, 120.14, 122.47, 132.00, 134.09, 147.73, 159.22, 165.74, 168.54; FAB-MS (*m*/*z*, relative intensity) 405 (MH$^+$, 18), 135 (100). Anal. ($C_{23}H_{32}O_6$) C, H.

(*E*)-[{2-(Hydroxymethyl)-4-[4-methyl-3-(methylethyl)pentylidene]-5-oxo-2,3 −dihydrofur-2-yl}methyl 3-Methoxybenzoate ((*E*)-9, (*E*)-V, R^1 = 3-(OMe)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$). According to general procedure G, (*E*)-**IV** (R^2 = CH$_2$CH(*i*-Pr)$_2$; 197 mg, 0.73 mmol) and 3-methoxybenzoyl chloride (187 mg, 1.10 mmol) were reacted to give (*E*)-**9** ((*E*)-**V**, R^1 = 3-(OMe)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$; 182 mg, 61% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.85−0.98 (m, 12 H, C=CHCH$_2$CH(CH(C*H*$_3$)$_2$)$_2$), 1.20−1.29 (m, 1 H, C=CHCH$_2$C*H*(CH(CH$_3$)$_2$)$_2$), 1.74−1.90 (m, 2 H, C=CHCH$_2$CH(C*H*(CH$_3$)$_2$)$_2$), 2.13−2.21 (m, 2 H, C=CHC*H*$_2$CH(CH(CH$_3$)$_2$)$_2$), 2.84 (dd, J = 17.1, 2.2 Hz, 1 H, H-3$_a$), 2.98 (dd, J = 17.1, 2.4 Hz, 1 H, H-3$_b$), 3.80−3.92 (m, 2 H, HOC*H*$_2$C), 3.92 (s, 3 H, C*H*$_3$OC$_6$H$_4$C(CO)CH$_2$C), 4.57 (s, 2 H, CH$_3$OC$_6$H$_4$C(CO)C*H*$_2$C), 6.87−6.96 (m, 1 H, C=C*H*CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 7.18−7.22, 7.34−7.45, and 7.56−7.66 (m, 4 H, CH$_3$OC$_6$*H*$_4$C(CO)CH$_2$C); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.28, 21.56, 28.65, 29.07, 29.12, 30.05, 50.19, 55.35, 64.78, 66.12, 83.12, 114.06, 119.90, 122.01, 124.73, 129.39, 130.20, 143.87, 159.44, 165.99, 169.78; FAB-MS (*m*/*z*, relative intensity) 405 (MH$^+$, 38), 135 (100). Anal. ($C_{23}H_{32}O_6$·0.2H_2O) C, H.

(*Z*)-[{2-(Hydroxymethyl)-4-[4-methyl-3-(methylethyl)pentylidene]-5-oxo-2,3 −dihydrofur-2-yl}methyl 3-Methoxybenzoate ((*Z*)-9, (*Z*)-V, R^1 = 3-(OMe)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$). According to general procedure G, (*Z*)-**IV** (R^2 = CH$_2$CH(*i*-Pr)$_2$, 195 mg, 0.72 mmol) and 3-methoxybenzoyl chloride (148.1 mg, 0.87 mmol) were reacted to give (*Z*)-**9** ((*Z*)-**V**, R^1 = 3-(OMe)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$; 167 mg, 57% yield) as a colorless oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.90−0.99 (m, 12 H, C=CHCH$_2$CH(CH(C*H*$_3$)$_2$)$_2$), 1.12−1.21 (m, 1 H, C=CHCH$_2$C*H*(CH(CH$_3$)$_2$)$_2$), 1.78−1.91 (m, 2 H, C=CHCH$_2$CH(C*H*(CH$_3$)$_2$)$_2$), 2.62−2.72 and 2.83−3.07 (m, 4 H, C=CHC*H*$_2$CH(CH(CH$_3$)$_2$)$_2$ and H-3$_{ab}$), 3.82 (AB q, J = 12.2 Hz, 2 H, HOC*H*$_2$C), 3.93 (s, 3 H, C*H*$_3$OC$_6$H$_4$C(CO)CH$_2$C), 4.55 (AB q, J = 12.2 Hz, 2 H, CH$_3$OC$_6$H$_4$C(CO)C*H*$_2$C), 6.31−6.37 (m, 1 H, C=C*H*CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 7.18−7.22, 7.39−7.46, and 7.60−7.69 (m, 4 H, CH$_3$OC$_6$*H*$_4$C(CO)CH$_2$C); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.44, 21.60, 26.27, 29.21, 29.34, 33.29, 51.05, 55.38, 64.64, 65.85, 82.34, 114.23, 119.75, 122.01, 122.43, 129.39, 130.28, 147.76, 159.45, 166.05, 168.55; FAB-MS (*m*/*z*, relative intensity) 405 (MH$^+$, 26), 135 (100). Anal. ($C_{23}H_{32}O_6$) C, H.

(*E*)-[{2-(Hydroxymethyl)-4-[4-methyl-3-(methylethyl)pentylidene]-5-oxo-2,3 -dihydrofuryl}methyl 4-Methoxybenzoate ((*E*)-10, (*E*)-V, R^1 = 4-(OMe)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$). According to general procedure G, (*E*)-**IV** (R^2 = CH$_2$CH(*i*-Pr)$_2$; 200 mg, 0.74 mmol) and 4-methoxybenzoyl chloride (189 mg, 1.11 mmol) were reacted to give (*E*)-**10** ((*E*)-**V**, R^1 = 4-(OMe)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$; 173 mg, 58% yield) as a colorless oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.86−0.98 (m, 12 H, C=CHCH$_2$CH(CH(C*H*$_3$)$_2$)$_2$), 1.21−1.28 (m, 1 H, C=CHCH$_2$C*H*(CH(CH$_3$)$_2$)$_2$), 1.75−1.91 (m, 2 H, C=CHCH$_2$CH(C*H*(CH$_3$)$_2$)$_2$), 2.11−2.25 (m, 2 H, C=CHC*H*$_2$CH(CH(CH$_3$)$_2$)$_2$), 2.83 (dd, J = 17.3, 2.2 Hz, 1 H, H-3$_a$), 2.98 (dd, J = 17.1, 2.4 Hz, 1 H, H-3$_b$), 3.84 (AB q, $J \approx$ 12 Hz, H, HOC*H*$_2$C), 3.94 (s, 3 H, C*H*$_3$OC$_6$H$_4$C(CO)CH$_2$C), 4.54 (AB q, J = 12.0 Hz, 2 H, CH$_3$OC$_6$H$_4$C(CO)C*H*$_2$C), 6.87−7.01 (m, 1 H, C=C*H*CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 7.17 (d, J = 9.0 Hz, 2 H, CH$_3$OC$_6$*H*$_4$C(CO)CH$_2$C), 8.02 (d, J = 8.8 Hz, 2 H, CH$_3$OC$_6$*H*$_4$C(CO)CH$_2$C); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.28, 21.57, 28.63, 29.07, 29.13, 30.04, 50.20, 55.39, 64.72, 65.68, 83.21, 113.65, 121.26, 124.75, 131.76, 143.83, 163.65, 165.90, 169.81; FAB-MS (*m*/*z*, relative intensity) 405 (MH$^+$, 26), 135 (100). Anal. ($C_{23}H_{32}O_6$·0.2H_2O) C, H.

(*Z*)-[{2-(Hydroxymethyl)-4-[4-methyl-3-(methylethyl)pentylidene]-5-oxo-2,3-dihydrofur-2-yl}methyl 4-Methoxybenzoate ((*Z*)-10, (*Z*)-V, R^1 = 4-(OMe)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$). According to general procedure G, (*Z*)-**IV** (R^2 = CH$_2$CH(*i*-Pr)$_2$; 201 mg, 0.74 mmol) and 4-methoxybenzoyl chloride (151.2 mg, 0.89 mmol) were reacted to give (*Z*)-**10** ((*Z*)-**V**, R^1 = 4-(OMe)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$; 167 mg, 56% yield) as a colorless oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.92, 0.93, 0.97, and 0.98 (d, J = 6.8 Hz, 12 H, C=CHCH$_2$CH(CH(C*H*$_3$)$_2$)$_2$), 1.13−1.21 (m, 1 H, C=CHCH$_2$C*H*(CH(CH$_3$)$_2$)$_2$), 1.78−1.91 (m, 2 H, C=CHCH$_2$CH(C*H*(CH$_3$)$_2$)$_2$), 2.18 (br s, 1 H, *H*OCH$_2$C), 2.65−3.07 (m, 4 H, C=CHC*H*$_2$CH(CH(CH$_3$)$_2$)$_2$ and *H*-3$_{ab}$), 3.81 (AB q, J = 12.2 Hz, 2 H, HOC*H*$_2$C), 3.94 (s, 3 H, C*H*$_3$OC$_6$H$_4$C(CO)CH$_2$C), 4.52 (AB q, J = 12.0 Hz, 2 H, CH$_3$OC$_6$H$_4$C(CO)C*H*$_2$C), 6.31−6.37 (m, 1 H, C=C*H*CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 6.99 (d, J = 9.0 Hz, 2 H, CH$_3$OC$_6$*H*$_4$C(CO)CH$_2$C), 8.04 (d, J = 8.8 Hz, 2 H, CH$_3$OC$_6$*H*$_4$C(CO)CH$_2$C); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.43, 21.61, 26.27, 29.22, 29.32, 33.27, 51.05, 55.38, 64.54, 65.48, 82.49, 113.64, 121.34, 122.53, 131.76, 147.64, 163.62, 165.94, 168.63; FAB-MS (*m*/*z*, relative intensity) 405 (MH$^+$, 25), 135 (100). Anal. ($C_{23}H_{32}O_6$) C, H.

(*E*)-{2-(Hydroxymethyl)-4-[4-methyl-3-(methylethyl)pentylidene]-5-oxo-2,3-dihydrofur-2-yl}methyl 2-Hydroxybenzoate ((*E*)-11, (*E*)-VI, R^1 = 2-(OH)Ph, R^2 = CH$_2$CH(*i*-Pr)$_2$). A solution of (*E*)-**V** ((*E*)-**8**, R^1 = 2-(OMe)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$; 118 mg, 0.29 mmol) in CH_2Cl_2 (10 mL) was treated at −78 °C with dropwise addition of BBr_3 (1.2 mL, 1 M in CH_2Cl_2) and stirred at the same temperature for 2 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (1.3 mL), and the mixture was extracted with Et_2O (1 × 30 mL). The organic layer was then washed with potassium phosphate buffer (pH 7, 1 × 10 mL) and brine (1 × 10 mL), dried over $MgSO_4$, and concentrated in vacuo. Purification by silica gel flash column chromatography gave (*E*)-**11** ((*E*)-**VI**, R^1 = 2-(OH)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$; 97 mg, 85% yield): oil; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.87−1.99 (m, 12 H, C=CHCH$_2$-

CH(CH(CH_3)$_2$)$_2$), 1.23−1.37 (m, 1 H, C═CHCH$_2$C*H*(CH(CH$_3$)$_2$)$_2$), 1.74−1.92 (m, 2 H, C═CHCH$_2$CH(C*H*(CH$_3$)$_2$)$_2$), 2.17−2.23 (m, 2 H, C═CHC*H*$_2$CH(CH(CH$_3$)$_2$)$_2$), 2.85 (dm, J = 17.3 Hz, 1 H, H-3$_a$), 3.00 (dm, J = 17.3 Hz, 1 H, H-3$_b$), 3.89 (AB q, J = 12.0 Hz, 2 H, HOC*H*$_2$C), 4.60 (s, 2 H, HOC$_6$H$_4$C(CO)C*H*$_2$C), 6.92−6.98 (m, 2 H, C═C*H*CH$_2$CH(CH(CH$_3$)$_2$)$_2$ and HOC$_6$*H*$_4$C(CO)-CH$_2$C), 7.07 (br d, J = 8.1 Hz, 1 H, HOC$_6$*H*$_4$C(CO)CH$_2$C), 7.53−7.60 and 7.78−7.81 (m, 2 H, HOC$_6$*H*$_4$C(CO)CH$_2$C); ^{13}C NMR (62.9 MHz, CDCl$_3$) δ 19.27, 21.58, 28.71, 29.07, 29.15, 30.00, 50.23, 64.91, 66.09, 82.75, 111.42, 117.62, 119.29, 124.41, 129.70, 136.17, 144.25, 161.64, 169.44, 169.52; FAB-MS (*m*/*z*, relative intensity) 391 (MH$^+$, 73), 121 (100). Anal. (C$_{22}$H$_{30}$O$_6$) C, H.

(*E*)-{2-(Hydroxymethyl)-4-[4-methyl-3-(methylethyl)pentylidene]-5-oxo-2,3-dihydrofur-2-yl}methyl 3-Hydroxybenzoate ((*E*)-12, (*E*)-VI, R^1 = 3-(OH)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$). A solution of (*E*)-**V** ((*E*)-**9**, R^1 = 3-(OMe)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$; 132 mg, 0.33 mmol) in CH$_2$Cl$_2$ (10 mL) was treated at −78 °C with dropwise addition of BBr$_3$ (1.3 mL, 1.3 mmol, 1 M in CH$_2$Cl$_2$), stirred at the same temperature for 2 h, and then warmed to −10 °C for 1.5 h. The reaction was then quenched with saturated aqueous NaHCO$_3$ (1.5 mL), and the mixture was extracted with Et$_2$O (1 × 30 mL). The organic layer was then washed with potassium phosphate buffer (pH 7, 2 × 10 mL) and brine (1 × 10 mL), dried over MgSO$_4$, and concentrated in vacuo. Purification by silica gel flash column chromatography gave (*E*)-**12** ((*E*)-**VI**, R^1 = 3-(OH)-C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$; 82 mg, 64% yield) as a semisolid paste: IR (CHCl$_3$) 3385 (OH), 2964 (CH), 2886 (CH), 1728 (C═O), 1672 (C═C) cm^{-1}; ^{1}H NMR (250 MHz, CDCl$_3$) δ 0.84, 0.88, 0.89, and 0.95 (d, J = 6.8 Hz, 12 H, C═CHCH$_2$CH(CH-(C*H*$_3$)$_2$)$_2$), 1.19−1.28 (m, 1 H, C═CHCH$_2$C*H*(CH(CH$_3$)$_2$)$_2$), 1.68−1.89 (m, 3 H, C═CHCH$_2$CH(C*H*(CH$_3$)$_2$)$_2$ and *H*OC$_6$H$_4$C(CO)-CH$_2$C), 2.15−2.17 (m, 2 H, C═CHC*H*$_2$CH(CH(CH$_3$)$_2$)$_2$), 2.83 (dd, J = 17.1, 2.2 Hz, 2 H, H-3$_a$), 2.99 (dd, J = 17.1, 2.4 Hz, 2 H, H-3$_b$), 3.89 (AB q, J = 12.2 Hz, 2 H, HOC*H*$_2$C), 4.56 (AB q, J = 11.7 Hz, 2 H, HOC$_6$H$_4$C(CO)C*H*$_2$C), 6.30 (br s, 1 H, *H*OC$_6$H$_4$C-(CO)CH$_2$C), 6.90−6.96 (m, 1 H, C═C*H*CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 7.13−7.17, 7.38−7.41, and 7.47−7.49 (m, 3 H, HOC$_6$*H*$_4$C(CO)-CH$_2$C), 7.62 (br d, J = 7.82 Hz, 1 H, HOC$_6$*H*$_4$C(CO)CH$_2$C); ^{13}C NMR (62.9 MHz, CDCl$_3$) δ 19.35, 21.68, 28.80, 29.13, 29.23, 30.16, 50.28, 64.84, 66.25, 83.59, 116.20, 120.83, 122.04, 124.82, 129.80, 130.32, 144.39, 155.89, 165.90, 170.44; FAB-MS (*m*/*z*, relative intensity) 391 (MH$^+$, 75), 121 (100). Anal. (C$_{22}$H$_{30}$O$_6$·0.5H$_2$O) C, H.

(*E*)-[2-(Hydroxymethyl)-5-oxo-4-(phenylmethylene)-2,3-dihydrofur-2-yl]methyl 4-Methyl-3-(methylethyl)pentanoate ((*E*)-14, (*E*)-V, R^1 = CH$_2$CH(*i*-Pr)$_2$, R^2 = Ph). According to general procedure G, (*E*)-**IV** (R^2 = Ph; 114 mg, 0.49 mmol) and 4-methyl-3-(methylethyl)pentanoyl chloride[25] (130.9 mg, 0.74 mmol) were reacted to give (*E*)-**14** ((*E*)-**V**, R^1 = CH$_2$CH(*i*-Pr)$_2$, R^2 = Ph; 53 mg, 29% yield): oil; ^{1}H NMR (250 MHz, CDCl$_3$) δ 0.80−1.02 (m, 12 H, ((C*H*$_3$)$_2$CH)$_2$CHCH$_2$C(O)OCH$_2$C), 1.60−1.66 (m, 1 H, ((CH$_3$)$_2$CH)$_2$C*H*CH$_2$C(O)OCH$_2$C), 1.70−1.82 (m, 2 H, ((CH$_3$)$_2$C*H*)$_2$-CHCH$_2$C(O)OCH$_2$C), 2.28 (d, 2 H, J = 5.6 Hz ((CH$_3$)$_2$-CH)$_2$CHC*H*$_2$C(O)OCH$_2$C), 3.12 (dd, J = 17.8, 2.7 Hz, 1 H, H-3$_a$), 3.31 (dd, J = 17.6, 2.9 Hz, 1 H, H-3$_b$), 3.84 (AB q, J = 12.2 Hz, 2 H, HOC*H*$_2$C), 4.36 (AB q, J = 12.0 Hz, 2 H, ((CH$_3$)$_2$CH)$_2$CHCH$_2$C(O)OC*H*$_2$C), 7.50−7.67 (m, 6 H, C═C*HPh*); ^{13}C NMR (62.9 MHz, CDCl$_3$) δ 18.59, 18.66, 21.21, 29.26, 32.21, 46.81, 64.75, 65.36, 83.16, 123.86, 128.82, 129.95, 134.21, 137.20, 170.84, 174.51; FAB-MS (*m*/*z*, relative intensity) 375 (MH$^+$, 64), 57 (100). Anal. (C$_{22}$H$_{30}$O$_5$·0.07H$_2$O) C, H.

(*E*)-[2-(Hydroxymethyl)-5-oxo-4-(2-phenylethylidene)-2,3-dihydrofur-2-yl]methyl 4-Methyl-3-(methylethyl)pentanoate ((*E*)-15, (*E*)-V, R^1 = CH$_2$CH(*i*-Pr)$_2$, R^2 = CH$_2$Ph). According to general procedure G, (*E*)-**IV** (R^2 = CH$_2$Ph; 116 mg, 0.47 mmol) and 4-methyl-3-(methylethyl)pentanoyl chloride[25] (125.1 mg, 0.71 mmol) were reacted to give (*E*)-**15** ((*E*)-**V**, R^1 = CH$_2$CH(*i*-Pr)$_2$, R^2 = CH$_2$Ph; 77 mg, 42% yield): oil; ^{1}H NMR (250 MHz, CDCl$_3$) δ 0.88 and 0.97 (br d, $J \approx$ 6.8 Hz, 12 H, ((C*H*$_3$)$_2$CH)$_2$CHCH$_2$C(O)-OCH$_2$C), 1.60−1.66 (m, 1 H, ((CH$_3$)$_2$CH)$_2$C*H*CH$_2$C(O)OCH$_2$C), 1.70−1.82 (m, 2 H, ((CH$_3$)$_2$C*H*)$_2$CHCH$_2$C(O)OCH$_2$C), 2.04 (br s, 1 H, *H*OCH$_2$C), 2.28 (d, 2 H, J = 5.6, ((CH$_3$)$_2$CH)$_2$CHC*H*$_2$C(O)-OCH$_2$C), 3.12 (dd, J = 17.8, 2.7 Hz, 1 H, H-3$_a$), 3.31 (dd, J = 17.6, 2.9 Hz, 1 H, H-3$_b$), 3.84 (AB q, J = 12.2 Hz, 2 H, HOC*H*$_2$C), 4.36 (AB q, J = 12.0 Hz, 2 H ((CH$_3$)$_2$CH)$_2$CHCH$_2$C(O)OC*H*$_2$C), 7.50−7.67 (m, 6 H, C═C*HPh*); ^{13}C NMR (62.9 MHz, CDCl$_3$) δ 18.63, 18.66, 18.70, 18.74, 21.28, 29.28, 29.34, 29.85, 32.69, 36.22, 46.85, 64.73, 65.33, 82.98, 126.63, 126.72, 128.25, 128.70, 128.77, 137.17, 139.21, 169.37, 174.47; FAB-MS (*m*/*z*, relative intensity) 389 (MH$^+$, 59), 57 (100). Anal. (C$_{23}$H$_{32}$O$_5$·0.2H$_2$O) C, H.

General Procedure for the Synthesis of VIII. Procedure H. A solution of **VII**[30,31] (1 equiv) in THF (3−5 mL/mmol) at −78 °C was treated dropwise with LHMDS (2 equiv, 1 M in THF). After the solution was stirred at −78 °C for 15 min, R^{2}CHO (1.5 equiv) was added and stirring continued for 30 min more at −78 °C. The reaction was monitored by TLC, quenched by slow addition of a saturated aqueous solution of NH$_4$Cl, and allowed to warm to room temperature. The layers were separated, and the aqueous layer was extracted with Et$_2$O (3×). The combined organics were washed with H$_2$O (1×) and brine (1×), dried over MgSO$_4$, and concentrated in vacuo. Purification by silica gel flash column chromatography gave **VIII** as a mixture of diastereomers, which were used directly in the next step.

3-[1-Hydroxy-4-methyl-3-(methylethyl)pentyl]-5-[(4-methoxyphenoxy)methyl]-5-[(phenylmethoxy)methyl]-3,4,5-trihydrofuran-2-one (VIII, R^2 = CH$_2$CH(*i*-Pr)$_2$). According to general procedure H, **VII** (800 mg, 2.3 mmol) and 4-methyl-3-(methylethyl)pentan-1-one[25] (399 mg, 2.8 mmol) were reacted to give **VIII** (R^2 = CH$_2$CH(*i*-Pr)$_2$; 692 mg, 61% yield).

3-(1-Hydroxy-3-phenoxypropyl)-5-[(4-methoxyphenoxy)methyl]-5-[(phenylmethoxy)methyl]-3,4,5-trihydrofuran-2-one (VIII, R^2 = PhCH$_2$CH$_2$). According to general procedure H, **VII** (600 mg, 1.8 mmol) and hydrocinnamaldehyde (0.28 mL, 2.1 mmol) were reacted to give **VIII** (R^2 = PhCH$_2$CH$_2$; 1.35 g, 83% yield) as a colorless oil.

3-[Hydroxy-(2-methoxyphenyl)methyl]-5-[(4-methoxyphenoxy)methyl]-5-[(phenylmethoxy)methyl]-3,4,5-trihydrofuran-2-one (VIII, R^2 = 2-(OMe)C$_6$H$_4$). According to general procedure H, **VII** (1.0 g, 2.9 mmol) and *o*-anisaldehyde (473 mg, 3.5 mmol) were reacted to give **VIII** (R^2 = 2-(OMe)C$_6$H$_4$; 1.38 g, 100% yield) as a colorless oil.

3-[Hydroxy-(3-methoxyphenyl)methyl]-5-[(4-methoxyphenoxy)methyl]-5-[(phenylmethoxy)methyl]-3,4,5-trihydrofuran-2-one (VIII, R^2 = 3-(OMe)C$_6$H$_4$). According to general procedure H, **VII** (1.0 g, 2.9 mmol) and *m*-anisaldehyde (0.42 mL, 3.5 mmol) were reacted to give **VIII** (R^2 = 3-(OMe)C$_6$H$_4$; 1.25 g, 89% yield) as a colorless oil.

3-[Hydroxy-(4-methoxyphenyl)methyl]-5-[(4-methoxyphenoxy)methyl]-5-[(phenylmethoxy)methyl]-3,4,5-trihydrofuran-2-one (VIII, R^2 = (4-(OMe)C$_6$H$_4$). According to general procedure H, **VII** (1.0 g, 2.9 mmol) and *p*-anisaldehyde (0.42 mL, 3.5 mmol) were reacted to give **VIII** (R^2 = 4-(OMe)C$_6$H$_4$; 1.15 g, 82% yield) as a colorless oil.

3-{Hydroxy-[2-(phenylmethoxy)phenyl]methyl}-5-[(4-methoxyphenoxy)methyl]-5-[(phenylmethoxy)methyl]-3,4,5-trihydrofuran-2-one (VIII, R^2 = 2-(PhCH$_2$O)C$_6$H$_4$). According to general procedure H, **VII** (1.0 g, 2.9 mmol) and 2-(benzyloxy)benzaldehyde (742 mg, 3.5 mmol) were reacted to give **VIII** (R^2 = 2-(PhCH$_2$O)-C$_6$H$_4$; 1.35 g, 83% yield) as a colorless oil.

3-{Hydroxy-[3-(phenylmethoxy)phenyl]methyl}-5-[(4-methoxyphenoxy)methyl]-5-[(phenylmethoxy)methyl]-3,4,5-trihydrofuran-2-one (VIII, R^2 = 3-(PhCH$_2$O)C$_6$H$_4$. According to general procedure H, **VII** (1.0 g, 2.9 mmol) and 3-(benzyloxy)benzaldehyde (742 mg, 3.5 mmol) were reacted to give **VIII** (R^2 = 3-(PhCH$_2$O)-C$_6$H$_4$; 1.24 g, 76% yield) as a colorless oil.

3-{Hydroxy-[4-(phenylmethoxy)phenyl]methyl}-5-[(4-methoxyphenoxy)methyl]-5-[(phenylmethoxy)methyl]-3,4,5-trihydrofuran-2-one (VIII, R^2 = 4-(PhCH$_2$O)C$_6$H$_4$. According to general procedure H, **VII** (1.0 g, 2.9 mmol) and 4-(benzyloxy)benzaldehyde (742 mg, 3.5 mmol) were reacted to give **VIII** (R^2 = 4-(PhCH$_2$O)-C$_6$H$_4$; 1.25 g, 79% yield) as a colorless oil.

General Procedure for the Synthesis of IX. Procedure I. Intermediate **VIII** was then taken up in dichloromethane (3−5 mL/mmol) and treated with triethylamine (1.7 equiv) and methanesulfonyl chloride (1 equiv). After the solution was stirred for 30 min at room temperature, DBU (2.5 equiv) was added, and the reaction was monitored by TLC. Concentration in vacuo and purification by silica gel flash column chromatography gave **IX**. In most cases only the *E*-isomer was formed; when the *Z*-isomer was detected in small amounts, it was not characterized.

(*E*)-5-[(4-Methoxyphenoxy)methyl]-3-[4-methyl-3-(methylethyl)pentylidene]-5-[(phenylmethoxy)methyl]-4,5-dihydrofuran-2-one ((*E*)-IX, R^2 = $CH_2CH(i\text{-}Pr)_2$) and (*Z*)-5-[(4-Methoxyphenoxy)methyl]-3-[4-methyl-3-(methylethyl)pentylidene]-5-[(phenylmethoxy)methyl]-4,5-dihydrofuran-2-one ((*Z*)-IX, R^2 = $CH_2CH(i\text{-}Pr)_2$). According to general procedure I, **VIII** (R^2 = $CH_2CH(i\text{-}Pr)_2$; 692 mg, 1.43 mmol) was reacted to give (*E*)-**IX** (R^2 = $CH_2CH(i\text{-}Pr)_2$; 240 mg, 36% yield) and (*Z*)-IX (R^2 = $CH_2CH(i\text{-}Pr)_2$; 257 mg, 39% yield).

Data for (*E*)-IX (R^2 = $CH_2CH(i\text{-}Pr)_2$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 and 0.86 (s, 6 H,C═CHCH$_2$CH(CH(CH_3)$_2$)$_2$), 0.90 and 0.92 (d, J = 1.5 Hz, 6 H, C═CHCH$_2$CH(CH(CH_3)$_2$)$_2$), 1.22 (p, J = 5.5 Hz, 1 H, C═CHCH$_2$C*H*(CH(CH$_3$)$_2$)$_2$), 1.74−1.85 (m, 2 H, C═CHCH$_2$CH(C*H*(CH$_3$)$_2$)$_2$), 2.14 (dd, J = 7.4, 5.8 Hz, 2 H, C═CHC*H*$_2$CH(CH(CH$_3$)$_2$)$_2$), 2.88 (dq, J = 17.1, 2.5 Hz, 2 H, H-4$_{ab}$), 3.68 (dd, J = 22.7, 10.2 Hz, 2 H, CC*H*$_2$OCH$_2$C$_6$H$_5$), 3.76 (s, 3 H, CCH$_2$OC$_6$H$_4$OC*H*$_3$), 4.05 (dd, 1 H, J = 23.1, 9.8 Hz, 2 H, CC*H*$_2$OC$_6$H$_4$OCH$_3$) 4.59 (m, 2 H, CCH$_2$OC*H*$_2$C$_6$H$_5$), 6.82 (s, 5 H, CCH$_2$OC$_6$H$_4$OC*H*$_3$ and C═C*H*CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 7.27−7.36 (m, 5 H, CCH$_2$OCH$_2$C$_6$*H*$_5$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.23, 19.30, 21.51, 21.53, 28.58, 29.09, 29.14, 30.56, 50.20, 55.59, 70.65, 72.02, 73.61, 82.76, 114.53, 115.60, 125.28, 127.52, 127.70, 128.33, 137.50, 142.81, 152.45, 154.20, 170.05; FAB-MS (*m*/*z*, relative intensity) 466 (MH$^+$, 36), 91 (100). Anal. ($C_{29}H_{38}O_5$) C, H.

Data for (*Z*)-IX (R^2 = $CH_2CH(i\text{-}Pr)_2$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (d, J = 2.8 Hz, 3 H, C═CHCH$_2$CH(CH(CH_3)$_2$)$_2$), 0.89 (d, J = 2.7 Hz, 3 H, C═CHCH$_2$CH(CH(CH_3)$_2$)$_2$), 0.92 (d, J = 1.6 Hz, 3 H, C═CCH$_2$CH(CH(CH_3)$_2$)$_2$), 0.93 (d, J = 1.5 Hz, 3 H, C═CHCH$_2$CH(CH(CH_3)$_2$)$_2$), 1.13 (m, 1 H, C═CHCH$_2$C*H*(CH(CH$_3$)$_2$)$_2$), 1.76−1.84 (m, 2 H, C═CHCH$_2$CH(C*H*(CH$_3$)$_2$)$_2$), 2.75−2.76 (m, 2 H, C═CHC*H*$_2$CH(CH(CH$_3$)$_2$)$_2$), 2.91 (dq, J = 16.4, 2.0 Hz, 2 H, H-4$_{ab}$), 3.66 (dd, J = 21.5, 10.2 Hz, 2 H, CC*H*$_2$OCH$_2$C$_6$H$_5$), 3.77 (s, 3 H, CCH$_2$OC$_6$H$_4$OC*H*$_3$), 4.02 (dd, 1 H, J = 26.8, 9.7 Hz, 2 H, CC*H*$_2$OC$_6$H$_4$OCH$_3$) 4.59 (m, 1 H, CCH$_2$OC*H*$_2$C$_6$H$_5$), 6.23 (t, J = 7.4 Hz, 1 H, C═C*H*CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 6.82 (s, 4 H, CCH$_2$OC$_6$H$_4$OC*H*$_3$), 7.27−7.36 (m, 5 H, CCH$_2$OCH$_2$C$_6$*H*$_5$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.36, 19.42, 21.57, 21.61, 26.18, 29.26, 29.31, 33.86, 51.12, 55.61, 70.50, 71.88, 73.59, 82.10, 114.54, 115.64, 123.16, 127.54, 127.69, 128.34, 159, 146.66, 152.52, 154.19, 168.90; FAB-MS (*m*/*z*, relative intensity) 466 (MH$^+$, 58), 91 (100). Anal. ($C_{29}H_{38}O_5$) C, H.

(*E*)-5-[(4-Methoxyphenoxy)methyl]-5-[(phenylmethoxy)methyl]-3-(phenylpropylidene)-4,5-dihydrofuran-2-one ((*E*)-IX, R^2 = $PhCH_2CH_2$) and (*Z*)-5-[(4-Methoxyphenoxy)methyl]-5-[(phenylmethoxy)methyl]-3-(phenylpropylidene)-4,5-dihydrofuran-2-one ((*Z*)-IX, R^2 = $PhCH_2CH_2$). According to general procedure I, **VIII** (R^2 = $PhCH_2CH_2$; 747 mg, 1.63 mmol) was reacted to give (*E*)-**IX** (R^2 = $PhCH_2CH_2$; 224 mg, 30% yield) and (*Z*)-**IX** (R^2 = $PhCH_2CH_2$; 201 mg, 27% yield) as colorless oils.

Data for (*E*)-IX (R^2 = $PhCH_2CH_2$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (irregular q, 2 H, C═CHC*H*$_2$CH$_2$C$_6$H$_5$), 2.61 (dm, J = 17.1 Hz, 1 H, H-4$_a$), 2.67 (dm, J = 17.1 Hz, 1 H, H-4$_b$), 2.77 (t, J ≈ 7.3 Hz, 2 H, C═CHCH$_2$C*H*$_2$C$_6$H$_5$), 3.56 (AB q, J = 10.3 Hz, 2 H, CC*H*$_2$OCH$_2$C$_6$H$_5$), 3.74 (s, 3 H, CCH$_2$OC$_6$H$_4$OC*H*$_3$), 3.92 (AB q, J = 9.7 Hz, CC*H*$_2$OC$_6$H$_4$OCH$_3$), 4.54 (br s, 2 H, CCH$_2$OC*H*$_2$C$_6$H$_5$), 6.73−6.82 (m, 6 H, C═C*H*CH$_2$CH$_2$C$_6$*H*$_5$), 7.10−7.34 (m, 9 H, CCH$_2$OC$_6$*H*$_4$OCH$_3$ and CCH$_2$OCH$_2$C$_6$*H*$_5$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.32, 32.09, 34.19,55.69, 70.48, 71.89, 73.64, 82.23, 114.62, 115.70, 126.24, 127.30, 127.59, 127.80, 128.43, 128.48, 137.61, 139.45, 140.61, 152.51, 154.30, 169.84; FAB-MS (*m*/*z*, relative intensity) 459 (MH$^+$, 17), 458 (M•$^+$, 28), 91 (100). Anal. ($C_{29}H_{30}O_5$·0.2H_2O) C, H.

Data for (*Z*)-IX (R^2 = $PhCH_2CH_2$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.75 (irregular t, J ≈ 7.5 Hz, 2 H, C═CHC*H*$_2$CH$_2$C$_6$H$_5$), 2.84 (dm, J = 16.5 Hz, 1 H, H-4$_a$), 2.90 (dm, J = 16.5 Hz, 1 H, H-4$_b$), 3.05 (dm, J ≈ 7.5 Hz, 1 H, C═CHCH$_2$C*H*HC$_6$H$_5$), 3.07 (dm, J ≈ 7.5 Hz, 1 H, C═CHCH$_2$CH*H*C$_6$H$_5$), 3.62 (AB q, J = 10.3 Hz, 2 H, CC*H*$_2$OCH$_2$C$_6$H$_5$), 3.74 (s, 3 H, CCH$_2$OC$_6$H$_4$OC*H*$_3$), 3.97 (AB q, J = 9.7 Hz, CC*H*$_2$OC$_6$H$_4$OCH$_3$), 4.55 (AB q, J = 12.1 Hz, 2 H, CCH$_2$OC*H*$_2$C$_6$H$_5$), 6.18 (tt, J = 7.6, 2.3 Hz, 1 H, C═C*H*CH$_2$CH$_2$C$_6$H$_5$), 6.76−6.82 (m, 4 H, CCH$_2$OC$_6$*H*$_4$OCH$_3$), 7.14−7.34 (m, 10 H, CCH$_2$OCH$_2$C$_6$*H*$_5$ and CCH$_2$OCH$_2$C$_6$*H*$_5$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.89, 33.71, 35.05, 55.69, 70.39, 71.84, 73.62, 82.34, 114.62, 115.70, 125.14, 126.02, 127.59, 127.78, 128.37, 128.41, 128.49, 137.65, 140.95, 142.93, 152.53, 154.28, 168.76; FAB-MS (*m*/*z*, relative intensity) 459 (MH$^+$, 22), 458 (M•$^+$, 37), 91 (100). Anal. ($C_{29}H_{30}O_5$) C, H.

(*E*)-3-[(2-Methoxyphenyl)methylene]-5-[(4-methoxyphenoxy)methyl]-5-[(phenylmethoxy)methyl]-4,5-dihydrofuran-2-one ((*E*)-IX, R^2 = 2-(MeO)C_6H_4). According to general procedure I, **VIII** (R^2 = 2-(MeO)C_6H_4; 1.38 g, 2.88 mmol) was reacted to give (*E*)-**IX** (R^2 = 2-(MeO)C_6H_4; 921 mg, 71% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.12 (dd, J = 17.7, 2.9 Hz, 1 H, H-4$_a$), 3.20 (dd, J = 17.7, 2.9 Hz, 1 H, H-4$_b$), 3.64−3.74 (AB q, J = 10.2 Hz, 2 H, CC*H*$_2$OCH$_2$C$_6$H$_5$ containing δ 3.71 (s, 3 H, CCH$_2$OC$_6$H$_4$OC*H*$_3$)), 3.81 (s, 3 H, C═CHC$_6$H$_4$OC*H*$_3$), 4.04 (AB q, 2 H, J = 9.8 Hz, 2 H, CC*H*$_2$OC$_6$H$_4$OCH$_3$), 4.56 (s, 2 H, CCH$_2$OC*H*$_2$C$_6$H$_5$), 6.75−6.80 (m, 4 H, CCH$_2$OC$_6$*H*$_4$OCH$_3$), 6.90 (d, J = 8.3 Hz, 1 H, C═CHC$_6$*H*$_4$OCH$_3$), 6.96 (t, J = 7.5 Hz, 1 H, C═CHC$_6$*H*$_4$OCH$_3$), 7.23−7.28 (m, 5 H, CCH$_2$OCH$_2$C$_6$*H*$_5$), 7.31−7.36 (m, 1 H, C═CHC$_6$*H*$_4$OCH$_3$), 7.42 (dd, J = 7.7, 1.3 Hz, 1 H, C═CHC$_6$*H*$_4$OCH$_3$), 8.02 (t, J = 2.8 Hz, 1 H, C═C*H*C$_6$H$_4$OCH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.69, 55.37, 55.49, 70.40, 71.78, 73.49, 82.80, 110.88, 114.45, 115.57, 120.25, 123.52, 129.34, 127.46, 127.60, 128.25, 128.90, 131.20, 137.44, 152.34, 154.12, 158.29, 171.22; FAB-MS (*m*/*z*, relative intensity) 461 (MH$^+$, 60), 460 (M•$^+$, 51), 91 (100). Anal. ($C_{28}H_{28}O_6$·0.8H_2O) C, H.

(*E*)-3-[(3-Methoxyphenyl)methylene]-5-[(4-methoxyphenoxy)methyl]-5-[(phenylmethoxy)methyl]-4,5-dihydrofuran-2-one ((*E*)-IX, R^2 = 3-(MeO)C_6H_4). According to general procedure I, **VIII** (R^2 = 3-(MeO)C_6H_4; 1.25 g, 2.6 mmol) was reacted to give (*E*)-**IX** (R^2 = 3-(MeO)Ph; 460 mg, 38% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.17 (dd, J = 17.6, 2.9 Hz, 1 H, H-4$_a$), 3.25 (dd, J = 17.6, 2.9 Hz, 1 H, H-4$_b$), 3.68−3.74 (m, 2 H, CC*H*$_2$OCH$_2$C$_6$H$_5$ containing δ 3.72 s, 3 H, C═CHC$_6$H$_4$OC*H*$_3$), 3.81 (s, 3 H, CCH$_2$OC$_6$H$_4$OC*H*$_3$), 4.06 (AB q, 2 H, J = 9.8 Hz, 2 H, CC*H*$_2$OC$_6$H$_4$OCH$_3$), 4.57 (s, 2 H, CCH$_2$OC*H*$_2$C$_6$H$_5$), 6.75−6.80 (m, 4 H, CCH$_2$OC$_6$*H*$_4$OCH$_3$), 6.93 (dd, J = 8.1, 2.2 Hz, 1 H, C═CHC$_6$*H*$_4$OCH$_3$), 7.00 (br s, 1 H, C═CHC$_6$*H*$_4$OCH$_3$), 7.08 (d, J = 7.8 Hz, 1 H, C═CHC$_6$*H*$_4$OCH$_3$), 7.20−7.35 (m, 6 H, CCH$_2$OCH$_2$C$_6$*H*$_5$ and C═CHC$_6$*H*$_4$OCH$_3$), 7.52 (t, J = 2.8 Hz, 1 H, C═C*H*C$_6$H$_4$OCH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.75, 55.24, 55.58, 70.56, 71.85, 73.61, 83.07, 112.00, 114.54, 115.18, 115.66, 121.08, 124.97, 127.56, 128.36, 129.80, 135.85, 136.32, 136.50, 137.40, 152.36, 154.25, 159.70, 171.11; FAB-MS (*m*/*z*, relative intensity) 461 (MH$^+$, 58), 460 (M•$^+$, 58), 91 (100). Anal. ($C_{28}H_{28}O_6$) C, H.

(*E*)-3-[(4-Methoxyphenyl)methylene]-5-[(4-methoxyphenoxy)methyl]-5-[(phenylmethoxy)methyl]-4,5-dihydrofuran-2-one ((*E*)-IX, R^2 = 4-(MeO)C_6H_4). According to general procedure I, **VIII** (R^2 = 4-(MeO)C_6H_4; 1.15 g, 2.4 mmol) was reacted to give (*E*)-**IX** (R^2 = 4-(MeO)Ph; 716 mg, 85% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.12 (dd, J = 17.5, 2.6 Hz, 1H, H-4$_a$), 3.19 (dd, J = 17.5, 2.6 Hz, 1H, H-4$_b$), 3.66−3.76 (m, 2 H, CC*H*$_2$OCH$_2$C$_6$H$_5$ containing s, 3 H, CCH$_2$OC$_6$H$_4$OC*H*$_3$), 3.78 (s, 3 H, C═CHC$_6$H$_4$OC*H*$_3$), 4.05 (AB q, 2 H, J = 9.8 Hz, 2 H, CC*H*$_2$OC$_6$H$_4$OCH$_3$), 4.55 (s, 2 H, CCH$_2$OC*H*$_2$C$_6$H$_5$), 6.75−6.80 (m, 4 H, CCH$_2$OC$_6$*H*$_4$OCH$_3$), 6.92 (d, 2 H, C═CHC$_6$*H*$_4$OCH$_3$), 7.22−7.29 (m, 5 H, CCH$_2$OCH$_2$C$_6$*H*$_5$), 7.43 (d, 2 H, C═CHC$_6$*H*$_4$OCH$_3$), 7.51 (br t, J ≈ 2.3 Hz, 1 H, 2 H, C═C*H*C$_6$H$_4$OCH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.57, 55.12, 55.38, 70.44, 71.77, 73.40, 82.69, 114.18, 114.38, 115.53, 121.52, 127.13, 127.39, 127.54, 128.18, 131.66, 136.10, 137.36, 152.27, 154.06, 160.65, 171.35;

FAB-MS (*m*/*z*, relative intensity) 461 (MH^+, 57), 91 (100). Anal. ($C_{28}H_{28}O_6$) C, H.

(*E*)-5-[(4-Methoxyphenoxy)methyl]-5-[(phenylmethoxy)methyl]-3-{[2-(phenylmethoxy)phenyl]methylene}-4,5-dihydrofuran-2-one ((*E*)-IX, R^2 = 2-($PhCH_2O$)C_6H_4). According to general procedure I, **VIII** (R^2 = 2-($PhCH_2O$)C_6H_4; 1.35 g, 2.43 mmol) was reacted to give (*E*)-**IX** (R^2 = 2-($PhCH_2O$)C_6H_4; 906 mg, 71% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.12 (dd, J = 17.7, 2.9 Hz, 1 H, H-4_a), 3.20 (dd, J = 17.7, 2.9 Hz, 1 H, H-4_b), 3.70 (AB q, J = 10.3 Hz, 2 H, $CCH_2OCH_2C_6H_5$), 3.76 (s, 3 H, $CCH_2OC_6H_4OCH_3$), 4.06 (AB q, J = 9.7 Hz, 2 H, $CCH_2OC_6H_4OCH_3$), 4.59 (s, 2 H, $CCH_2OCH_2C_6H_5$), 5.16 (s, 2 H, $C{=}CHC_6H_4OCH_2C_6H_5$), 6.81 (s, 4 H, $CCH_2OC_6H_4OCH_3$), 6.97−7.02 (m, 2 H, $C{=}CHC_6H_4OCH_2C_6H_5$), 7.27−7.48 (m, 12 H, $C{=}CHC_6H_4OCH_2C_6H_5$ and $CCH_2OCH_2C_6H_5$), 8.09 (t, J = 2.8 Hz, 1 H, $C{=}CHC_6H_4OCH_2C_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.98, 55.69, 70.41, 70.44, 70.47, 71.89, 73.68, 82.86, 112.66, 114.58, 115.67, 120.69, 124.19, 124.37, 127.15, 127.61, 127.75, 127.99, 128.39, 128.65, 129.32, 131.15, 131.58, 136.43, 137.54, 152.48, 154.25, 157.48, 171.22; FAB-MS (*m*/*z*, relative intensity) 537 (MH^+, 15), 536 ($M\bullet^+$, 15), 91 (100). Anal. ($C_{34}H_{32}O_6$) C, H.

(*E*)-5-[(4-Methoxyphenoxy)methyl]-5-[(phenylmethoxy)methyl]-3-{[3-(phenylmethoxy)phenyl]methylene}-4,5-dihydrofuran-2-one ((*E*)-IX, R^2 = 3-($PhCH_2O$)C_6H_4). According to general procedure I, **VIII** (R^2 = 3-($PhCH_2O$)C_6H_4; 1.24 g, 2.24 mmol) was reacted to give (*E*)-**IX** (R^2 = 3-($PhCH_2O$)C_6H_4; 911 mg, 77% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.09 (dd, J = 17.9, 2.8 Hz, 1 H, H-4_a), 3.18 (dd, J = 17.9, 2.8 Hz, 1 H, H-4_b), 3.68−3.73 (m, 2 H, $CCH_2OCH_2C_6H_5$), 3.73 (s, 3 H, $CCH_2OC_6H_4OCH_3$), 4.05 (AB q, 2 H, J = 9.9 Hz, 2 H, $CCH_2OC_6H_4OCH_3$), 4.58 (s, 2 H, $CCH_2OCH_2C_6H_5$), 5.08 (s, 2 H, $C{=}CHC_6H_4OCH_2C_6H_5$), 6.80 (s, 4 H, $CCH_2OC_6H_4OCH_3$), 7.01−7.11 and 7.27−7.43 (m, 14 H, $C{=}CHC_6H_4OCH_2C_6H_5$ and $CCH_2OCH_2C_6H_5$), 7.53 (br t, 1 H, $C{=}CHC_6H_4OCH_2C_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.62, 55.48, 69.97, 70.45, 71.76, 73.50, 83.00, 114.47, 115.59, 116.09, 116.24, 122.85, 124.99, 127.22, 127.50, 127.67, 127.92, 128.28, 128.51 129.76, 135.78, 136.18, 136.50, 137.36, 152.29, 154.17, 158.76; FAB-MS (*m*/*z*, relative intensity) 537 (MH^+, 23), 536 ($M\bullet^+$, 24), 91 (100). Anal. ($C_{34}H_{32}O_6\cdot 0.2H_2O$) C, H.

(*E*)-5-[(4-Methoxyphenoxy)methyl]-5-[(phenylmethoxy)methyl]-3-{[4-(phenylmethoxy)phenyl]methylene}-4,5-dihydrofuran-2-one ((*E*)-IX, R^2 = 4-($PhCH_2O$)C_6H_4). According to general procedure I, **VIII** (R^2 = 4-($PhCH_2O$)C_6H_4; 1.25 g, 2.25 mmol) was reacted to give (*E*)-**IX** (R^2 = 4-($PhCH_2O$)C_6H_4; 503 mg, 41% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.14 (dd, J = 17.7, 2.8 Hz, 1 H, H-4_a), 3.22 (dd, J = 17.7, 2.8 Hz, 1 H, H-4_b), 3.70−3.77 (m, 2 H, $CCH_2OCH_2C_6H_5$ containing δ 3.72 s, 3 H, $CCH_2OC_6H_4OCH_3$), 4.05−4.17 (m, 2 H, $CCH_2OC_6H_4OCH_3$), 4.61 (s, 2 H, $CCH_2OCH_2C_6H_5$), 5.12 (s, 2 H, $C{=}CHC_6H_4OCH_2C_6H_5$), 6.83 (s, 4 H, $CCH_2OC_6H_4OCH_3$), 7.05 (d, J = 8.8 Hz, 2 H, $C{=}CHC_6H_4OCH_2C_6H_5$), 7.28−7.50 (m, 12 H, $C{=}CHC_6H_4OCH_2C_6H_5$ and $CCH_2OCH_2C_6H_5$), 7.56 (br t, J = 2.6 Hz, 1 H, $C{=}CHC_6H_4OCH_2C_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.76, 55.60, 710.01, 70.57, 71.91, 73.63, 82.84, 114.55, 115.21 115.68, 121.75, 127.37, 127.58, 127.74, 128.11, 128.36, 128.60, 131.83, 136.28, 136.34, 137.48, 152.43, 154.24 159.96, 171.52; FAB-MS (*m*/*z*, relative intensity) 537 (MH^+, 13), 536 ($M\bullet^+$, 10), 91 (100). Anal. ($C_{34}H_{32}O_6$) C, H.

General Procedure for the Synthesis of X. Procedure J. CAN (3 equiv) was added to a stirring solution of **IX** (1 equiv) in acetonitrile (8 mL/mmol of **IX**) and water (2 mL/mmol of **IX**) at 0 °C. The reaction was monitored by TLC and, after being stirred for 30 min, quenched with a saturated aqueous $NaHCO_3$ solution and warmed to room temperature. The resulting aqueous solution was extracted with EtOAc (3×), dried over $MgSO_4$, and concentrated in vacuo. Purification by silica gel flash column chromatography gave intermediate **X** as an oil which was used directly without further purification.

(*E*)-5-(Hydroxymethyl)-3-[4-methyl-3-(methylethyl)pentylidene]-5-[(phenylmethoxy)methyl]-4,5-dihydrofuran-2-one ((*E*)-X, R^2 = $CH_2CH(i\text{-}Pr)_2$). According to general procedure J, (*E*)-**IX** (R^2 = $CH_2CH(i\text{-}Pr)_2$; 660 mg, 1.4 mmol) was reacted to give (*E*)-**X** (R^2 = $CH_2CH(i\text{-}Pr)_2$; 381 mg, 78% yield) as a colorless oil.

(*Z*)-5-(Hydroxymethyl)-3-[4-methyl-3-(methylethyl)pentylidene]-5-[(phenylmethoxy)methyl]-4,5-dihydrofuran-2-one ((*Z*)-X, R^2 = $CH_2CH(i\text{-}Pr)_2$). According to general procedure J, (*Z*)-**IX** (R^2 = $CH_2CH(i\text{-}Pr)_2$; 1.0 g, 2.1 mmol) was reacted to give (*Z*)-**X** (R^2 = $CH_2CH(i\text{-}Pr)_2$; 370 mg, 49% yield) as a colorless oil.

(*E*)-5-(Hydroxymethyl)-5-[(phenylmethoxy)methyl]-3-(phenylpropylidene)-4,5-dihydrofuran-2-one ((*E*)-X, R^2 = $PhCH_2CH_2$). According to general procedure J, (*E*)-**IX** (R^2 = $PhCH_2CH_2$; 224 mg, 0.49 mmol) was reacted to give (*E*)-**X** (R^2 = $PhCH_2CH_2$; 100 mg, 57% yield) as a colorless oil.

(*E*)-5-(Hydroxymethyl)-3-[(2-methoxyphenyl)methylene]-5-[(phenylmethoxy)methyl]-4,5-dihydrofuran-2-one ((*E*)-X, R^2 = 2-(MeO)C_6H_4). According to general procedure J, (*E*)-**IX** (R^2 = 2-(MeO)Ph; 921 mg, 2.0 mmol) was reacted to give (*E*)-**X** (R^2 =2-(MeO)C_6H_4; 560 mg, 80% yield) as a colorless oil.

(*E*)-5-(Hydroxymethyl)-3-[(3-methoxyphenyl)methylene]-5-[(phenylmethoxy)methyl]-4,5-dihydrofuran-2-one ((*E*)-X, R^2 = 3-(MeO)C_6H_4). According to general procedure J, (*E*)-**IX** (R^2 = 3-(MeO)C_6H_4; 460 mg, 1.0 mmol) was reacted to give (*E*)-**X** (R^2 = 3-(MeO)C_6H_4; 232 mg, 66% yield) as a colorless oil.

(*E*)-5-(Hydroxymethyl)-3-[(4-methoxyphenyl)methylene]-5-[(phenylmethoxy)methyl]-4,5-dihydrofuran-2-one ((*E*)-X, R^2 = 4-(MeO)C_6H_4). According to general procedure J, (*E*)-**IX** (R^2 = 4-(MeO)C_6H_4; 480 mg, 1.0 mmol) was reacted to give (*E*)-**X** (R^2 = 4-(MeO)C_6H_4; 122 mg, 34% yield) as a colorless oil.

(*E*)-5-(Hydroxymethyl)-5-[(phenylmethoxy)methyl]-3-{[2-(phenylmethoxy)phenyl]methylene}-4,5-dihydrofuran-2-one ((*E*)-X, R^2 = 2-($PhCH_2O$)C_6H_4). According to general procedure J, (*E*)-**IX** (R^2 = 2-($PhCH_2O$)C_6H_4; 906 mg, 1.7 mmol) was reacted to give (*E*)-**X** (R^2 = 2-($PhCH_2O$)C_6H_4; 631 mg, 88% yield) as a colorless oil.

(*E*)-5-(Hydroxymethyl)-5-[(phenylmethoxy)methyl]-3-{[3-(phenylmethoxy)phenyl]methylene}-4,5-dihydrofuran-2-one ((*E*)-X, R^2 = 3-($PhCH_2O$)C_6H_4). According to general procedure J, (*E*)-**IX** (R^2 = 3-($PhCH_2O$)C_6H_4; 900 mg, 1.7 mmol) was reacted to give (*E*)-**X** (R^2 = 3-($PhCH_2O$)C_6H_4; 631 mg, 88% yield) as a colorless oil.

(*E*)-5-(Hydroxymethyl)-5-[(phenylmethoxy)methyl]-3-{[4-(phenylmethoxy)phenyl]methylene}-4,5-dihydrofuran-2-one ((*E*)-X, R^2 = 4-($PhCH_2O$)C_6H_4). According to general procedure J, (*E*)-**IX** (R^2 = 4-($PhCH_2O$)C_6H_4; 503 mg, 0.94 mmol) was reacted to give (*E*)-**X** (R^2 = 4-($PhCH_2O$)C_6H_4; 242 mg, 60% yield) as a colorless oil.

General Procedure for the Synthesis of XI. Procedure K. A solution of (*E*)-**X** (1 equiv) in dichloromethane (12 mL/mmol) was treated with Et_3N (3 equiv), acid chloride (1.5 equiv), and a catalytic amount of DMAP (0.1 equiv). The reaction was stirred at room temperature and monitored by TLC, and upon completion it was concentrated in vacuo. Purification by silica gel flash column chromatography gave (*E*)-**XI**.

(*Z*)-{4-[4-Methyl-3-(methylethyl)pentylidene]-5-oxo-2-[(phenylmethoxy)methyl]-2,3-dihydrofur-2-yl}methyl 2-(Phenylmethoxy)benzoate ((*Z*)-XI, R^1 = 2-($PhCH_2O$)C_6H_4, R^2 = $CH_2CH(i\text{-}Pr)_2$). According to general procedure K, (*Z*)-**X** (R^2 = $CH_2CH(i\text{-}Pr)_2$; 100 mg, 0.28 mmol) and 2-($PhCH_2O$)PhCOCl (103 mg, 0.42 mmol) were reacted in CH_2Cl_2 (4 mL) to give (*Z*)-**XI** (R^1 = 2-($PhCH_2O$)C_6H_4, R^2 = $CH_2CH(i\text{-}Pr)_2$; 109 mg, 68% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82, 0.83, 0.87, and 0.88 (d, J = 6.8 Hz, 12 H, $C{=}CHCH_2CH(CH(CH_3)_2)_2$), 1.05 (p, $J \approx$ 5.5 Hz, 1 H, $C{=}CHCH_2CH(CH(CH_3)_2)_2$), 1.70−1.80 (m, 2 H, $C{=}CHCH_2CH(CH(CH_3)_2)_2$), 2.51−2.60 (m, 1 H, $C{=}CHCH_2CH(CH(CH_3)_2)_2$), 2.69−2.80 (m, 3 H, $C{=}CHCH_2CH(CH(CH_3)_2)_2$ and H-$3_{a,b}$), 3.50 (AB q, J = 10.1 Hz, 2 H, $CCH_2OCH_2C_6H_5$), 4.41 (AB q, J = 11.7 Hz, 2 H, $CCH_2OC(O)C_6H_4OCH_2C_6H_5$), 4.50 (d, J = 2.9 Hz, 2 H, $CCH_2OCH_2C_6H_5$), 5.12 (s, 2 H, $CCH_2OC(O)C_6H_4OCH_2C_6H_5$), 6.08−6.13 (m, 1 H, $C{=}CHCH_2CH(CH(CH_3)_2)_2$), 6.94−6.99 (m, 2 H, $CCH_2OC(O)C_6H_4OCH_2C_6H_5$), 7.25−7.45 (m, 11 H, $CCH_2OC(O)C_6H_4OCH_2C_6H_5$ and $CCH_2OCH_2C_6H_5$), 7.77 (dd, J = 7.7, 1.8 Hz, 1 H, $CCH_2OC(O)C_6H_4OCH_2C_6H_5$); ^{13}C NMR (100

MHz, $CDCl_3$) δ 19.31, 19.47, 21.58, 21.65, 26.19, 29.27, 29.36, 33.90, 51.13, 65.93, 70.54, 71.70, 73.58, 81.51, 113.56, 119.70, 120.48, 122.90, 127.24, 127.56, 127.73, 127.91, 128.37, 128.58, 132.12, 133.81, 136.49, 137.57, 146.94, 158.39, 165.60, 168.77; FAB-MS (*m*/*z*, relative intensity) 571 (MH^+, 5), 91 (100). Anal. ($C_{36}H_{42}O_6 \cdot 0.5H_2O$) C, H.

(*Z*)-{4-[4-Methyl-3-(methylethyl)pentylidene]-5-oxo-2-[(phenylmethoxy)methyl]-2,3-dihydrofur-2-yl}methyl 3-(Phenylmethoxy)benzoate ((*Z*)-XI, R^1 = 3-($PhCH_2O$)C_6H_4, R^2 = $CH_2CH(i\text{-}Pr)_2$). According to general procedure K, (*Z*)-**X** (R^2 = $CH_2CH(i\text{-}Pr)_2$; 110 mg, 0.31 mmol) and 3-($PhCH_2O$)PhCOCl (162 mg, 0.66 mmol) were reacted in CH_2Cl_2 (6 mL) to give (*Z*)-**XI** (R^1 = 3-($PhCH_2O$)C_6H_4, R^2 = $CH_2CH(i\text{-}Pr)_2$; 149 mg, 84% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 and 0.87 (t, J = 6.8 Hz, 12 H, C=$CHCH_2CH(CH(CH_3)_2)_2$), 1.08 (p, J = 5.5 Hz, 1 H, C=$CHCH_2CH(CH(CH_3)_2)_2$), 1.70−1.80 (m, 2 H, C=$CHCH_2$-$CH(CH(CH_3)_2)_2$), 2.54−2.61 (m, 1 H, C=$CHCHHCH(CH(CH_3)_2)_2$), 2.79−2.86 (m, 2 H, C=$CHCHHCH(CH(CH_3)_2)_2$ and H-3_a), 2.94 (dd, J = 16.6, 2.4 Hz, 1 H, H-3_b), 3.62 (AB q, J = 10.0 Hz, 2 H, $CCH_2OCH_2C_6H_5$), 4.46 (AB q, J = 11.8 Hz, 2 H, $CCH_2OC(O)$-$C_6H_4OCH_2C_6H_5$), 4.58 (s, 2 H, $CCH_2OCH_2C_6H_5$), 5.09 (s, 2 H, $CCH_2OC(O)C_6H_4OCH_2C_6H_5$), 6.18−6.24 (m, 1 H, C=$CHCH_2CH$-$(CH(CH_3)_2)_2$), 7.18 (dd, J = 8.2, 2.6 Hz, 1 H, $CCH_2OC(O)C_6H_4$-$OCH_2C_6H_5$), 7.27−7.46 (m, 10 H, $CCH_2OC(O)C_6H_4OCH_2C_6H_5$ and $CCH_2OCH_2C_6H_5$), 7.56−7.60 (m, 2 H, $CCH_2OC(O)C_6H_4OCH_2C_6H_5$), 7.73−7−75 (m, 1 H, $CCH_2OC(O)C_6H_4OCH_2C_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.29, 21.65, 26.23, 29.26, 29.36, 34.11, 51.12, 66.39, 70.16, 71.65, 73.69, 81.46, 115.26, 116.01, 120.50, 121.75, 122.35, 122.72, 123.15, 127.54, 127.65, 127.85, 128.08, 128.20, 128.43, 128.66, 129.92, 130.68, 136.44, 147.16, 158.71, 165.78, 168.71; FAB-MS (*m*/*z*, relative intensity) 571 (MH^+, 7), 91 (100). Anal. ($C_{36}H_{42}O_6 \cdot 0.1H_2O$) C, H.

(*E*)-{4-[4-Methyl-3-(methylethyl)pentylidene]-5-oxo-2-[(phenylmethoxy)methyl]-2,3-dihydrofur-2-yl}methyl 4-(Phenylmethoxy)benzoate ((*E*)-XI, R^1 = 4-($PhCH_2O$)C_6H_4, R^2 = $CH_2CH(i\text{-}Pr)_2$). According to general procedure K, (*E*)-**X** (R^2 = $CH_2CH(i\text{-}Pr)_2$; 150 mg, 0.41 mmol) and 4-($PhCH_2O$)PhCOCl (151 mg, 0.61 mmol) were reacted to give (*E*)-**XI** (R^1 = 4-($PhCH_2O$)-C_6H_4, R^2 = $CH_2CH(i\text{-}Pr)_2$; 240 mg, 100% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.76, 0.79, 0.82, and 0.85 (d, 6.8 Hz, 12 H, C=$CHCH_2CH(CH(CH_3)_2)_2$), 1.15 (p, J = 5.6 Hz, 1 H, C=$CHCH_2CH(CH(CH_3)_2)_2$), 1.73 (m, 2 H, C=$CHCH_2CH$-$(CH(CH_3)_2)_2$), 2.07 (m, 2 H, C=$CHCH_2CH(CH(CH_3)_2)_2$), 2.74 (dd, J = 17.1, 2.5 Hz, 1 H, H-3_a), 2.87 (dd, J = 17.1, 2.5 Hz, 1 H, H-3_b), 3.64 (AB q, J = 10.0 Hz, 2 H, $CCH_2OCH_2C_6H_5$), 4.44 (AB q, J = 11.8 Hz, 2 H, $CCH_2OC(O)C_6H_4OCH_2C_6H_5$), 4.58 (s, 2 H, $CCH_2OCH_2C_6H_5$), 5.10 (s, 2 H, $CCH_2OC(O)C_6H_4OCH_2C_6H_5$), 6.80 (tt, J = 7.3, 2.7 Hz, 1 H, C=$CHCH_2CH(CH(CH_3)_2)_2$), 6.95 (d, J = 8.9 Hz, 2 H, $CCH_2OC(O)C_6H_4OCH_2C_6H_5$), 7.24−7.43 (m, 10 H, $CCH_2OC(O)C_6H_4OCH_2C_6H_5$ and $CCH_2OCH_2C_6H_5$), 7.89 (d, J = 8.9 Hz, 2 H, $CCH_2OC(O)C_6H_4OCH_2C_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.21, 19.26, 21.38, 21.52, 28.54, 29.02, 29.07, 30.72, 50.14, 66.24, 70.16, 71.80, 73.65, 82.24, 114.48, 121.81, 125.04, 127.35, 127.60, 127.79, 128.13, 128.37, 128.59, 131.73, 136.05, 137.26, 143.07, 162.69, 165.53, 169.87; FAB-MS (*m*/*z*, relative intensity) 571 (MH^+, 11), 91 (100). Anal. ($C_{36}H_{42}O_6$) C, H.

(*Z*)-{4-[4-Methyl-3-(methylethyl)pentylidene]-5-oxo-2-[(phenylmethoxy)methyl]-2,3-dihydrofur-2-yl}methyl 4-(Phenylmethoxy)benzoate ((*Z*)-XI, R^1 = 4-($PhCH_2O$)C_6H_4, R^2 = $CH_2CH(i\text{-}Pr)_2$). According to general procedure K, (*Z*)-**X** (R^2 = $CH_2CH(i\text{-}Pr)_2$; 160 mg, 0.44 mmol) and 4-($PhCH_2O$)PhCOCl (162 mg, 0.66 mmol) were reacted in CH_2Cl_2 (6 mL) to give (*Z*)-**XI** (R^1 = 4-($PhCH_2O$)C_6H_4, R^2 = $CH_2CH(i\text{-}Pr)_2$; 152 mg, 61% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83, 0.84, 0.88, and 0.89 (d, J = 6.8 Hz, 12 H, C=$CHCH_2CH(CH(CH_3)_2)_2$), 1.09 (p, J = 5.5 Hz, 1 H, C=$CHCH_2CH(CH(CH_3)_2)_2$), 1.74 (m, 2 H, C=$CHCH_2CH(CH(CH_3)_2)_2$), 2.54−2.64 (m, 1 H, C=$CHCHHCH$-$(CH(CH_3)_2)_2$), 2.74−2.84 (m, 2 H, C=$CHCHHCH(CH(CH_3)_2)_2$ and H-3_a), 2.92 (dd, J = 16.2, 2.5 Hz, 1 H, H-3_b), 3.62 (AB q, J = 10.0 Hz, 2 H, $CCH_2OCH_2C_6H_5$), 4.44 (AB q, J = 11.8 Hz, 2 H, $CCH_2OC(O)C_6H_4OCH_2C_6H_5$), 4.59 (s, 2 H, $CCH_2OCH_2C_6H_5$), 5.12 (s, 2 H, $CCH_2OC(O)C_6H_4OCH_2C_6H_5$), 6.19−6.23 (m, 1 H, C=$CHCH_2CH(CH(CH_3)_2)_2$), 6.97 (d, J = 8.9 Hz, 2 H, CCH_2OC-$(O)C_6H_4OCH_2C_6H_5$), 7.27−7.45 (m, 10 H, $CCH_2OC(O)C_6H_4$-$OCH_2C_6H_5$ and $CCH_2OCH_2C_6H_5$), 7.92 (d, J = 8.9 Hz, 2 H, $CCH_2OC(O)C_6H_4OCH_2C_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.29, 19.45, 21.55, 21.66, 26.19, 29.25, 29.34, 34.03, 51.09, 66.07, 70.08, 71.71, 73.66, 81.58, 114.51, 121.97, 122.85, 127.40, 127.64, 127.80, 128.19, 128.40, 128.64, 131.78, 132.78, 136.10, 137.37, 146.93, 162.71, 165.60, 168.74; FAB-MS (*m*/*z*, relative intensity) 571 (MH^+, 6), 91 (100). Anal. ($C_{36}H_{42}O_6$) C, H.

(*E*)-{5-Oxo-2-[(phenylmethoxy)methyl]-4-(3-phenylpropylidene)-2,3-dihydrofur-2-yl}methyl 4-Methyl-3-(methylethyl)pentanoate ((*E*)-XI, R^1 = $CH_2CH(i\text{-}Pr)_2$, R^2 = $PhCH_2CH_2$). According to general procedure K, (*E*)-**X** (R^2 = $PhCH_2CH_2$; 100 mg, 0.28 mmol) and 4-methyl-3-(methylethyl)pentanoyl chloride[25] (74 mg, 0.42 mmol) were reacted in CH_2Cl_2 (4 mL) to give (*E*)-**XI** (R^1 = $CH_2CH(i\text{-}Pr)_2$, R^2 = $PhCH_2CH_2$; 108 mg, 78% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.79 and 0.88 (d, J = 6.64 Hz, 12 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 1.55 (p, $J \approx$ 5.70 Hz, 1 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 1.73 (m, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 2.14 (d, J = 5.6 Hz, CCH_2OC-$(O)CH_2CH(CH(CH_3)_2)_2$), 2.42−2.52 (m, 3 H, C=$CHCH_2CH_2C_6H_5$ and H-3_a), 2.62 (d, J = 16.6 Hz, 1 H, H-3_b), 2.78 (t, $J \approx$ 7 Hz, C=$CHCH_2CH_2C_6H_5$), 3.48 (AB q, J = 9.76 Hz, 2 H, $CCH_2OCH_2C_6H_5$), 4.14 (AB q, J = 12.3 Hz, 2 H, $CCH_2OC(O)$-$CH_2CH(CH(CH_3)_2)_2$), 4.52 (s, 2 H, $CCH_2OCH_2C_6H_5$), 6.76 (br t, 1 H, C=$CHCH_2CH_2C_6H_5$), 7.12−7.38 (m, 10 H, C=$CHCH_2CH_2C_6H_5$ and $CCH_2OCH_2C_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.70, 21.32, 29.31, 29.35, 30.41, 32.11, 32.76, 34.17, 46.85, 65.83, 71.75, 73.70, 76.71, 77.04, 77.35, 81.93, 126.29, 126.99, 127.63, 127.88, 128.45, 128.51, 137.35, 139.62, 140.49, 169.54, 174.24; FAB-MS (*m*/*z*, relative intensity) 493 (MH^+, 27), 91 (100). Anal. ($C_{31}H_{40}O_5$) C, H.

(*E*)-{4-[(2-Methoxyphenyl)methylene]-5-oxo-2-[(phenylmethoxy)methyl]-2,3-dihydrofur-2-yl}methyl 4-Methyl-3-(methylethyl)pentanoate ((*E*)-XI, R^1 = $CH_2CH(i\text{-}Pr)_2$, R^2 = 2-(MeO)C_6H_4). According to general procedure K, (*E*)-**X** (R^2 = 2-(MeO)C_6H_4; 560 mg, 1.6 mmol) and 4-methyl-3-(methylethyl)-pentanoyl chloride[25] (424 mg, 2.4 mmol) were reacted to give (*E*)-**XI** (R^1 = $CH_2CH(i\text{-}Pr)_2$, R^2 = 2-(MeO)C_6H_4; 790 mg, 100% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.73, 0.76, 0.83, 0.85 (d, J = 6.8 Hz, 12 H, $CCH_2OC(O)CH_2CH$-$(CH(CH_3)_2)_2$), 1.53 (p, J = 5.8 Hz, 1 H, $CCH_2OC(O)CH_2CH$-$(CH(CH_3)_2)_2$), 1.68 (septet, J = 6.8 Hz, 2 H, $CCH_2OC(O)CH_2CH$-$(CH(CH_3)_2)_2$), 2.14 (d, J = 5.8 Hz, 2 H, $CCH_2OC(O)CH_2CH$-$(CH(CH_3)_2)_2$), 2.99 (dd, J = 17.6, 2.9 Hz, 1 H, H-3_a), 3.15 (dd, J = 17.6, 2.9 Hz, 1 H, H-3_b), 3.61 (AB q, J = 10.9 Hz, 2 H, $CCH_2OCH_2C_6H_5$), 3.87 (s, 1 H, C=$CHC_6H_4OCH_3$), 4.27 (AB q, J = 11.9 Hz, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 4.57 (s, 2 H, $CCH_2OCH_2C_6H_5$), 6.94 (d, J = 8.3 Hz, 1 H, C=$CHC_6H_4OCH_3$), 6.99 (t, J = 2.9 Hz, 1 H, C=$CHC_6H_4OCH_3$), 7.26−7.40 (m, 7 H, $CCH_2OCH_2C_6H_5$ and C=$CHC_6H_4OCH_3$), 8.01 (t, J = 2.9 Hz, 1 H, C=$CHC_6H_4OCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.58, 21.21, 29.21, 32.68, 32.90, 34.03, 46.71, 55.36, 65.90, 71.73, 73.62, 82.08, 110.89, 120.28, 123.42, 123.61, 127.57, 127.77, 128.34, 128.89, 131.32, 131.37, 137.22, 158.36, 170.38, 171.11, 174.23; FAB-MS (*m*/*z*, relative intensity) 495 (MH^+, 34), 91 (100). Anal. ($C_{30}H_{38}O_6$) C, H.

(*E*)-{4-[(3-Methoxyphenyl)methylene]-5-oxo-2-[(phenylmethoxy)methyl]-2,3-dihydrofur-2-yl}methyl 4-Methyl-3-(methylethyl)pentanoate ((*E*)-XI, R^1 = $CH_2CH(i\text{-}Pr)_2$, R^2 = 3-(MeO)C_6H_4). According to general procedure K, (*E*)-**X** (R^2 = 3-(MeO)C_6H_4; 232 mg, 0.66 mmol) and 4-methyl-3-(methylethyl)-pentanoyl chloride[25] (174 mg, 0.99 mmol) were reacted to give (*E*)-**XI** (R^1 = $CH_2CH(i\text{-}Pr)_2$, R^2 = 3-(MeO)C_6H_4; 230 mg, 70% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.73, 0.76, 0.82, 0.83 (d, J = 6.8 Hz, 12 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 1.48−1.55 (m, 1 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 1.68 (septet, J = 6.3 Hz, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 2.14 (d, J = 5.8 Hz, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 3.01 (dd, J =

17.6, 2.9 Hz, 1 H, H-3$_a$), 3.16 (dd, J = 17.6, 2.9 Hz, 1 H, H-3$_b$), 3.58 (AB q, J = 10.2 Hz, 2 H, CCH_2OCH$_2$C$_6$H$_5$), 3.83 (s, 1 H, C=CHC$_6$H$_4$OCH_3), 4.24 (AB q, J = 12.1 Hz, 2 H, CCH_2OC(O)CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 4.57 (s, 2 H, CCH$_2$OCH_2C$_6$H$_5$), 6.96 (dd, J = 8.1, 2.4 Hz, 1 H, C=CHC$_6$$H_4OCH_3$), 6.99 (br t, 1 H, C=CHC$_6$$H_4$-OCH$_3$), 7.07 (br d, J = 7.8 Hz, 1 H, C=CHC$_6$$H_4OCH_3$), 7.26−7.38 (m, 6 H, CCH$_2$OCH$_2$C$_6$$H_5$ and C=CHC$_6$$H_4OCH_3$), 7.49 (t, J = 2.8 Hz, 1 H, C=CHC$_6$H$_4$OCH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$) δ 21.15, 21.27, 29.32, 32.74, 46.82, 55.28, 65.90, 71.74, 73.71, 82.31, 115.27, 115.62, 122.40, 124.66, 127.48, 127.83, 128.43, 135.74, 136.39, 136.70, 137.20, 159.77, 170.89, 174.23; FAB-MS (*m*/*z*, relative intensity) 495 (MH$^+$, 34), 91 (100). Anal. (C$_{30}$H$_{38}$O$_6$) C, H.

(*E*)-{4-[(4-Methoxyphenyl)methylene]-5-oxo-2-[(phenylmethoxy)methyl]-2,3-dihydrofur-2-yl}methyl 4-Methyl-3-(methylethyl)pentanoate ((*E*)-XI, R^1 = CH$_2$CH(*i*-Pr)$_2$, R^2 = 4-(MeO)C$_6$H$_4$). According to general procedure K, (*E*)-**X** (R^2 = 4-(MeO)C$_6$H$_4$; 122 mg, 0.34 mmol) and 4-methyl-3-(methylethyl)-pentanoyl chloride[25] (90 mg, 0.51 mmol) were reacted to give (*E*)-**XI** (R^1 = CH$_2$CH(*i*-Pr)$_2$, R^2 = 4-(MeO)C$_6$H$_4$; 110 mg, 64% yield) as a colorless oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.72 and 0.76 (d, J = 6.7 Hz, 6 H, CCH$_2$OC(O)CH$_2$CH(CH(CH_3)$_2$)$_2$), 0.81−0.85 (m, 6 H, CCH$_2$OC(O)CH$_2$CH(CH(CH_3)$_2$)$_2$), 1.52 (p, J = 5.8 Hz, 1 H, CCH$_2$OC(O)CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 1.68 (irregular septet, 2 H, CCH$_2$OC(O)CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 2.14 (d, J = 5.8 Hz, 2 H, CCH$_2$-OC(O)CH_2CH(CH(CH$_3$)$_2$)$_2$), 3.00 (dd, J = 17.5, 2.8 Hz, 1 H, H-3$_a$), 3.16 (dd, J = 17.5, 2.8 Hz, 1 H, H-3$_b$), 3.62 (AB q, J = 10.0 Hz, 2 H, CCH_2OCH$_2$C$_6$H$_5$), 3.85 (s, 3 H, C=CHC$_6$H$_4$OCH_3), 4.28 (AB q, J = 12.0 Hz, 2 H, CCH_2OC(O)CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 4.57 (s, 2 H, CCH$_2$OCH_2C$_6$H$_5$), 6.96 (d, $J \approx$ 12 Hz, 2 H, C=CHC$_6$$H_4OCH_3$), 7.25−7.35 (m, 5 H, CCH$_2$OCH$_2$C$_6$$H_5$), 7.45 (d, $J \approx$ 12 Hz, 2 H, C=CHC$_6$$H_4OCH_3$), 7.51 (t, 1 H, J = 2.7 Hz, C=CHC$_6$H$_4$OCH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$) δ 18.66, 21.27, 29.29, 32.78, 46.84, 55.45, 66.00, 71.86, 73.76, 82.07, 114.38, 121.29, 127.27, 127.76, 128.45, 031.92, 136.46, 136.59, 137.28, 160.94, 171.35, 174.33; FAB-MS (*m*/*z*, relative intensity) 495 (MH$^+$, 21), 91 (100). Anal. (C$_{30}$H$_{38}$O$_6$·0.2H$_2$O) C, H.

(*E*)-(5-Oxo-2-[(phenylmethoxy)methyl]-4-{[2-(phenylmethoxy)phenyl]methylene}-2,3-dihydrofur-2-yl)methyl 4-Methyl-3-(methylethyl)pentanoate ((*E*)-XI, R^1 = CH$_2$CH(*i*-Pr)$_2$, R^2 = 2-(PhCH$_2$O)C$_6$H$_4$). According to general procedure K, (*E*)-**X** (R^2 = 2-(PhCH$_2$O)C$_6$H$_4$; 496 mg, 1.1 mmol) and 4-methyl-3-(methylethyl)pentanoyl chloride[25] (240 mg, 1.3 mmol) were reacted to give (*E*)-**XI** (R^1 = CH$_2$CH(*i*-Pr)$_2$, R^2 = 2-(PhCH$_2$O)Ph; 439 mg, 70% yield) as a colorless oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.71 and 0.73 (d, J = 6.8 Hz, 6 H, CCH$_2$OC(O)CH$_2$CH(CH(CH_3)$_2$)$_2$), 0.81 (t, J = 6.8 Hz, 6 H, CCH$_2$OC(O)CH$_2$CH(CH(CH_3)$_2$)$_2$), 1.55 (p, J = 5.8 Hz, 1 H, CCH$_2$OC(O)CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 1.61−1.74 (m, 2 H, CCH$_2$OC(O)CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 2.16 (d, J = 5.7 Hz, 2 H, CCH$_2$OC(O)CH_2CH(CH(CH$_3$)$_2$)$_2$), 3.00 (dd, J = 17.7, 2.9 Hz, 1 H, H-3$_a$), 3.15 (dd, J = 17.7, 3.0 Hz, 2 H, H-3$_b$), 3.60 (AB q, J = 10.0 Hz, 2 H, CCH_2OCH$_2$C$_6$H$_5$), 4.27 (s, 2 H, CCH_2OC(O)-CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 4.57 (s, 2 H, CCH$_2$OCH_2C$_6$H$_5$), 5.15 (s, 2 H, C=CHC$_6$H$_4$OCH_2C$_6$H$_5$), 6.98−7.03 (m, 2 H, C=CHC$_6$$H_4$-OCH$_2C_6H_5$), 7.26−7.45 (m, 12 H, C=CHC$_6$$H_4OCH_2C_6$$H_5$ and CCH$_2$OCH$_2$C$_6$$H_5$), 8.09 (t, J = 2.8 Hz, 1 H, C=CHC$_6$H$_4$-OCH$_2$C$_6$H$_5$); ^{13}C NMR (100 MHz, CDCl$_3$) δ 18.62, 21.15, 21.17, 29.23, 32.71, 33.05, 46.75, 65.88, 70.32, 71.75, 73.65, 81.98, 112.60, 120.64, 123.92, 127.06, 127.59, 127.79, 127.94, 128.36, 128.57, 129.16, 131.22, 131.42, 136.31, 137.25, 157.46, 170.93, 174.24; FAB-MS (*m*/*z*, relative intensity) 571 (MH$^+$, 4), 91 (100). Anal. (C$_{36}$H$_{42}$O$_6$·0.8H$_2$O) C, H.

(*E*)-(5-Oxo-2-[(phenylmethoxy)methyl]-4-{[3-(phenylmethoxy)phenyl]methylene}-2,3-dihydrofur-2-yl)methyl 4-methyl-3-(methylethyl)pentanoate ((*E*)-XI, R^1 = CH$_2$CH(*i*-Pr)$_2$, R^2 = 3-(PhCH$_2$O)C$_6$H$_4$). According to general procedure K, (*E*)-**X** (R^2 = 4-(PhCH$_2$O)C$_6$H$_4$; 359 mg, 0.83 mmol) and 4-methyl-3-(methylethyl)pentanoyl chloride[25] (219 mg, 1.2 mmol) were reacted to give (*E*)-**XI** (R^1 = CH$_2$CH(*i*-Pr)$_2$, R^2 = 3-(PhCH$_2$O)Ph; 366 mg, 77% yield) as a colorless oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.74, 0.77, 0.83 (d, J = 6.8 Hz, 12 H, CCH$_2$OC(O)CH$_2$CH(CH(CH_3)$_2$)$_2$), 1.53 (p, J = 5.8 Hz, 1 H, CCH$_2$OC(O)CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 1.62−1.74 (m, 2 H, CCH$_2$OC(O)CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 2.15 (d, J = 5.7 Hz, 2 H, CCH$_2$OC(O)CH_2CH(CH(CH$_3$)$_2$)$_2$), 2.93 (dd, J = 17.8, 2.8 Hz, 1 H, H-3$_a$), 3.10 (dd, J = 17.8, 2.9 Hz, 1 H, H-3$_b$), 3.60 (AB q, J = 10.0 Hz, 2 H, CCH_2OCH$_2$C$_6$H$_5$), 4.26 (s, 2 H, CCH_2-OC(O)CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 4.58 (s, 2 H, CCH$_2$OCH_2C$_6$H$_5$), 5.11 (s, 2 H, C=CHC$_6$H$_4$OCH_2C$_6$H$_5$), 7.04−7.09 (m, 3 H, C=CHC$_6$$H_4$-OCH$_2C_6H_5$), 7.28−7.44 (m, 11 H, C=CHC$_6$$H_4OCH_2C_6$$H_5$ and CCH$_2$OCH$_2$C$_6$$H_5$), 7.51 (t, J = 2.8 Hz, 1 H, C=CHC$_6$H$_4$-OCH$_2$C$_6$H$_5$); ^{13}C NMR (100 MHz, CDCl$_3$) δ 18.56, 21.17, 21.20, 21.26, 29.24, 32.72, 46.78, 65.87, 70.08, 71.69, 73.67, 82.29, 116.18, 116.42, 122.90,124.68, 127.25, 127.65, 127.87, 128.03, 128.41 128.61, 129.86, 135.72, 136.40, 136.53, 137.18, 158.86, 170.87, 174.20, 180.30; FAB-MS (*m*/*z*, relative intensity) 571 (MH$^+$, 9), 91 (100). Anal. (C$_{36}$H$_{42}$O$_6$·0.3H$_2$O) C, H.

(*E*)-(5-Oxo-2-[(phenylmethoxy)methyl]-4-{[4-(phenylmethoxy)phenyl]methylene}-2,3-dihydrofur-2-yl)methyl 4-Methyl-3-(methylethyl)pentanoate ((*E*)-XI, R^1 = CH$_2$CH(*i*-Pr)$_2$, R^2 = 4-(PhCH$_2$O)C$_6$H$_4$). According to general procedure K, (*E*)-**X** (R^2 = 4-(PhCH$_2$O)C$_6$H$_4$; 242 mg, 0.56 mmol) and 4-methyl-3-(methylethyl)pentanoyl chloride[25] (148 mg, 0.84 mmol) were reacted to give (*E*)-**XI** (R^1 = CH$_2$CH(*i*-Pr)$_2$, R^2 = 4-(PhCH$_2$O)C$_6$H$_4$; 213 mg, 66% yield) as a colorless oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.74 and 0.77 (d, J = 6.8 Hz, 6 H, CCH$_2$OC(O)CH$_2$CH(CH(CH_3)$_2$)$_2$), 0.83 (d, J = 6.0 Hz, 6 H, CCH$_2$OC(O)CH$_2$CH(CH(CH_3)$_2$)$_2$), 1.54 (p, J = 5.8 Hz, 1 H, CCH$_2$OC(O)CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 1.69 (irregular septet, 2 H, CCH$_2$OC(O)CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 2.15 (d, J = 5.8 Hz, 2 H, CCH$_2$OC(O)CH_2CH(CH(CH$_3$)$_2$)$_2$), 3.01 (dd, J = 17.6, 2.7 Hz, 2 H, H-3$_a$), 3.16 (dd, J = 17.6, 2.8 Hz, 2 H, H-3$_b$), 3.62 (AB q, J = 9.9 Hz, 2 H, CCH_2OCH$_2$C$_6$H$_5$), 4.29 (AB q, J = 11.9 Hz, 2 H, CCH_2OC(O)CH$_2$CH(CH(CH$_3$)$_2$)$_2$), 4.58 (s, 2 H, C=CHC$_6$H$_4$OCH_2C$_6$H$_5$), 5.11 (s, 2 H, CCH$_2$OCH_2C$_6$H$_5$), 7.03 (d, J = 8.8 Hz, 2 H, C=CHC$_6$$H_4OCH_2C_6H_5$), 7.27−7.45 (m, 12 H, C=CHC$_6$$H_4OCH_2C_6$$H_5$ and CCH$_2$OCH$_2$C$_6$$H_5$), 7.52 (t, J = 2.6 Hz, 1 H, C=CHC$_6$H$_4$OCH$_2$C$_6$H$_5$); ^{13}C NMR (100 MHz, CDCl$_3$) δ 18.55, 18.63, 21.16, 21.19, 29.23, 29.31, 32.72, 32.86, 46.76, 65.94, 70.00, 71.79, 73.67, 82.04, 115.24, 121.41, 127.34, 127.42, 127.63, 127.83, 128.10, 128.39, 128.59, 131.81, 136.23, 136.37, 137.22, 160.01, 171.28, 174.25; FAB-MS (*m*/*z*, relative intensity) 571 (MH$^+$, 9), 91 (100). Anal. (C$_{36}$H$_{42}$O$_6$·0.3H$_2$O$_6$) C, H.

General Procedure for the Synthesis of XII. Procedure L. Boron trichloride (3 equiv) was added slowly to a stirring solution of **XI** (1 equiv) in dichloromethane (20 mL/mmol of **XI**) at −78 °C. The reaction was monitored by TLC, and upon completion, the reaction mixture was slowly quenched with a saturated aqueous NaHCO$_3$ solution, diluted with dichloromethane (20 mL/mmol of **XI**), and warmed to room temperature. The layers were separated, and the aqueous layer was further extracted with dichloromethane (2×). The combined organics were dried over MgSO$_4$ and concentrated in vacuo. Purification by silica gel flash column chromatography gave **XII**.

(*Z*)-{2-(Hydroxymethyl)-4-[4-methyl-3-(methylethyl)pentylidene]-5-oxo-2,3-dihydrofur-2-yl}methyl 2-Hydroxybenzoate ((*Z*)-11, (*Z*)-XII, R^1 = 2-(OH)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$). According to general procedure L, (*Z*)-**XI** (R^1 = 2-(PhCH$_2$O)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$; 109 mg, 0.40 mmol) was reacted to give (*Z*)-**11** ((*Z*)-**XII**, R^1 = 2-(HO)C$_6$H$_4$, R^2 = CH$_2$CH(*i*-Pr)$_2$; 32 mg, 43% yield) as a white solid: mp 60 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.85, 0.86, 0.89, and 0.90 (d, J = 6.8 Hz, 12 H, C=CHCH$_2$CH-(CH(CH_3)$_2$)$_2$), 1.10 (p, J = 5.6 Hz, 1 H, C=CHCH$_2$CH(CH-(CH$_3$)$_2$)$_2$), 1.77 irregular septet, 2 H, C=CHCH$_2$CH(CH(CH$_3$)$_2$)$_2$), 2.25 (t, J = 6.1 Hz, 1 H, CCH$_2$OH), 2.59−2.67 (m, 1 H, C=CHCHHCH(CH(CH$_3$)$_2$)$_2$), 2.74−2.85 (m, 2 H, H-3$_a$ and C=CHCHHCH(CH(CH$_3$)$_2$)$_2$), 2.95 (ddd, J = 16.6, 5.0, 2.5 Hz, 1 H, H-3$_b$), 3.72 (br dd, J = 12.1, 5.8 Hz, 1 H, CCHHOH), 3.80 (br dd, J = 12.1, 5.8 Hz, 1 H, CCHHOH), 4.49 (AB m, 2 H, CCH_2-OC(O)C$_6$H$_4$OH), 6.29 (tt, J = 7.4, 2.2 Hz, 1 H, C=CHCH$_2$CH-(CH(CH$_3$)$_2$)$_2$), 6.85−6.89 (m, 1 H, CCH$_2$OC(O)C$_6$$H_4$OH), 6.98 (dd, J = 8.7, < 1 Hz, 1 H, CCH$_2$OC(O)C$_6$$H_4$OH), 7.45−7.49 (m, 1 H, CCH$_2$OC(O)C$_6$$H_4$OH), 7.74 (dd, J = 8.0, 1.7 Hz, 1 H, CCH$_2$OC-

(O)C_6H_4OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.33, 19.46, 21.57, 21.65, 26.36, 29.29, 29.37, 33.25, 51.13, 64.83, 65.98, 82.18, 111.62, 117.74, 119.38, 122.38,129.87, 136.27, 148.18, 161.79 168.59,169.62; FAB-MS (*m*/*z*, relative intensity) 391 (MH^+, 30), 121 (100). Anal. ($C_{22}H_{30}O_6$) C, H.

(*Z*)-{2-(Hydroxymethyl)-4-[4-methyl-3-(methylethyl)pentylidene]-5-oxo-2,3-dihydrofur-2-yl}methyl 3-Hydroxybenzoate ((*Z*)-12, (*Z*)-XII, R^1 = 3-(OH)C_6H_4, R^2 = $CH_2CH(i\text{-}Pr)_2$). According to general procedure L, (*Z*)-**XI** (R^1 = 3-($PhCH_2O$)C_6H_4, R^2 = $CH_2CH(i\text{-}Pr)_2$; 140 mg, 0.25 mmol) was reacted to give (*Z*)-**12** ((*Z*)-**XII**, R^1 = 3-(OH)C_6H_4, R^2 = $CH_2CH(i\text{-}Pr)_2$; 40 mg, 40% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81 and 0.83 (d, J = 6.8 Hz, 6 H, C=CHCH_2CH(CH(CH_3)$_2$)$_2$), 0.87 (t, J = 6.8 Hz, 6 H, C=CHCH_2CH(CH(CH_3)$_2$)$_2$), 1.10 (p, J = 5.5 Hz, 1 H, C=CHCH_2C*H*(CH(CH_3)$_2$)$_2$), 1.75 (m, 2 H, C=CHCH_2-CH(C*H*(CH_3)$_2$)$_2$), 2.59−2.65 (m, 1 H, C=CHC*H*HCH(CH(CH_3)$_2$)$_2$), 2.70−2.82 (m, 2 H, C=CHCH*H*CH(CH(CH_3)$_2$)$_2$ and H-3$_a$), 2.96 (dm, J = 16.4 Hz, 1 H, H-3$_b$), 3.09 (br s, 1 H CCH_2OH), 3.75 (br dd, J = 12.1, 4.3 Hz, 1 H, CC*H*HOH), 3.82 (br dd, J = 12.1, 4.3 Hz, 1 H, CCH*H*OH), 4.45 (AB q, J = 11.9 Hz, 2 H, CCH_2OC-(O)C_6H_4OH), 6.27 (irregular tt, 1 H, C=C*H*CH_2CH(CH(CH_3)$_2$)$_2$), 6.69 (s, 1 H, $CCH_2OC(O)C_6H_4OH$), 7.09 (ddd, 1 H, J = 8.1, 2.5, 0.9 Hz, $CCH_2OC(O)C_6H_4$OH), 7.29 (dd, J = 8.4, 7.4 Hz, 1 H, $CCH_2OC(O)C_6H_4$OH), 7.49−7.54 (m, 2 H, $CCH_2OC(O)C_6H_4$OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.27, 19.44, 21.53, 21.62, 26.38, 29.24, 29.35, 33.32, 51.09, 64.60, 65.98, 82.98, 116.32, 120.92, 121.87, 122.53, 129.78, 130.30, 148.42, 156.12, 166.23, 169.58; FAB-MS (*m*/*z*, relative intensity) 391 (MH^+, 63), 121 (100). Anal. ($C_{22}H_{30}O_6$) C, H.

(*E*)-{2-(Hydroxymethyl)-4-[4-methyl-3-(methylethyl)pentylidene]-5-oxo-2,3-dihydrofur-2-yl}methyl 4-Hydroxybenzoate ((*E*)-13, (*E*)-XII, R^1 = 4-(OH)C_6H_4, R^2 = $CH_2CH(i\text{-}Pr)_2$). According to general procedure L, (*E*)-**XI** (R^1 = 4-($PhCH_2O$)C_6H_4, R^2 = $CH_2CH(i\text{-}Pr)_2$; 230 mg, 0.40 mmol) was reacted to give (*E*)-**13** ((*E*)-**XII**, R^1 = 4-(HO)C_6H_4, R^2 = $CH_2CH(i\text{-}Pr)_2$; 93 mg, 60% yield) as a white solid: mp 117−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.78, 0.81, 0.84, and 0.87 (d, J = 6.8 Hz, 12 H, C=CHCH_2CH(CH(CH_3)$_2$)$_2$), 1.16 (p, J = 5.6 Hz, 1 H, C=CHCH_2C*H*(CH(CH_3)$_2$)$_2$), 1.73 (m, 2 H, C=CHCH_2CH-(C*H*(CH_3)$_2$)$_2$), 2.05−2.15 (m, 2 H, C=CHCH_2CH(CH(CH_3)$_2$)$_2$), 2.76 (dd, J = 17.3, 2.4 Hz, 1 H, H-3$_a$), 2.92 (dd, J = 17.3, 2.4 Hz, 1 H, H-3$_b$), 3.07 (br s, 1 H, CCH_2OH), 3.79 (AB q, J = 12.2 Hz, 2 H, CCH_2OH), 4.45 (AB q, J = 12.0 Hz, 2 H, C$CH_2OC(O)C_6H_4$-OH), 6.81−6.87 (m, 3 H, $CCH_2OC(O)C_6H_4$OH and C=C*H*CH_2-CH(CH(CH_3)$_2$)$_2$), 7.50 (br s, 1 H, $CCH_2OC(O)C_6H_4OH$), 7.80 (d, J = 8.8 Hz, 2 H, $CCH_2OC(O)C_6H_4$OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.27, 21.42, 21.60, 28.76, 29.08, 29.18, 30.08, 50.25, 64.57, 65.76, 84.05, 115.45, 120.75, 124.82, 132.05, 144.81, 161.15, 166.22, 171.05; FAB-MS (*m*/*z*, relative intensity) 391 (MH^+, 60), 121 (100). Anal. ($C_{22}H_{30}O_6$·0.5H_2O) C, H.

(*Z*)-{2-(Hydroxymethyl)-4-[4-methyl-3-(methylethyl)pentylidene]-5-oxo-2,3-dihydrofur-2-yl}methyl 4-Hydroxybenzoate ((*Z*)-13, (*Z*)-XII, R^1 = 4-(OH)C_6H_4, R^2 = $CH_2CH(i\text{-}Pr)_2$). According to general procedure L, (*Z*)-**XI** (R^1 = 4-($PhCH_2O$)C_6H_4, R^2 = $CH_2CH(i\text{-}Pr)_2$; 148 mg, 0.26 mmol) was reacted to give (*Z*)-**13** ((*Z*)-**XII**, R^1 = 4-(HO)C_6H_4, R^2 = $CH_2CH(i\text{-}Pr)_2$; 60 mg, 58% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84, 0.85, 0.88, and 0.89 (d, J = 6.8 Hz, 12 H, C=CHCH_2CH(CH-(CH_3)$_2$)$_2$), 1.10 (p, J = 5.5 Hz, 1 H, C=CHCH_2C*H*(CH(CH_3)$_2$)$_2$), 1.76 (m, 2 H, C=CHCH_2CH(C*H*(CH_3)$_2$)$_2$), 2.59−2.68 (m, 1 H, H-3$_a$), 2.72−2.82 (m, 2 H, H-3$_b$ and C=CHC*H*HCH(CH(CH_3)$_2$)$_2$), 2.97 (ddd, J = 16.6, 4.8, 2.4 Hz, 1 H, C=CHCH*H*CH(CH(CH_3)$_2$)$_2$), 3.74 (AB q, J = 12.2 Hz, 2 H, CCH_2OH), 4.43 (AB q, J = 12.0 Hz, 2 H, C$CH_2OC(O)C_6H_4$OH), 6.30 (tt, J = 7.5, 2.2 Hz, 1 H, C=C*H*CH_2CH(CH(CH_3)$_2$)$_2$), 6.84 (m, 2 H, $CCH_2OC(O)C_6H_4$OH), 7.01 (br s, 1 H, $CCH_2OC(O)C_6H_4OH$), 7.84 (m, 2 H, CCH_2OC-(O)C_6H_4OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.32, 19.43, 21.56, 21.62, 26.42, 29.27, 29.33, 33.32, 51.09, 64.40, 65.50, 83.06, 115.44, 120.92, 122.48, 132.09, 148.61, 161.02, 166.28, 169.66; FAB-MS (*m*/*z*, relative intensity) 391 (MH^+, 53), 121 (100). Anal. ($C_{22}H_{30}O_6$) C, H.

(*E*)-[2-(Hydroxymethyl)-5-oxo-4-(3-phenylpropylidene)-2,3-dihydrofur-2-yl]methyl 4-Methyl-3-(methylethyl)pentanoate ((*E*)-16, (*E*)-XII, R^1 = $CH_2CH(i\text{-}Pr)_2$, R^2 = $PhCH_2CH_2$). According to general procedure L, (*E*)-**XI** (R^1 = $CH_2CH(i\text{-}Pr)_2$, R^2 = $PhCH_2CH_2$; 104 mg, 0.22 mmol) was reacted to give (*E*)-**14** ((*E*)-**XII**, R^1 = $CH_2CH(i\text{-}Pr)_2$, R^2 = $PhCH_2CH_2$; 61 mg, 68% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.80 and 0.89 (d, J = 6.64 Hz, 12 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 1.57 (p, J = 5.80 Hz, 1 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 1.73 (m, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 2.18 (d, J = 5.8 Hz, CCH_2-$OC(O)CH_2CH(CH(CH_3)_2)_2$), 2.42−2.53 (m, 3 H, C=CHCH_2-$CH_2C_6H_5$ and H-3$_a$), 2.61 (dm, $J \approx$ 16 Hz, 1 H, H-3$_b$), 2.80 (t, J = 7.4 Hz, C=CHC$H_2CH_2C_6H_5$), 3.58 (AB q, J = 12.3 Hz, 2 H, CCH_2-OH), 4.13 (AB q, J = 11.9 Hz, 2 H, C$CH_2OC(O)CH_2CH$(CH-$(CH_3)_2)_2$), 6.74 (m, 1 H, C=C$HCH_2CH_2C_6H_5$), 7.14−7.32 (m, 5 H, C=$CHCH_2CH_2C_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.64, 18.69, 21.28, 21.30, 29.29, 29.34, 29.63, 32.13, 32.73, 34.12, 46.85, 64.10, 65.28, 83.06, 126.29, 126.92, 128.40, 128.50, 140.19, 140.48, 169.70, 174.62; FAB-MS (*m*/*z*, relative intensity) 403 (MH^+, 100). Anal. ($C_{24}H_{34}O_5$) C, H.

(*E*)-{2-(Hydroxymethyl)-4-[(2-methoxyphenyl)methylene]-5-oxo-2,3-dihydrofur-2-yl}methyl 4-Methyl-3-(methylethyl)pentanoate ((*E*)-17, (*E*)-XII, R^1 = $CH_2CH(i\text{-}Pr)_2$, R^2 = 2-(MeO)C_6H_4). According to general procedure L, (*E*)-**XI** (R^1 = CH_2CH-$(i\text{-}Pr)_2$, R^2 = 2-(MeO)C_6H_4; 790 mg, 1.6 mmol) was reacted to give (*E*)-**17** ((*E*)-**XII**, R^1 = $CH_2CH(i\text{-}Pr)_2$, R^2 = 2-(MeO)C_6H_4; 474 mg, 75% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.74, 0.77, 0.84, and 0.85 (d, J = 6.8 Hz, 12 H, $CCH_2OC(O)CH_2$-$CH(CH(CH_3)_2)_2$), 1.54 (p, $J \approx$ 5.7 Hz, 1 H, $CCH_2OC(O)$-$CH_2CH(CH(CH_3)_2)_2$), 1.69 (septet, $J \approx$ 6.5 Hz, 2 H, $CCH_2OC(O)$-$CH_2CH(CH(CH_3)_2)_2$), 2.17 (dd, J = 5.8, 1.3 Hz, 2 H, $CCH_2OC(O)$-$CH_2CH(CH(CH_3)_2)_2$), 2.34 (br s,1 H, CCH_2OH), 2.97 (dd, J = 17.6, 2.8 Hz, 1 H, H-3$_a$), 3.12 (dd, J = 17.6, 3.0 Hz, 1 H, H-3$_b$), 3.70 (br dd, J = 12.9, 4.7 Hz, 1 H, CC*H*HOH), 3.78 (br dd, J = 12.9, 4.7 Hz, 1 H, CCH*H*OH), 3.87 (s, 1 H, C=$CHC_6H_4OCH_3$), 4.26 (AB q, J = 11.9 Hz, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 6.93 (d, J = 8.3 Hz, 1 H, C=$CHC_6H_4OCH_3$), 6.99 (t, J = 7.9 Hz, 1 H, C=$CHC_6H_4OCH_3$), 7.35−7.43 (m, 2 H, C=$CHC_6H_4OCH_3$), 8.02 (t, J = 2.9 Hz, 1 H, C=C*H*$C_6H_4OCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.65, 21.22, 29.32 32.29, 32.78, 46.83, 55.50, 64.81, 65.48, 83.14, 111.01, 120.39, 123.43, 123.45, 129.02, 131.56, 132.10, 158.50, 171.21, 174.74; FAB-MS (*m*/*z*, relative intensity) 405 (MH^+, 100), 57 (23). Anal. ($C_{30}H_{38}O_6$) C, H.

(*E*)-{2-(Hydroxymethyl)-4-[(3-methoxyphenyl)methylene]-5-oxo-2,3-dihydrofur-2-yl}methyl 4-Methyl-3-(methylethyl)pentanoate ((*E*)-18, (*E*)-XII, R^1 = $CH_2CH(i\text{-}Pr)_2$, R^2 = 3-(MeO)C_6H_4). According to general procedure L, (*E*)-**18** ((*E*)-**XII** R^1 = $CH_2CH(i\text{-}Pr)_2$, R^2 = 3-(MeO)C_6H_4; 222 mg, 0.45 mmol) was reacted to give (*E*)-**XII** ((*E*)-**18**, R^1 = $CH_2CH(i\text{-}Pr)_2$, R^2 = 3-(MeO)-C_6H_4; 140 mg, 77% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.72, 0.75, (d, J = 6.8 Hz, 6 H, $CCH_2OC(O)CH_2CH$-$(CH(CH_3)_2)_2$), 0.81, 0.83 (s, 6 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 1.51 (p, $J \approx$ 5.7 Hz, 1 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 1.67 (septet, $J \approx$ 6.5 Hz, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 2.15 (d, J = 5.7 Hz, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 2.80 (s, 1 H, CCH_2OH), 3.03 (dd, J = 17.7, 2.6 Hz, 1 H, H-3$_a$), 3.23 (dd, J = 17.7, 2.6 Hz, 1 H, H-3$_b$), 3.72 (br t, 2 H, CCH_2OH), 3.82 (s, 1 H, C=$CHC_6H_4OCH_3$), 4.25 (AB q, J = 12.0 Hz, 2 H, CCH_2OC-(O)$CH_2CH(CH(CH_3)_2)_2$), 6.94 (dd, J = 8.2, 1.9 Hz, 1 H, C=$CHC_6H_4OCH_3$), 6.99 (s, 1 H, C=$CHC_6H_4OCH_3$), 7.07 (d, J = 6.8 Hz, 1 H, C=$CHC_6H_4OCH_3$), 7.34 (t, J = 7.9 Hz, 1 H, C=$CHC_6H_4OCH_3$), 7.53 (br t, 1 H, C=C*H*$C_6H_4OCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.63, 21.20, 29.27, 32.12, 32.74, 46.84, 55.30, 64.69, 65.50, 83.54, 115.48, 115.59, 122.49, 124.53, 129.87, 135.60, 137.03, 159.76, 171.20, 174.61; FAB-MS (*m*/*z*, relative intensity) 405 (MH^+, 100), 57 (76). Anal. ($C_{30}H_{38}O_6$) C, H.

(*E*)-{2-(Hydroxymethyl)-4-[(4-methoxyphenyl)methylene]-5-oxo-2,3-dihydrofur-2-yl}methyl 4-Methyl-3-(methylethyl)pentanoate ((*E*)-19, (*E*)-XII, R^1 = $CH_2CH(i\text{-}Pr)_2$, R^2 = 4-(MeO)C_6H_4). According to general procedure L, (*E*)-**XI** (R^1 = CH_2CH-$(i\text{-}Pr)_2$, R^2 = 4-(MeO)C_6H_4; 100 mg, 0.2 mmol) was reacted to

give (*E*)-**19** ((*E*)-**XII**, $R^1 = CH_2CH(i\text{-}Pr)_2$, $R^2 = 4\text{-}(MeO)C_6H_4$; 50 mg, 60%) as a white powder: mp 97−99 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.75, 0.77, 0.84, 0.85 (d, $J = 6.8$ Hz, 12 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 1.55 (p, $J = 5.8$ Hz, 1 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 1.70 (sept, $J \approx 6.6$ Hz, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 2.18 (d, $J = 5.8$ Hz, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 2.21 (t, $J = 6.9$ Hz, 1 H, CCH_2OH), 3.01 (dd, $J = 17.5$, 2.8 Hz, 1 H, H-3_a), 3.18 (dd, $J = 17.5$, 2.8 Hz, 1 H, H-3_b), 3.72 (dd, $J = 12.1$, 6.8 Hz, 2 H, $CCHHOH$), 3.78 (dd, $J = 12.1$, 6.8 Hz, 2 H, $CCHHOH$), 3.86 (s, 1 H, $C{=}CHC_6H_4OCH_3$), 4.27 (AB q, $J = 11.9$ Hz, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 6.94−6.98 (m, 2 H, $C{=}CHC_6H_4OCH_3$), 7.44−7.48 (m, 2 H, $C{=}CHC_6H_4OCH_3$), 7.53 (t, $J = 2.8$ Hz, 1 H, $C{=}CHC_6H_4OCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.68, 21.26, 29.33, 32.26, 32.79, 46.87, 61.11, 64.90, 65.48, 83.05, 114.47, 120.93, 127.15, 131.97, 137.18, 161.10, 161.76, 174.76; FAB-MS (*m*/*z*, relative intensity) 405 (MH^+, 41), 57 (100). Anal. ($C_{30}H_{38}O_6 \cdot 0.1H_2O$) C, H.

(*E*)-{2-(Hydroxymethyl)-4-[(2-hydroxyphenyl)methylene]-5-oxo-2,3-dihydrofur-2-yl}methyl 4-Methyl-3-(methylethyl)pentanoate ((*E*)-20, (*E*)-XII, $R^1 = CH_2CH(i\text{-}Pr)_2$, $R^2 = 2\text{-}(OH)C_6H_4$). According to general procedure L, (*E*)-**XI** ($R^1 = CH_2CH(i\text{-}Pr)_2$, $R^2 = 2\text{-}(PhCH_2O)C_6H_4$; 430 mg, 0.75 mmol) was reacted to give (*E*)-**20** ((*E*)-**XII**, $R^1 = CH_2CH(i\text{-}Pr)_2$, $R^2 = 2\text{-}(HO)C_6H_4$; 130 mg, 44% yield) as a yellow foam: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.74, 0.76, 0.83, and 0.84 (d, $J = 6.8$ Hz, 12 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 1.54 (p, $J = 5.8$ Hz, 1 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 1.69 (m, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 1.94 (br s, 1 H, CCH_2OH), 2.18 (d, $J = 5.8$ Hz, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 2.93 (br s, 1 H, $C{=}CHC_6H_4OH$), 3.00 (dd, $J = 17.6$, 2.8 Hz, 2 H, H-3_a), 3.19 (dd, $J = 17.6$, 2.9 Hz, 2 H, H-3_b), 3.75 (AB q, $J = 12.1$ Hz, 2 H, CCH_2OH), 4.26 (AB q, $J = 12.0$ Hz, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 6.89−6.92 (m, 2 H, $C{=}CHC_6H_4OH$), 7.22−7.28 (m, 1 H, $C{=}CHC_6H_4OH$), 7.36 (m, 1 H, $C{=}CHC_6H_4OH$), 8.11 (t, $J = 2.8$ Hz, 1 H, $C{=}CHC_6H_4OH$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.62, 18.68, 21.22, 21.24, 29.31, 32.23, 32.78, 46.90, 64.76, 65.44, 83.90, 116.45, 120.32, 121.67, 122.89, 129.01, 131.77, 132.84, 155.98, 172.61, 174.91; FAB-MS (*m*/*z*, relative intensity) 391 (MH^+, 66), 57 (100). Anal. ($C_{22}H_{30}O_6$) C, H.

(*E*)-{2-(Hydroxymethyl)-4-[(3-hydroxyphenyl)methylene]-5-oxo-2,3-dihydrofur-2-yl}methyl 4-Methyl-3-(methylethyl)pentanoate ((*E*)-21, ((*E*)-XII, $R^1 = CH_2CH(i\text{-}Pr)_2$, $R^2 = 3\text{-}(OH)C_6H_4$). According to general procedure L, (*E*)-**XI** ($R^1 = CH_2CH(i\text{-}Pr)_2$, $R^2 = 3\text{-}(PhCH_2O)C_6H_4$; 360 mg, 0.63 mmol) was reacted to give (*E*)-**21** ((*E*)-**XII**, $R^1 = CH_2CH(i\text{-}Pr)_2$, $R^2 = 3\text{-}(HO)C_6H_4$; 146 mg, 59% yield) as a white solid: mp 45−47 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.72 and 0.74 (d, $J = 6.8$ Hz, 6 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 0.81 (d, $J = 6.8$ Hz, 6 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 1.53 (p, $J = 5.8$ Hz, 1 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 1.67 (septet, $J = 6.7$ Hz, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 2.18 (d, $J = 5.7$ Hz, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 3.00 (dd, $J = 17.9$, 2.7 Hz, 1 H, H-3_a), 3.25 (dd, $J = 17.9$, 2.7 Hz, 1 H, H-3_b), 3.50 (br t, 1 H, CCH_2OH), 3.72 (br dd, $J \approx 11.6$, 4.0 Hz, 1 H, $CCHHOH$), 3.82 (br dd, $J \approx 11.6$, 4.0 Hz, 1 H, $CCHHOH$), 4.25 (AB q, $J = 12.0$ Hz, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 6.88−7.00 (m, 3 H, $C{=}CHC_6H_4OH$), 7.22−7.28 (m, 4 H, $C{=}CHC_6H_4OH$), 7.47 (t, $J = 2.6$ Hz, 1 H, $C{=}CHC_6H_4OH$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.59, 18.66, 21.20, 21.22, 29.28 32.12, 32.79, 46.93, 64.59, 65.58, 83.97, 116.74, 117.55, 122.47, 124.12, 130.06, 135.48, 137.44, 156.38, 172.01, 175.02; FAB-MS (*m*/*z*, relative intensity) 391 (MH^+, 100), 57 (100). Anal. ($C_{22}H_{30}O_6$) C, H.

(*E*)-{2-(Hydroxymethyl)-4-[(4-hydroxyphenyl)methylene]-5-oxo-2,3-dihydrofur-2-yl}methyl 4-Methyl-3-(methylethyl)pentanoate ((*E*)-22, (*E*)-XII, $R^1 = CH_2CH(i\text{-}Pr)_2$, $R^2 = 4\text{-}(OH)C_6H_4$). According to general procedure L, (*E*)-**XI** ($R^1 = CH_2CH(i\text{-}Pr)_2$, $R^2 = 4\text{-}(PhCH_2O)C_6H_4$; 200 mg, 0.35 mmol) was reacted to give (*E*)-**22** ((*E*)-**XII**, $R^1 = CH_2CH(i\text{-}Pr)_2$, $R^2 = 4\text{-}(HO)C_6H_4$; 81 mg, 60% yield) as a white foam: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.74 and 0.76 (d, $J = 6.8$ Hz, 6 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 0.83 (d, $J = 6.8$ Hz, 6 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 1.55 (p, $J = 5.8$ Hz, 1 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 1.70 (irregular septet, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 2.20 (d, $J = 5.8$ Hz, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 2.98 (dd, $J = 17.5$, 2.6 Hz, 1 H, H-3_a), 3.19 (dd, $J = 17.5$, 2.6 Hz, 1 H, H-3_b), 3.45 (br t, $J = 5.7$ H, 1 H, CCH_2OH), 3.74 (dd, $J = 12.2$, 6.0 Hz, 1 H, $CCHHOH$), 3.86 (dd, $J = 12.2$, 6.0 Hz, 1 H, $CCHHOH$), 4.29 (AB q, $J = 11.9$ Hz, 2 H, $CCH_2OC(O)CH_2CH(CH(CH_3)_2)_2$), 6.87 (d, $J = 8.7$ Hz, 2 H, $C{=}CHC_6H_4OH$), 7.27 (d, $J = 8.9$ Hz, 2 H, $C{=}CHC_6H_4OH$), 7.43 (t, $J = 2.6$ Hz, 1 H, $C{=}CHC_6H_4OH$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.62, 18.68, 21.22, 21.25, 29.29, 31.17, 32.80, 46.92, 64.78, 65.56, 83.66, 116.08, 120.39, 126.59, 132.29, 137.58, 158.22, 172.37, 175.00; FAB-MS (*m*/*z*, relative intensity) 391 (MH^+, 100), 57 (73). Anal. ($C_{22}H_{30}O_6 \cdot 0.2H_2O$) C, H.

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Supporting Information Available: Combustion analysis results for compounds **III**−**VI**, and **IX**, **XI**−**XII** and ^{1}H and ^{13}C NMR spectra of compounds **1**−**22**. This material is available free of charge via the Internet at http://pubs.acs.org.

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