Highly Substituted α-Silylated Cyclopentanones from Ethyl Levulinate: An Entry to a Methylenomycin B Analog

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The transformation of α-diphenylmethylsilylated ethyl levulinate acetal, 1, to a series of α-silylated cyclopentanones has been studied. The approach was based on a three-step process in which 1 was initially transformed into α-(diphenylmethylsilyl)-γ-(ethylenedioxy) ketones by its reaction with Grignard reagents. A novel highly substituted 2,3-dihydrofuran was also obtained as a secondary product. Deprotonation–trimethylsilylation of these ketones under kinetic conditions produced 3-silylated-2-silyl enol ethers in a regio- and stereoselective manner. The *Z* isomer was shown to predominate. These enol ethers were stereoselectively transformed into α-silylated cyclopentanones by a $TiCl_4$-promoted intramolecular Mukaiyama reaction. The geometry of the silyl enol ethers determined the stereochemistry of the cyclic ketone products, and the integrity of the diphenylmethylsilyl group was maintained. A methylenomycin B analog was prepared in one pot from one of the polyfunctional ketones by means of a β-alkoxy elimination followed by a Peterson-type α-methylenation with formaldehyde. This analog, 3-methyl-5-methylene-2-(2-phenylethyl)-2-cyclopenten-1-one, 12, showed in vitro cytotoxicity against CHO-K1 cells.

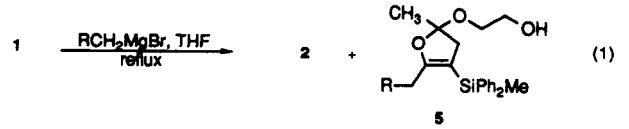
The synthetic utility of α-silyl ketones has only been recently explored. These compounds have been shown to be useful in highly regio- and stereoselective entries to alkenes,[1] silyl enol ethers,[2] and others.[3] They cannot be directly prepared from ketones in one step because of the high oxophilicity of silicon.[4] Some of the more important previous approaches for their preparation have included the oxidation of β-hydroxysilanes,[5] the Lewis acid catalyzed rearrangement of α,β-epoxysilanes,[6] and the reaction of esters or other derivatives with silicon-containing organometallic reagents.[7] A 1,3 oxygen to carbon silyl rearrangement of an enol ether has also been employed in the case of bulky trialkylsilyl groups.[8] The discovery by Larson and Fuentes that the silylation of esters with diphenylmethylchlorosilane could lead to C-silylation rather than O-silylation has made a large variety of α-silyl esters readily available.[9] These intermediates were also shown to react with a single equivalent of a Grignard reagent to produce β-keto silanes.[10]

The intramolecular Mukaiyama reaction[11] has been used as an entry to important cyclic systems.[12] Usually, the enol silyl ether is prepared via the conjugate addition of a ketal-containing organocuprate to an enone. This produces a regiocontrolled enolate that can be trapped with a silylating agent. Treatment of the resulting enol ether with a Lewis acid yields the cyclized product under mild nonbasic conditions in an irreversible and stereoselective fashion.

Along these lines we have worked out a sequence in which β-keto silanes **2a–f** can be transformed into highly substituted α-silylated cyclopentanones **4a–f** as illustrated in Scheme I. The key aspect of this transformation is the regiospecific preparation of enol silyl ethers **3a–f**, which in turn cyclize to the cycloalkanones under Lewis acid catalysis. The role of the diphenylmethylsilyl moiety is 3-fold. First, it controls the regioselectivity of the formation of the enol silyl ether. In addition, it influences the stereoselectivity of the cyclization, and finally it forms part of the product, which is an α-silylated cyclic ketone that can be further transformed.

Results and Discussion

The requisite α-(diphenylmethylsilyl)-γ-(ethylenedioxy) ketones, **2a–f** were prepared by the modification of the procedure of Larson et al.[13] (eq 1). The readily available



C-silylated ethyl levulinate acetal 1 was reacted with several Grignard reagents to yield the α-silylated monoprotected diketones. The results are summarized in Table I. Some Grignard double addition product was observed

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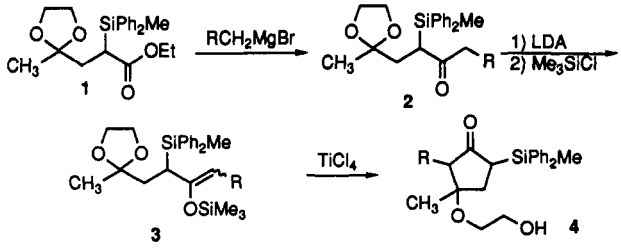
Scheme I



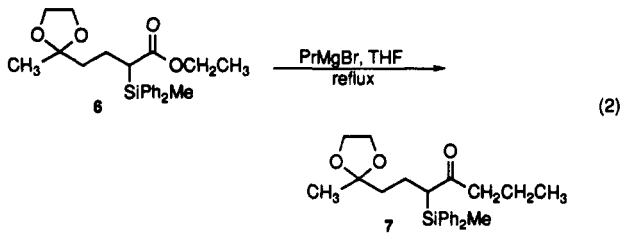
R = Et-, Bu-, iPr-, allyl, $CH_2{=}CH(CH_2)_2$-, $Ph(CH_2)_2$-

Table I. Reaction of Grignard Reagents with 1

reagent	ketone	yield[a]	ether	yield[a]
$CH_3(CH_2)_2MgBr$	**2a**	87		8[b]
$CH_3(CH_2)_4MgBr$	**2b**	70	**5b**	26
$(CH_3)_2CHCH_2MgBr$	**2c**	33	**5c**	33
$CH_2{=}CH(CH_2)_2MgBr$	**2d**	68	**5d**	17
$CH_2{=}CH(CH_2)_3MgBr$	**2e**	70	**5e**	26
$Ph(CH_2)_3MgBr$	**2f**	63	**5f**	27

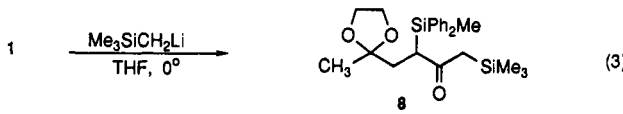
[a] Percent, isolated. [b] Double addition product.

when the *n*-propyl reagent was used. In addition, the yield dropped (ketone **2c**) when the more hindered isobutyl reagent was used. A novel highly substituted 2,3-dihydrofuran **5b–f**, which was easily separated by flash chromatography, was also obtained as a secondary product. When the homologous ethyl 2-(diphenylmethylsilyl)-4-acetylbutyrate ethylene ketal (**6**) was reacted in the same manner with *n*-propylmagnesium bromide, a 73% yield of ketone **7** was obtained (eq 2) and no six-membered cyclic



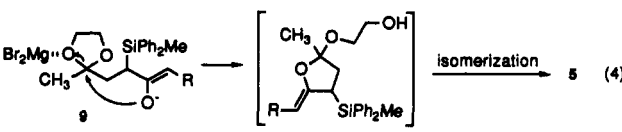
(2)

ether could be observed. Despite the fact that alkyllithium reagents promote double addition when reacted with α-silylated esters,[1] the reaction of **1** with [(trimethylsilyl)-methyl]lithium produced 36% of the bis(silyl) ketone **8** with 40% starting material recovered (eq 3). In this case as well the formation of a cyclic ether could not be detected.



(3)

It is known that Grignard reagents in solution exist in equilibrium with dialkylmagnesium and magnesium dihalide (Schlenk equilibrium).[14] Since enolate **9** is formed by excess Grignard reagent,[2] the magnesium bromide could then activate the ketal oxygen and provide the driving force for the formation of **5**. This is shown in eq 4. The



(4)

absence of the corresponding 2,3-dihydrofuran when the trimethylsilyl lithium reagent was used would favor this proposed role for $MgBr_2$.

Table II. Preparation of TMS Enol Ethers 3a–f

R group	product	yield[a]	*Z*:*E* ratio[b]	δ silyl C *Z*:*E*[c]
CH_3CH_2–	**3a**	97	79:21	25.3, 30.4
$CH_3(CH_2)_3$–	**3b**	99	80:20	25.4, 30.1
$(CH_3)_2CH$–	**3c**	99	93:7	25.4, 30.1
$CH_2{=}CHCH_2$–	**3d**	96	78:22	25.4, 30.6
$CH_2{=}CH(CH_2)_2$–	**3e**	94	82:18	25.2, 30.2
$Ph(CH_2)_2$–	**3f**	93	95:5	25.5, 30.4

[a] Percent, isolated. [b] Determined by ^1H NMR or GC analysis. [c] ppm.

The infrared carbonyl stretching absorption for β-keto silanes **2a–f** ranged from 1689 to 1694 cm^{-1}. The ^1H NMR spectra showed that the α-(diphenylmethylsilyl) methine protons in **2a–f** resonate between 2.90 and 3.10 ppm. Due to the presence of diastereotopic and overlapping resonances, the complete assignments of the proton and carbon NMR spectra required the assistance of two-dimensional techniques. For example, in **2e** we observed a correlation for the diasterotopic β methylene alkyl protons at δ 1.38 and 1.12 ppm. A correlation between these protons and their carbon at δ 21.9 ppm was found. An attached proton test (APT)[15] for this compound allowed the distinction between the ketal methyl at δ 23.3 and the C(7) methylene carbon at δ 21.9 ppm. The majority of these compounds demonstrated nonequivalency in the ^{13}C NMR for the phenyls attached to silicon giving rise to separate carbon signals for each ring.

The kinetic TMS enol ethers **3a–f** were prepared by LDA deprotonation at 0 °C followed by the addition of trimethylchlorosilane. This regiospecific transformation effectively yielded *Z*/*E* isomer mixtures. These yields along with some pertinent spectral data are summarized in Table II. Although superior selectivity could be obtained at lower temperatures and with more hindered bases, such conditions could lower the yield. It is noteworthy that the *Z* isomer is the major product, since the *E* isomer should be favored under these reaction conditions.[16] The finding that the (diphenylmethylsilyl)-alkyl-containing group inverts the stereoselectivity is consistent with the observation of Heathcock et al. that the *E*/*Z* selectivity is affected by the size of the alkyl groups.[17]

^1H NMR has been widely used to establish the geometry of trisubstituted enol ethers based on the vinyl proton resonances.[16] This proton usually resonates at a lower field for the *E* relative to the *Z* isomer. This method for ascertaining stereochemistry is not always conclusive. This is particularly true when the differences in chemical shift become less pronounced due to the bulk of the alkyl groups. This effect and the complications produced by signal overlapping were the case for enol ethers **3a–f**. However, the ^{13}C NMR resonances for the allylic diphenylmethylsilylated carbons allowed the unambiguous determination of the geometry of the double bond. As shown in Table II, a Δδ of approximately 5 ppm is consistently observed and is typical for the allylic carbons.[17] The *E* silyl enol ethers resonate at lower field, ca. 25.2–25.5 vs 30.1–30.6 ppm for the *Z* isomers.

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Table III. Preparation of Silylated Cyclopentanones 4a–f

R group	ketone	yield[a]	ratio[b]
CH_3CH_2–	**4a**	70	74:26
$CH_3(CH_2)_3$–	**4b**	66	82:18
$(CH_3)_2CH$–	**4c**	40	100:0
CH_2=$CHCH_2$–	**4d**	64	80:20
CH_2=$CH(CH_2)_2$–	**4e**	62	79:21
$Ph(CH_2)_2$–	**4f**	70	75:13:12

[a] Percent, isolated. [b] Diastereomeric ratio determined by ^1H NMR.

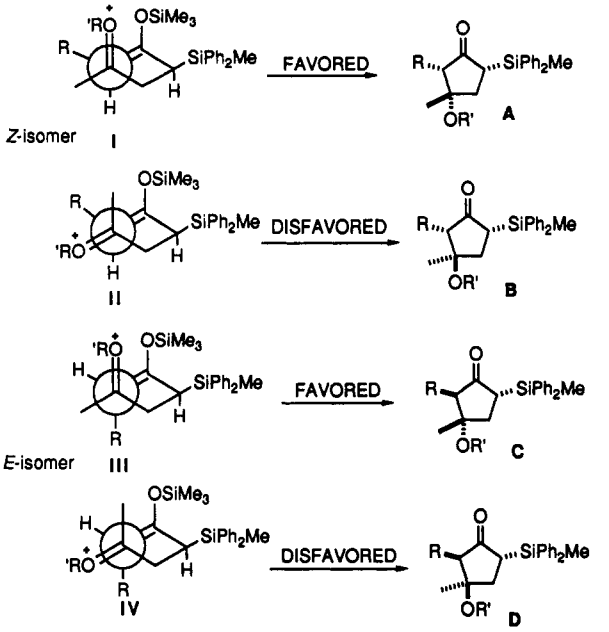
The proton NMR assignments for enol ethers **3a–f** also required the assistance of 2D techniques. As a typical example, the C,H COSY spectrum of **3e** permitted the proper correlation between the diastereomeric methylene protons adjacent to the ketal moiety. The signals at δ 1.66 and 2.13 ppm for these protons correlate with the carbon at δ 35.1 ppm. The carbon signal at δ 26.7 ppm correlates with the protons at δ 2.04 and 1.77 ppm. The correlation of these protons with the internal vinyl proton at 5.67 ppm is observed on the COSY spectra.

Silyl enol ethers **3a–f** were subjected to an intramolecular Mukaiyama cyclization process. These systems have an internal ketal and a silyl enol ether with the proper arrangement for Lewis acid promoted annulation. Thus, the addition of titanium tetrachloride in dichloromethane at −78 °C to these compounds produced the desired cycloalkanones **4a–f**. As summarized in Table III the isolated yields were good and high diastereoselectivities were observed. Again, a lower yield was obtained for the branched ketone **4c**. In general, the reactions required short periods for completion and the diphenylmethylsilyl group always remained intact. However, desilylation was found to occur at longer reaction times. For example, if **3e** was reacted under these conditions for 3.5 h, a ratio of 3:1 for the desilylated vs silylated cyclopentanones was observed, whereas at 1.5 h the silylated cyclopentanone could be isolated in 62% yield.

Comparison of Tables II and III in terms of the *Z*/*E* isomeric ratio for enol ethers **3a–f** with the corresponding diastereoisomeric ratio of cyclopentanones **5a–f** shows their dependence on the initial geometry of the silyl enol ethers. To gain some insight into this, we examined the diastereomeric ratio for an *E*-enriched silyl enol ether.[18] Thus, a 36:64 *Z*/*E* mixture of **3a** was cyclized under identical conditions to give two isomeric ketones **5a** in a 37:63 ratio. Separation and characterization of both isomers showed them to be spectroscopically identical to that obtained initially (Table III). This time the previously called minor isomer was more abundant. These results imply a high stereoselectivity in the cyclization reaction.[19]

In order to gain some insight into the stereochemistry of the products, the NOESY spectra of cyclopentanones **4a**, **4c**, and **4e** was obtained. In the case of **4c**, for example, a clear dipolar interaction between the C(3) methyl at δ 1.37 ppm and both the C(2) and C(5) α protons at δ 2.71 and 1.99 ppm, respectively, was observed. Also, both protons had similar dipolar interactions with each other. Comparable results were observed for the major components of **4a** and **4c**. On the basis of these observations, we concluded that the C(3) methyl and the protons at C(2) and C(5) are located on the same face of the ring (see compound **A**, Scheme II).

Scheme II



Similarly, a NOESY analysis was performed on the minor isomer of **5a**. Again a clear dipolar interaction between the C(3) methyl at 1.32 ppm and the C(5) α proton at 2.58 ppm was observed. This time no correlation was found between the C(3) methyl and the C(2) α proton at 1.73 ppm as on the previous systems. These results allowed us to conclude that on this diastereomer the C(3) methyl and the C(5) proton are on the same face while the C(2) proton now occupies the opposite face of the molecule (see compound **C**, Scheme II). Furthermore, this isomer showed a ^{13}C NMR signal for the C(3) methyl at 19.1 ppm. An examination of other minor isomers shows the same chemical shift for this carbon. All of the major isomers showed the equivalent signal between 23.3 and 24.2 ppm. This finding suggest a trans relationship between the methyl and ethyl groups of the minor isomers while a cis relationship exists for the major ones.[20] This is also in agreement with the proposed stereochemical relationship of the products.

The stereoselectivity observed here can be interpreted in terms of the four possible transition states illustrated in Scheme II. The oxyphilic titanium tetrachloride can drive the reaction through an oxocarbenium ion intermediate.[21] The *Z* enol ether should react via transition state **I** or **II**. Isomer **A** should predominate since transition state **I** has the topology for which the sequential coordination of the strong Lewis acid to both oxygens prior to the carbon–carbon bond formation leads to a gauche arrangement between the enol and the electrophile.[22] Accordingly, and for the same reason, the *E* isomer would

(18) Attempts to equilibrate the lithium enolate with HMPA to improve the ratio of the *E* isomer produced considerable desilylation of the diphenylmethylsilyl group. Consequently, the reaction was carried out using LDA prepared in hexane containing 15% THF (Munchhof, M. J.; Heathcock, C. H. *Tetrahedron Lett.* **1992**, 8005). A change in the *Z*/*E* ratio from 79:21 to 36:64 is in agreement with the observation that increased concentration of hexane can dramatically change and even invert the *Z*/*E* ratio on the preparation of lithium enolates.

(19) Enol ether **3c** is again an exception. In this case, the bulky isopropyl group only allows the cyclopentanone **4c** to form in a 40% yield. However, only a single diastereomer is observed. Interestingly, the preparation of ketone **4f** produced a major diastereomer along with two minor ones.

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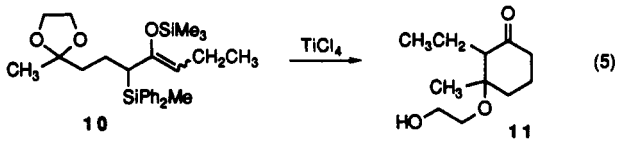
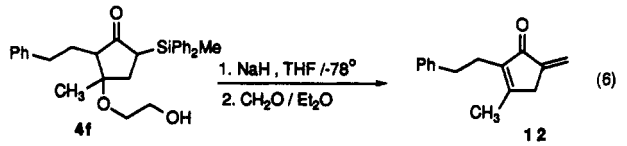
favor transition states **III** over transition state **IV** producing stereoisomer **C**. The application of the Kocienski nomenclature for intramolecular Mukaiyama reactions allows the classification of this annulation process as a 5-exo$_e$,endo$_n$.[21,23]

When the higher homolog **10** was reacted under the same conditions, a 51% of the desilylated cyclohexanone **11** with a 93:7 diastereomeric ratio was obtained (eq 5).



(5)

In order to explore the utility of this methodology, we transformed **4f** into a methylenomycin B antibiotic[24] analog. This "one-pot" transformation is shown in eq 6.



(6)

One equiv of NaH produced a β-alkoxy elimination of **4f** to give an α-(diphenylmethylsilyl)cyclopentenone. An additional equivalent of base followed by the addition of formaldehyde promoted a Peterson-type olefination[25] of this product yielding compound **12**. This compound is a benzyl-derivatized methylenomycin B analog which exhibited in vitro cytotoxicity with an ED_{50} value of 2.05 μg/mL against CHO-K1 cells.

Conclusions

We have demonstrated that highly substituted α-silylated cyclopentanones can be prepared by an intramolecular Mukaiyama reaction. The diphenylmethylsilyl group efficiently directs the regiochemistry of the TMS enol ether formation and controls the stereoselectivity of the key cyclization step. These α-silylated cyclopentanones can be further transformed into other interesting systems as exemplified by the preparation of a methylenomycin B analog.

Experimental Section

General. All reactions were carried out on a three-necked, round-bottom flask equipped with nitrogen inlet, magnetic bar, rubber septum, reflux condenser, and dropping funnel. This standard apparatus was flame-dried under a stream of nitrogen and allowed to cool to room temperature. All solvents were purified before use. Hexane and THF were distilled from sodium benzophenone ketyl. Dichloromethane was distilled from CaH_2. Esters **1** and **6** were prepared by the procedure of Larson et al.[13] Flash chromatography was performed as described by Still using Kieselgel 60 (230–400 mesh)[26] but with a cold-jacketed column (0 °C). Unless otherwise noted all compounds purified by chromatography were sufficiently pure (by ^{1}H NMR analysis) for use in subsequent reactions. Melting points are uncorrected. Infrared spectra were recorded neat using sodium chloride cells with either a Perkin-Elmer 283 or a Nicolet 6000 Series FT-IR spectrophotometer and are recorded in cm^{-1}. Chemical ionization mass spectra were measured with either a Hewlett-Packard 5995A or a Hewlett-Packard 5971A gas chromatography/mass spectrometers and were recorded as m/z (percent relative intensity). ^{1}H-NMR (300 MHz) and ^{13}C-NMR spectra (75 MHz) were recorded with either a General Electric QE-300 or a GN-300 spectrometer as solutions in deuterochloroform and are recorded in ppm with respect to tetramethylsilane. Analytical GC was carried out using either a Perkin-Elmer Sigma 1B gas chromatograph with a thermal conductivity detector, a Perkin-Elmer 8320, or a Varian 3300 capillary gas chromatograph with flame ionization detector.

General Procedure for the Preparation of 2,2-(Ethylenedioxy)-4-(diphenylmethylsilyl)alkanones. The standard apparatus was charged with 4 equiv of a Grignard solution in THF. The system was cooled with an ice–water bath and the silyl ester in THF added dropwise. The reaction mixture was refluxed for 72 h and cooled to 0 °C followed by the addition of moist ether. Cold water was added, and the heavy emulsion was slowly broken by continuous addition of cold water and pentane. The combined aqueous phase was back-extracted with pentane (2 × 25 mL) and the combined organic layer dried over anhyd sodium sulfate (5 min). After filtration, the solvent was removed at reduced pressure and the product purified by low-temperature flash chromatography.

7,7-(Ethylenedioxy)-5-(diphenylmethylsilyl)-4-octanone (2a) and 7,7-(Ethylenedioxy)-4-propyl-4-octanol. Following the general procedure, 1.93 g (5 mmol) of **1** was reacted with 21.7 mL (20 mmol) of a 0.92 M solution of propylmagnesium bromide. Low-temperature flash chromatography (ethyl acetate/pentane (10:90)) gave 1.67 g (87%) of ketone **2a**: IR (neat) 1689, 1244 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.59 (m, 2 H), 7.48 (m, 2 H), 7.37 (m, 6 H), 3.88–3.82 (m, 4 H), 3.07 (d, J = 11.2 Hz, 1 H), 2.59 (dd, J = 11.2, 14.4 Hz, 1 H), 2.09 (m, 1 H), 1.77 (m, 1 H), 1.73 (d, J = 14.5 Hz, 1 H), 1.23 (s, 3 H), 1.22 (m, 2 H), 0.62 (s, 3 H), 0.62 (t, J = 7.4 Hz, 3 H); ^{13}C-NMR ($CDCl_3$) δ 211.1, 134.8, 134.3, 129.8, 128.1, 128.0, 110.0, 64.5, 46.7, 41.0, 36.7, 23.7, 16.7, 13.6, –6.3. Anal. Calcd for $C_{23}H_{30}O_3Si$: C, 72.21; H, 7.90. Found: C, 72.08; H, 7.93. Also, 0.1 g (8%) of 7,7-(ethylenedioxy)-4-propyl-4-octanol was obtained: IR (neat) 3479 (OH) cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.94 (m, 4 H), 1.88 (br s, variable on dilution, 1 H), 1.70 (m, 2 H), 1.52 (m, 2 H), 1.38 (m, 4 H), 1.33 (s, 3 H), 1.31 (m, 4 H), 0.91 (t, J = 6.9 Hz, 6 H); ^{13}C-NMR ($CDCl_3$) δ 110.1, 73.7, 64.5, 41.6, 32.9, 32.7, 23.7, 16.7, 14.6; MS, m/z (rel intensity) 197 (7), 187 (38), 143 (39), 125 (19), 87 (100), 73 (14).

2,2-(Ethylenedioxy)-4-(diphenylmethylsilyl)-5-decanone (2b) and 5-(2-Hydroxyethoxy)-5-methyl-3-(diphenylmethylsilyl)-2-pentyl-2-oxacyclopentene (5b). Following the general procedure, 1.93 g (5 mmol) of **1** was reacted with 22.5 mL (20 mmol) of a 0.89 M solution of pentylmagnesium bromide. Low-temperature flash chromatography (ethyl acetate/pentane (10:90)) gave 1.44 g (70%) of ketone **2b**: IR (neat) 1693, 1254 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.47 (m, 2 H), 7.37 (m, 2 H), 7.21 (m, 6 H), 3.73–3.64 (m, 4 H), 2.99 (d, J = 10.8 Hz, 1 H), 2.49 (dd, J = 11.2, 14.4 Hz, 1 H), 1.99 (m, 1 H), 1.65 (m, 1 H), 1.63 (d, J = 14.2 Hz, 1 H), 1.27 (m, 1 H), 1.11 (s, 3 H), 1.08 (m, 2 H), 1.01 (m, 1 H), 0.84 (m, 2 H), 0.66 (t, J = 7.2 Hz, 3 H), 0.51 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 210.9, 134.5, 134.0, 129.5, 127.8, 127.7, 109.6, 64.2, 44.4, 40.7, 36.4, 31.0, 23.5, 22.6, 22.1, 13.6, –6.6. Anal. Calcd for $C_{25}H_{34}O_3Si$: C, 73.13; H, 8.35. Found: C, 73.07; H, 8.40. Also, 0.54 g (26%) of compound **5b** was obtained: IR (neat) 3440, 1630, 1251 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.51 (m, 4 H), 7.36 (m, 6 H), 3.70 (m, 2 H), 3.59 (m, 2 H), 2.67 (d, J = 16.3 Hz, 1 H), 2.61 (d, J = 16.4 Hz, 1 H), 2.26 (br s, 1 H, variable on dilution), 1.88 (t, J = 7.7 Hz, 2 H), 1.55 (s, 3 H), 1.32 (m, 2 H), 1.10 (m, 2 H), 1.00 (m, 2 H), 0.78 (t, J = 7.2 Hz, 3 H), 0.64 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 165.0, 136.5, 134.6, 129.1, 127.7, 109.4, 96.4, 63.4, 61.8, 44.9, 31.3, 28.7, 27.1, 25.3, 22.1, 13.8, –2.8. Anal. Calcd for $C_{25}H_{34}O_3Si$: C, 73.13; H, 8.35. Found: C, 72.98; H, 8.37.

7,7-(Ethylenedioxy)-2-methyl-5-(diphenylmethylsilyl)-4-octanone (2c) and 5-(2-Hydroxyethoxy)-2-isobutyl-5-methyl-3-(diphenylmethylsilyl)-2-oxacyclopentene (5c). Following the general procedure, 3.85 g (10 mmol) of **1** was reacted with 48.2 mL (40 mmol) of a 0.83 M solution of 2-methylpropylmagnesium bromide. Low-temperature flash chromatography (ethyl acetate/pentane (10:90)) gave 1.29 g (33%) of **2c**: IR (neat) 1693,

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1256 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.47 (m, 2 H), 7.42 (m, 2 H), 7.21 (m, 6 H), 3.72–3.63 (m, 4 H), 2.93 (d, J = 10.8 Hz, 1 H), 2.49 (dd, J = 11.1, 14.4 Hz, 1 H), 1.96 (dd, J = 6.6, 17.5 Hz, 1 H), 1.87–1.77 (m, 1 H), 1.66–1.58 (m, 1 H), 1.63 (d, J = 14.5 Hz, 1 H), 1.11 (s, 3 H), 0.67 (d, J = 6.6 Hz, 3 H), 0.52 (s, 3 H), 0.46 (d, J = 6.7 Hz, 3 H); ^{13}C-NMR ($CDCl_3$) δ 210.5, 134.7, 134.2, 129.7, 128.0, 109.9, 64.4, 53.5, 40.7, 36.5, 23.7, 23.1, 22.6, 22.4, –6.5. Anal. Calcd for $C_{24}H_{32}O_3Si$: C, 72.68; H, 8.13. Found: C, 72.60; H, 8.13. Also, 1.29 g (32.5%) of compound **5c** was obtained: mp 62.0–63.0 °C; IR (neat) 3430, 1628, 1254 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.50 (m, 4 H), 7.37 (m, 6 H), 3.71 (m, 2 H), 3.61 (m, 2 H), 2.67 (d, J = 16.4 Hz, 1 H), 2.59 (d, J = 16.3 Hz, 1 H), 2.10 (br s, variable on dilution, 1 H), 1.78 (s, 2 H), 1.77 (m, 1 H), 1.55 (s, 3 H), 0.70 (d, J = 5.8 Hz, 6 H), 0.65 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 164.0, 136.6, 134.8, 129.2, 127.8, 109.5, 97.7, 63.5, 62.0, 45.4, 37.3, 26.7, 25.2, 22.2, –2.6. Anal. Calcd for $C_{24}H_{32}O_3Si$: C, 72.68; H, 8.13. Found: C, 72.78; H, 8.17.

2,2-(Ethylenedioxy)-4-(diphenylmethylsilyl)-8-nonen-5-one (2d) and 2-(3-Butenyl)-5-(2-hydroxyethoxy)-5-methyl-3-(diphenylmethylsilyl)-2-oxacyclopentene (5d). Following the general procedure, 1.15 g (3 mmol) of **1** was reacted with 14.3 mL (12 mmol) of a 0.84 M solution of 3-butenylmagnesium bromide. The product was purified by low-temperature flash chromatography (ethyl acetate/pentane (35:65)) yielding 0.81 g (68%) of ketone **2d**: IR (neat) 1694, 1642, 1254 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.58 (m, 2 H), 7.47 (m, 2 H), 7.37 (m, 6 H), 5.52 (m, 1 H), 4.82 (d, J = 0.8 Hz, 1 H), 4.77 (m, 1 H), 3.88 (m, 2 H), 3.82 (m, 2 H), 3.09 (d, J = 10.9 Hz, 1 H), 2.59 (dd, J = 11.3, 14.4 Hz, 1 H), 2.19 (m, 1 H), 2.15 (m, 1 H), 1.86 (m, 1 H), 1.83 (m, 1 H), 1.75 (d, J = 14.4 Hz, 1 H), 1.23 (s, 3 H), 0.63 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 210.4, 138.8, 134.7, 134.0, 133.9, 129.8, 128.1, 128.0, 114.4, 109.8, 64.5, 64.5, 43.8, 40.9, 36.6, 27.4, 23.7, –6.5. Anal. Calcd for $C_{24}H_{30}O_3Si$: C, 73.06; H, 7.66. Found: C, 73.18; H, 7.68. Also, 0.20 g (17%) of compound **5d** was obtained: IR (neat) 3444, 1632, 1241 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.51 (m, 4 H), 7.34 (m, 6 H), 5.53 (m, 1 H), 4.84 (br s, 1 H), 4.80 (d, J = 0.5 Hz, 1 H), 3.68 (m, 2 H), 3.59 (m, 2 H), 2.68 (d, J = 16.4 Hz, 1 H), 2.59 (d, J = 16.4 Hz, 1 H), 2.19 (br s, variable on dilution, 1 H), 2.10 (m, 2 H), 1.99 (br d, J = 7.0 Hz, 2 H), 1.54 (s, 3 H), 0.64 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 163.9, 137.4, 136.5, 134.7, 129.2, 128.1, 128.0, 127.8, 114.8, 109.6, 97.2, 63.5, 62.0, 45.2, 31.5, 28.3, 25.3, –2.8. Anal. Calcd for $C_{24}H_{30}O_3Si$: C, 73.06; H, 7.66. Found: C, 72.95; H, 7.69.

2,2-(Ethylenedioxy)-4-(diphenylmethylsilyl)-9-decen-5-one (2e) and 5-(2-Hydroxyethoxy)-5-methyl-3-(diphenylmethylsilyl)-2-(4-pentenyl)-2-oxacyclopentene (5e). Following the general procedure, 3.08 g (8 mmol) of **1** was reacted with 39.5 mL (32 mmol) of a 0.81 M solution of 4-pentenylmagnesium bromide. Low-temperature flash chromatography (ethyl acetate/pentane (30:70)) gave 2.29 g (70%) of ketone **2e**: IR (neat) 1692, 1640, 1254 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.46 (m, 2 H), 7.34 (m, 2 H), 7.20 (m, 6 H), 5.43 (m, 1 H), 4.72 (m, 2 H), 3.67 (m, 4 H), 2.98 (d, J = 11.0 Hz, 1 H), 2.48 (dd, J = 11.3, 14.2 Hz, 1 H), 2.00 (m, 1 H), 1.70 (m, 1 H), 1.66 (m, 1 H), 1.61 (m, 2 H), 1.38 (m, 1 H), 1.12 (m, 1 H), 1.08 (s, 3 H), 0.50 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 210.4, 137.8, 134.3, 133.6, 129.3, 127.7, 127.5, 114.1, 109.5, 64.0, 64.0, 43.4, 40.4, 36.2, 32.5, 23.3, 21.9, –6.9. Anal. Calcd for $C_{25}H_{32}O_3Si$: C, 73.49; H, 7.89. Found: C, 73.52; H, 7.90. Also, 0.85 g (26%) of compound **5e** was obtained: IR (neat) 3435, 1630, 1252 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.41 (m, 4 H), 7.27 (m, 6 H), 5.47 (m, 1 H), 4.77 (dd, J = 1.3, 8.7 Hz, 1 H), 4.72 (br s, 1 H), 3.59 (m, 2 H), 3.48 (m, 2 H), 2.58 (d, J = 16.4 Hz, 1 H), 2.51 (d, J = 16.3 Hz, 1 H), 2.33 (br s, variable on dilution, 1 H), 1.79 (t, J = 7.8 Hz), 2 H, 1.67 (q, J = 7.1 Hz, 2 H), 1.45 (s, 3 H), 1.33 (m, 2 H), 0.54 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 164.7, 138.0, 136.5, 134.7, 129.2, 127.8, 114.5, 109.5, 96.8, 63.5, 62.0, 45.2, 33.3, 28.3, 26.8, 25.3, –2.8. Anal. Calcd for $C_{25}H_{32}O_3Si$: C, 73.49; H, 7.89. Found: C, 73.57; H, 7.91.

7,7-(Ethylenedioxy)-5-(diphenylmethylsilyl)-1-phenyl-4-octanone (2f) and 5-(2-Hydroxyethoxy)-5-methyl-3-(diphenylmethylsilyl)-2-(3-phenylpropyl)-2-oxacyclopentene (5f). Following the general procedure, 2.31 g (6 mmol) of **1** was reacted with 26.4 mL (24 mmol) of a 0.91 M solution of 3-phenylpropylmagnesium bromide. Low-temperature flash chromatography (ethyl acetate/pentane (12:88)) gave 1.74 g (63%) of ketone **2f**: IR (neat) 1694, 1254 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.58 (m, 2 H), 7.50–7.11 (m, 11 H), 7.03 (d, J = 7.0 Hz, 2 H), 3.88–3.70 (m, 4 H), 3.06 (d, J = 11.1 Hz, 1 H), 2.58 (dd, J = 11.3, 14.4 Hz, 1 H), 2.29 (t, J = 7.5 Hz, 2 H), 2.12 (m, 1 H), 1.82 (m, 1 H), 1.74 (d, J = 14.8 Hz, 1 H), 1.69 (m, 1 H), 1.48 (m, 1 H), 1.22 (s, 3 H), 0.62 (S, 3 H); ^{13}C-NMR ($CDCl_3$) δ 209.9, 141.5, 134.2, 133.6, 129.2, 127.9, 127.7, 127.6, 127.5, 127.4, 125.1, 109.2, 63.8, 43.4, 40.3, 36.3, 34.6, 24.3, 23.2, –6.9. Anal. Calcd for $C_{29}H_{34}O_3Si$: C, 75.94; H, 7.47. Found: C, 75.85; H, 7.53. Also, 0.74 g (27%) of compound **5f** was obtained: IR (neat) 3444, 1631, 1252 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.50 (m, 3 H), 7.38 (m, 6 H), 7.19 (m, 4 H), 7.01 (d, J = 6.9 Hz, 2 H), 3.70 (m, 2 H), 3.58 (m, 2 H), 2.68 (d, J = 16.4 Hz, 1 H), 2.61 (d, J = 16.4 Hz, 1 H), 2.28 (t, J = 7.9 Hz, 2 H), 2.12 (br s, variable on dilution, 1 H), 1.93 (t, J = 7.6 Hz, 2 H), 1.63 (m, 2 H), 1.55 (s, 3 H), 0.60 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 164.5, 141.7, 136.4, 134.6, 129.1, 128.1, 127.7, 125.5, 109.5, 96.8, 63.4, 61.8, 45.0, 35.4, 29.2, 28.5, 25.2, –3.0. Anal. Calcd for $C_{29}H_{34}O_3Si$: C, 75.94; H, 7.47. Found: C, 75.99; H, 7.53.

8,8-(Ethylenedioxy)-5-(diphenylmethylsilyl)-4-nonanone (7). Following the general procedure, 6.0 g (15 mmol) of **6** was reacted with 65.2 mL of a 0.92 M solution of propylmagnesium bromide. Low-temperature flash chromatography (ethyl acetate/pentane (10:90)) gave 4.34 g (73%) of the title ketone: IR (neat) 1688, 1254 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.58 (m, 2 H), 7.50 (m, 2 H), 7.36 (m, 6 H), 3.93–3.75 (m, 4 H), 2.98 (dd, J = 2.0, 11.3 Hz, 1 H), 2.13 (m, 1 H), 1.99 (m, 1 H), 1.80 (m, 1 H), 1.69–1.41 (m, 2 H), 1.54 (m, 1 H), 1.55–1.12 (m, 2 H), 1.21 (s, 3 H), 0.65 (s, 3 H), 0.63 (t, J = 7.4 Hz, 3 H); ^{13}C-NMR ($CDCl_3$) δ 21.6, 134.7, 134.3, 134.6, 134.5, 129.5, 127.9, 127.8, 109.5, 64.3, 64.2, 47.1, 46.3, 39.2, 23.3, 22.1, 16.7, 13.4, –6.3. Anal. Calcd for $C_{24}H_{32}O_3Si$: C, 72.68; H, 8.13. Found: C, 72.50; H, 8.18.

5,5-(Ethylenedioxy)-3-(diphenylmethylsilyl)-1-(trimethylsilyl)-2-hexanone (8). The standard apparatus was charged with 6.0 mL (6.6 mmol) of 1.1 M [(trimethylsilyl)methyl]lithium in hexane and cooled to 0 °C. Then, 1.16 g (3.0 mmol) of **1** in 3.0 mL of THF was added dropwise. The mixture was stirred overnight and then quenched with sodium sulfate decahydrate. The reaction mixture was poured into diethyl ether (25 mL) and cold water (50 mL), and the layers were separated. The aqueous layer was back-extracted with ethyl acetate (2 × 15 mL), the combined organic layers were dried over anhydrous sodium sulfate and filtered, and the solvent was removed at reduced pressure. Low-temperature flash chromatography (ethyl acetate/pentane (5:95–50:50)) gave 0.46 g (36%) of **8**: IR (neat) 1669, 1251 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.54 (m, 4 H), 7.33 (m, 6 H), 3.76 (m, 4 H), 3.01 (d, J = 10.0 Hz, 1 H), 2.62 (dd, J = 10.1, 14.4 Hz, 1 H), 1.74 (d, J = 12.3 Hz, 1 H), 1.56 (d, J = 15.9 Hz, 1 H), 1.55 (d, J = 12.1 Hz, 1 H), 1.21 (s, 3 H), 0.62 (s, 3 H), 0.02 (s, 9 H); ^{13}C-NMR ($CDCl_3$) δ 208.1, 134.5, 134.5, 134.3, 129.3, 129.1, 127.7, 127.6, 109.4, 63.9, 63.9, 43.0, 38.5, 35.0, 23.4, –1.2, –5.9. Anal. Calcd for $C_{24}H_{34}O_3Si_2$: C, 67.56; H, 8.03. Found: C, 67.38; H, 8.12.

General Procedure for the Preparation of 2,2-(Ethylenedioxy)-4-(diphenylmethylsilyl)-5-[(trimethylsilyl)oxy]-alkenes. A 0.75 M LDA solution in THF was cooled by means of an ice–water bath, and 0.5 equiv of the ketone in THF (0.5 M solution) was added dropwise. The solution was stirred at 0 °C for 3 h and the enolate quenched with chlorotrimethylsilane in THF (0.5 M solution). It was allowed to reach 25 °C overnight. The solvent was removed at reduced pressure, and dry hexane was added. The LiCl precipitate formed was removed by filtration (Celite/glass wool) under an atmosphere of nitrogen. The solvent was again removed at reduced pressure. The crude was relatively pure (^{1}H and ^{13}C NMR analysis) and was used immediately.

7,7-(Ethylenedioxy)-5-(diphenylmethylsilyl)-4-[(trimethylsilyl)oxy]-3-octene (3a). Following the general procedure, 1 mmol of LDA, 0.19 g (0.5 mmol) of **2a** in THF (1 mL), and 0.11 g (1.0 mmol) of chlorotrimethylsilane in 2.0 mL of THF was used. After workup, 0.22 g (97%) of a 79:21 Z/E mixture of **3a** was obtained. The crude was immediately used without further purification. Z isomer: IR (neat) 1654, 1252 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.60 (m, 2 H), 7.50 (m, 2 H), 7.32 (m, 6 H), 4.19 (m, 1 H), 3.87–3.69 (m, 3 H), 3.61–3.54 (m, 1 H), 2.75 (dd, J = 1.3, 10.9 Hz, 1 H), 2.11 (dd, J = 10.9, 14.3 Hz, 1 H), 1.91 (m, 1 H), 1.70 (m, 1 H), 1.72–1.52 (m, 1 H), 1.30, (s, 3 H), 0.72 (t, J = 7.4 Hz, 3 H), 0.57 (s, 3 H), 0.11 (s, 9 H); ^{13}C-NMR ($CDCl_3$) δ 150.9, 136.7, 136.7, 135.4, 135.0, 127.6, 127.4, 111.0, 105.5, 64.4, 64.2, 35.1, 25.3, 23.9, 20.7, 14.8, 0.2, –5.0. When the solvent was changed

to 15% THF in hexane a 36:64 *Z/E* ratio was obtained. *E* isomer: ^{13}C-NMR ($CDCl_3$) δ 150.4, 136.4, 136.0, 135.2, 135.1, 129.0, 128.8, 111.7, 107.6, 64.5, 64.2, 36.3, 30.4, 2406, 19.6, 14.4, 0.2, −4.7.

2,2-Ethylenedioxy-4-(diphenylmethylsilyl)-5-[(trimethylsilyl)oxy]-5-decene (3b). Following the general procedure, 4 mmol of LDA, 0.82 g (2.0 mmol) of **2b** in THF (4 mL), and 0.43 g (4.0 mmol) of chlorotrimethylsilane in 8.0 mL of THF were used. After workup, 0.96 g (99.7%) of a 80:20 *Z/E* mixture of **3b** was obtained. The crude was immediately used without further purification: IR (neat) 1649, 1254 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.59 (m, 2 H), 7.49 (m, 2 H), 7.30 (m, 6 H), 4.24 (t, *J* = 6.9 Hz, 1 H), 3.82–3.73 (m, 2 H), 3.72–3.67 (m, 1 H), 3.59–3.52 (m, 1 H), 2.73 (d, *J* = 10.8 Hz, 1 H), 2.13 (dd, *J* = 11.0, 14.4 Hz, 1 H), 1.90 (m, 1 H), 1.73 (m, 1 H), 1.67 (d, *J* = 14.3 Hz, 1 H), 1.30 (s, 3 H), 1.21 (m, 2 H), 1.15 (m, 2 H), 0.81 (t, *J* = 7.1 Hz, 3 H), 0.57 (s, 3 H), 0.14 (s, 9 H); ^{13}C-NMR ($CDCl_3$) δ 151.1, 136.6, 135.9, 135.1, 134.9, 129.0, 128.9, 127.5, 127.3, 110.9, 103.6, 64.3, 64.1, 34.9, 32.5, 27.0, 25.2, 23.8, 22.4, 14.0, 0.2, −5.1; ^{13}C-NMR (diagnostic signals for minor isomer) δ 150.4, 110.6, 105.7, 64.5, 64.1, 36.1, 32.1, 30.3, 26.0, 24.6, 22.4, 14.0, −4.8.

7,7-(Ethylenedioxy)-2-methyl-5-(diphenylmethylsilyl)-4-[(trimethylsilyl)oxy]-3-octene (3c). Following the general procedure, 1.6 mmol of LDA, 0.32 g (0.8 mmol) of **2c** in THF (1.6 mL), and 0.17 g (1.6 mmol) of chlorotrimethylsilane in 3.2 mL of THF were used. After workup, a quantitative yield of a 93:7 *Z/E* mixture of **3c** was obtained. The crude was immediately used without further purification: IR (neat) 1648, 1253 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.60 (m, 2 H), 7.50 (m, 2 H), 7.31 (m, 6 H), 4.09 (d, *J* = 9.5 Hz, 1 H), 3.82 (m, 2 H), 3.70 (m, 1 H), 3.57 (m, 1 H), 2.73 (d, *J* = 1.1, 10.8 Hz, 1 H), 2.27 (m, 1 H), 2.08 dd, *J* = 10.6, 14.0 Hz, 1 H), 1.64 (d, *J* = 14.0 Hz, 1 H), 1.32 (s, 3 H), 0.91 (d, *J* = 6.6 Hz, 3 H), 0.57 (s, 3 H), 0.48 (d, *J* = 6.6 Hz, 3 H), 0.17 (s, 9 H); ^{13}C-NMR (CDCl) δ 149.7, 136.7, 136.0, 135.3, 135.1, 129.0, 128.9, 127.6, 127.4, 112.0, 110.8, 64.2, 35.4, 27.1, 25.4, 23.9, 23.9, 0.30, −4.8; ^{13}C-NMR (diagnostic signals for minor isomer) δ 113.7, 64.5, 36.4, 30.1, 23.5, −4.7.

8,8-(Ethylenedioxy)-6-(diphenylmethylsilyl)-5-[(trimethylsilyl)oxy]-1,4-nonadiene (3d). Following the general procedure, 1.4 mmol of LDA, 0.28 g (0.7 mmol) of **2d** in THF (1.4 mL), and 0.15 g (1.4 mmol) of chlorotrimethylsilane in 2.8 mL of THF were used. After workup, 0.31 g (96%) of a 78:22 *Z/E* mixture of **3d** was obtained. The crude was immediately used without further purification: IR (neat) 1648, 1637, 1254 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.48 (m, 4 H), 7.34 (m, 6 H), 5.56 (m, 1 H), 4.89 (dd, *J* = 1.3, 18.4 Hz, 1 H), 4.82 (d, *J* = 9.4 Hz, 1 H), 4.26 (t, *J* = 7.2 Hz, 1 H), 3.82–3.69 (m, 3 H), 3.60–3.53 (m, 1 H), 2.78 (d, *J* = 10.8 Hz, 1 H), 2.66 (m, 1 H), 2.37 (m, 1 H), 2.14 (dd, *J* = 10.9, 14.2 Hz, 1 H), 1.69 (d, *J* = 14.3 Hz, 1 H), 1.29 (s, 3 H), 0.58 (s, 3 H), 0.14 (s, 9 H); ^{13}C-NMR ($CDCl_3$) δ 152.4, 138.1, 136.6, 136.1, 135.6, 135.2, 135.1, 135.0, 133.8, 129.4, 129.0, 129.0, 127.7, 127.6, 127.4, 113.8, 110.7, 100.9, 64.3, 64.2, 35.3, 31.8, 25.4, 24.0, 0.2, −5.0; ^{13}C-NMR (diagnostic signals for minor isomer) δ 151.7, 138.3, 114.5, 110.6, 102.9, 64.5, 36.5, 31.5, 30.6, 24.6, −4.7.

9,9-(Ethylenedioxy)-7-(diphenylmethylsilyl)-6-[(trimethylsilyl)oxy]-1,5-decadiene (3e). Following the general procedure, 2.2 mmol of LDA, 0.45 g (1.1 mmol) of **2e** in THF (12.2 mL), and 0.45 g (2.2 mmol) of chlorotrimethylsilane in 4.4 mL of THF were used. After workup, 0.50 g (94%) of a 82:18 *Z/E* mixture of **3e** was obtained. The crude was immediately used without further purification: IR (neat) 1648, 1640, 1251 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.59 (m, 2 H), 7.49 (m, 2 H), 7.30 (m, 6 H), 5.67 (m, 1 H), 4.94 (dd, *J* = 0.8, 13.2 Hz, 1 H), 4.88 (d, *J* = 10.5 Hz, 1 H), 4.23 (t, *J* = 6.5 Hz, 1 H), 3.81 (m, 2 H), 3.71 (m, 1 H), 3.58 (m, 1 H), 2.74, (d, *J* = 10.5 Hz, 1 H), 2.13 (dd, *J* = 11.0, 14.3 Hz, 1 H), 2.04 (m, 1 H), 1.82 (m, 2 H), 1.67 (m, 1 H), 1.66 (d, *J* = 14.3 Hz, 1 H), 1.29 (s, 3 H), 0.57 (s, 3 H), 0.13 (s, 9 H); ^{13}C-NMR ($CDCl_3$) δ 151.5, 138.6, 136.4, 135.8, 135.0, 134.8, 128.9, 128.8, 127.5, 127.3, 114.3, 110.6, 102.5, 64.1, 64.0, 35.1, 34.9, 25.2, 26.7, 23.8, 0.1, −5.2; ^{13}C-NMR (diagnostic signals for minor isomer) δ 150.9, 138.5, 114.1, 110.4, 104.6, 64.4, 36.1, 34.7, 30.2, 25.7, 24.6, −4.8.

7,7-(Ethylenedioxy)-5-(diphenylmethylsilyl)-1-phenyl-4-[(trimethylsilyl)oxy]-3-octene (3f). Following the general procedure, 3.6 mmol of LDA, 0.82 g (1.8 mmol) of **2f** in THF (3.6 mL), and 0.39 g (3.6 mmol) of chlorotrimethylsilane in 7.2 mL of THF were used. After workup, 0.89 g (93%) OF A 95:5 *Z/E* mixture of **3f** was obtained. The crude was immediately used without further purification: IR (neat) 1651, 1255 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.60 (m, 2 H), 7.51 (m, 2 H), 7.35–7.03 (m, 11 H), 4.23 (t, *J* = 6.7 Hz, 1 H), 3.78 (m, 2 H), 3.69 (m, 1 H), 3.55 (m, 1 H), 2.78 (dd, *J* = 1.0, 10.8 Hz, 1 H), 2.36 (m, 2 H), 2.26 (m, 1 H), 2.13 (dd, *J* = 10.9, 14.2 Hz, 1 H), 2.05 (m, 1 H), 1.67 (d, *J* = 14.1 Hz, 1 H), 1.27 (s, 3 H), 0.58 (s, 3 H), 0.11 (s, 9 H); ^{13}C-NMR ($CDCl_3$) δ 151.8, 142.4, 136.6, 135.9, 135.8, 135.3, 135.2, 135.0, 135.0, 129.1, 129.0, 128.9, 128.5, 128.3, 128.2, 128.1, 128.0, 127.6, 127.5, 127.4, 125.6, 110.8, 102.6, 64.3, 64.2, 36.5, 35.1, 25.5, 29.5, 23.9, 0.2, −5.1; ^{13}C-NMR (diagnostic signals for minor isomer) δ 151.2, 142.5, 125.9, 110.6, 104.8, 64.5, 36.2, 36.2, 35.3, 34.9, 34.4, 25.3, 29.3, 28.2, 24.6, 23.7, −4.9.

8,8-(Ethylenedioxy)-5-(diphenylmethylsilyl)-4-[(trimethylsilyl)oxy]-3-nonene (10). Following the general procedure, 4.0 mmol of LDA, 0.79 g (2.0 mmol) of **7** in THF (4 mL), and 0.43 g (4.0 mmol) of chlorotrimethylsilane in 8.0 mL of THF were used. After workup, 0.81 g (86%) of a 83:17 *Z/E* mixture of **10** was obtained. The crude was immediately used without further purification: IR (neat) 1649, 1251 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.55 (m, 2 H), 7.50 (m, 2 H), 7.31 (m, 6 H), 4.34 (t, *J* = 7.2 Hz), 1 H, 3.93–3.77 (m, 4 H), 2.39 (dd, *J* = 3.0, 11.6 Hz, 1 H), 1.91 (m, 2 H), 1.83 (m, 1 H), 1.74 (m, 1 H), 1.54 (m, 1 H), 1.53 (m, 1 H), 1.23 (s, 3 H), 0.77 (t, *J* = 7.5 Hz, 3 H), 0.58 (s, 3 H), 0.10 (s, 9 H); ^{13}C-NMR ($CDCl_3$) δ 150.6, 136.9, 136.7, 135.0, 134.8, 128.9, 128.8, 127.5, 127.3, 110.2, 107.1, 64.5, 64.4, 38.5, 29.7, 23.7, 21.9, 20.6, 15.1, 0.2, −4.9; MS *m/z* (relative intensity) 468 (M^+, 2), 198 (13), 197 (67), 195 (11), 155 (18), 119 (10), 111 (11), 110 (19), 109 (14), 105 (13), 99 (13), 97 (20), 96 (34), 87 (100); ^{13}C-NMR (diagnostic signals for minor isomer) δ 149.4, 110.1, 109.0, 38.7, 35.5, 23.8, 22.3, 19.4, 14.5, −4.7.

General Procedure for the Preparation 2-Alkyl-3-(2-hydroxyethoxy)-3-methyl-5-(diphenylmethylsilyl)cyclopentanones. The standard apparatus was charged with the enol silyl ether in CH_2Cl_2 (0.1 M solution). The solution was cooled by means of a dry ice/acetone bath, followed by a dropwise addition of a solution of $TiCl_4$ in CH_2Cl_2 (1.0 M, 1.2 equivalents). The mixture was stirred until the reaction was completed (TLC, 1–4 h) and then quenched with $NaHCO_3$. The reaction mixture was diluted with cold pentane (30 mL), rapidly washed with cold water (2 × 30 mL), and back-extracted with ethyl acetate (3 × 30 mL). The combined organic layers were dried over anhyd sodium sulfate and filtered. The solvent was removed at reduced pressure and the product purified by low-temperature flash chromatography.

2-Ethyl-3-(2-hydroxyethoxy)-3-methyl-5-(diphenylmethylsilyl)cyclopentanone (4a). Following the general procedure, 0.14 g (0.3 mmol) of **3a** in 3.0 mL of CH_2Cl_2 was reacted with 0.36 mL (0.36 mmol) of 1.0 M $TiCl_4$ in CH_2Cl_2 and stirred for 4 h. After low-temperature flash chromatography (ethyl acetate/pentane (15:85)), 0.08 g (70%) of **4a** was obtained as a 74:26 mixture of isomers. Major isomer: mp 79.0–80.5 °C; IR (neat) 3422, 1715, 1249 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.58 (m, 4 H), 7.38 (m, 6 H), 3.60 (s, 2 H), 3.29 (dt, *J* = 4.8, 9.4 Hz, 2 H), 2.70 (dt, *J* = 1.3, 9.3 Hz, 1 H), 2.16–2.00 (m, 2 H), 1.91 (dd, *J* = 4.4, 9.3 Hz, 1 H), 1.66–1.35 (m, 1 H), 1.23 (s, 3 H), 1.22 (br s, variable on dilution, 1 H), 1.07–0.76 (m, 1 H), 0.80 (t, *J* = 7.4 Hz, 3 H), 0.65 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 218.0, 135.8, 135.1, 135.0, 129.7, 129.5, 127.9, 127.8, 80.8, 63.4, 62.1, 60.3, 38.0, 35.3, 23.4, 16.9, 12.2, −4.4. Minor isomer: ^{1}H-NMR ($CDCl_3$) δ 7.58 (m, 4 H), 7.40 (m, 6 H), 3.61 (s, 2 H), 3.37 (m, 1 H), 3.28 (m, 1 H), 2.58 (t, *J* = 9.8 Hz, 1 H), 2.05 (m, 2 H), 1.74 (dd, *J* = 5.4, 7.6 Hz, 1 H), 1.63 (br s, variable on dilution, 1 H), 1.56 (m, 1 H), 1.25 (m, 1 H), 1.09 (s, 3 H), 0.90 (t, *J* = 7.4 Hz, 3 H), 0.66 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 215.9, 135.1, 134.9, 135.0, 129.8, 129.7, 127.9, 82.2, 62.8, 62.0, 60.3, 38.7, 35.2, 19.1, 17.0, 12.4, −4.7. Anal. Calcd for $C_{23}H_{30}O_3Si$: C, 72.12; H, 7.90. Found: C, 72.09; H, 7.95. When **3a** was used in a 36:64 *Z/E* ratio **4a** was now obtained in a 37:63 ratio of isomers.

2-Butyl-3-(2-hydroxyethoxy)-3-methyl-5-(diphenylmethylsilyl)cyclopentanone (4b). Following the general procedure, 0.68 g (1.4 mmol) of **3b** in 14 mL of CH_2Cl_2 was reacted with 1.68 mL (1.68 mmol) of 1.0 M $TiCl_4$ in CH_2Cl_2 and the resulting mixture stirred for 4 h. After low-temperature flash chromatography (ethyl acetate/pentane (15:85–50:50)), 0.38 g (66%) of **4b** was obtained as a 82:18 mixture of isomers: IR (neat) 3464, 1718,

1260 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.55 (m, 4 H), 7.36 (m, 6 H), 3.58 (m, 2 H), 3.28 (m, 2 H), 2.71 (dt, J = 1.3, 9.9 Hz, 1 H), 2.08 (m, 2 H), 2.01 (m, 1 H), 1.95 (s, 1 H, variable on dilution), 1.39–0.92 (m, 6 H), 1.31 (s, 3 H), 0.82 (t, J = 6.9 Hz, 3 H), 0.65 (s, 3 H), ^{13}C-NMR ($CDCl_3$) δ 218.3, 135.8, 135.1, 134.9, 135.0, 129.7, 129.5, 127.9, 127.8, 80.8, 63.4, 62.0, 60.3, 38.0, 35.2, 29.8, 23.4, 22.7, 23.3, 13.9, -4.4; ^{13}C-NMR (diagnostic signals for minor isomer) δ 216.2, 82.1, 81.9, 62.9, 62.8, 61.1, 58.5, 38.7, 36.6, 35.1, 32.9, 30.8, 29.8, 23.5, 21.8, 21.3, 19.2, 13.8, -4.7, -4.8. Anal. Calcd for $C_{25}H_{34}O_3Si$: C, 73.13; H, 8.35. Found: C, 73.11; H, 8.38.

3-(2-Hydroxyethoxy)-2-isopropyl-3-methyl-5-(diphenylmethylsilyl)cyclopentanone (4c). Following the general procedure, 0.33 g (0.7 mmol) of **3c** in 7.0 mL of CH_2Cl_2 was reacted with 0.84 mL (0.84 mmol) of 1.0 M $TiCl_4$ in CH_2Cl_2 and the resulting mixture stirred for 4 h. After low-temperature flash chromatography (ethyl acetate/pentane (15:85)), 0.11 g (40%) of **4c** was obtained: mp 99.0–100.5 °C; IR (neat) 3285, 1699, 1246 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.58 (m, 4 H), 7.37 (m, 6 H), 3.54 (m, 2 H), 3.35 (m, 1 H), 3.11 (m, 1 H), 2.71 (ddd, J = 1.5, 6.2, 10.7 Hz, 1 H), 2.16 (dd, J = 6.2, 13.7 Hz, 1 H), 2.04 (m, 1 H), 2.01, (d, J = 10.5 Hz, 1 H), 1.99 (m, 1 H), 1.74 (t, J = 6.4 Hz, variable on dilution, 1 H), 1.37 (s, 3 H), 1.08 (d, J = 6.9 Hz, 3 H), 0.95 (d, J = 6.8 Hz, 3 H), 0.65 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 218.8, 136.6, 135.1, 135.0, 129.6, 129.3, 127.9, 127.8, 82.2, 66.1, 62.9, 62.1, 37.9, 34.8, 26.3, 24.2, 23.1, 20.6, -4.6. Anal. Calcd for $C_{24}H_{32}O_3Si$: C, 72.68; H, 8.13. Found: C, 72.51; H, 8.21.

3-(2-Hydroxyethoxy)-3-methyl-5-(diphenylmethylsilyl)-2-(2-propenyl)cyclopentanone (4d). Following the general procedure, 0.28 g (0.6 mmol) of **3d** in 6.0 mL of CH_2Cl_2 was reacted with 0.72 mL (0.72 mmol) of 1.0 M $TiCl_4$ in CH_2Cl_2 and the resulting mixture stirred for 4 h. After low-temperature flash chromatography (ethyl acetate/pentane (30:70)), 0.15 g (64%) of **4d** was obtained as a 80:20 mixture of isomers: IR (neat) 3448, 1714, 1641, 1252 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.50 (m, 4 H), 7.28 (m, 6 H), 5.70 (m, 1 H), 4.86 (m, 2 H), 3.50 (m, 1 H), 3.43 (m, 1 H), 3.23 (m, 1 H), 3.06 (m, 1 H), 2.66 (dd, J = 6.6, 10.4 Hz, 1 H) 2.21–1.85 (m, 6 H), 1.25 (s, 3 H), 0.55 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 217.5, 137.2, 136.0, 135.0, 135.0, 134.9, 134.8, 129.8, 129.7, 129.6, 129.3, 127.9, 127.7, 115.2, 80.7, 63.1, 61.8, 60.6, 37.4, 34.7, 28.3, 23.3, -4.6; ^{13}C-NMR (diagnostic signals for minor isomer) δ 215.1, 136.7, 115.1, 82.0, 62.9, 62.8, 58.4, 38.7, 35.3, 28.2, 19.2, -4.8. Anal. Calcd for $C_{24}H_{30}O_3Si$: C, 73.05; H, 7.66. Found: C, 73.19; H, 7.67.

2-(3-Butenyl)-3-(2-hydroxyethoxy)-3-methyl-5-(diphenylmethylsilyl)cyclopentanone (4e) and 2-(3-Butenyl)-3-(2-hydroxyethoxy)-3-methylcyclopentanone. Following the general procedure, 1.30 g (2.7 mmol) of **3e** in 27.0 mL of CH_2Cl_2 was reacted with 3.24 mL (3.24 mmol) of 1.0 M $TiCl_4$ in CH_2Cl_2 and the resulting mixture stirred for 1.25 h. After low-temperature flash chromatography (ethyl acetate/pentane (30:70)), 0.68 g (62%) of **4e** was obtained as a 79:21 mixture of isomers: IR (neat) 3445, 1714, 1640, 1253 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.55 (m, 4 H), 7.38 (m, 6 H), 5.63 (m, 1 H), 4.95 (m, 2 H, 3.56 (m, 2 H), 3.28 (m, 2 H), 2.72 (t, J = 9.1 Hz, 1 H), 2.09 (m, 2 H), 2.06 (m, 2 H), 2.01 (m, 1 H), 1.90 (t, J = 6.1 Hz, variable on dilution, 1 H), 1.42 (m, 1 H), 1.31 (s, 3 H), 1.17 (m, 1 H), 0.64 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 217.9, 138.2, 135.9, 135.1, 135.0, 129.6, 129.4, 127.9, 127.8, 115.0, 80.8, 63.5, 62.0, 59.5, 37.9, 35.2, 31.4, 23.0, 23.3, -4.4; ^{13}C-NMR (diagnostic signals for minor isomer)) δ 138.4, 114.7, 82.1, 63.1, 63.0, 57.8, 38.8, 35.3, 23.4, 19.2, -4.7. Anal. Calcd for $C_{25}H_{32}O_3Si$: C, 73.49; H, 7.89. Found: C, 73.39; H, 7.90. When the reaction mixture was allowed to stir for 3.75 h, a 74:26 mixture of desilylated/silylated cyclopentanone was obtained. Spectral data of desilylated cyclopentanone: IR (neat) 3417, 1715, 1641 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 5.72 (m, 1 H), 4.96 (d, J = 17.2 Hz, 1 H), 4.91 (d, J = 10.1 Hz, 1 H), 3.58 (m, 2 H), 3.35 (m, 2 H), 2.28 (m, 1 H), 2.25 (m, 1 H), 2.15 (m, 2 H), 2.10 (m, 1 H), 2.05 (br s, variable on dilution, 1 H), 1.88 (dd, J = 5.0, 6.7 Hz, 1 H), 1.62 (m, 1 H), 1.55 (m, 2 H), 1.33 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 217.8, 138.5, 115.0, 81.7, 63.1, 62.1, 59.4, 34.4, 32.3, 29.9, 22.2, 21.5. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.77; H, 9.56.

3-(2-Hydroxyethoxy)-3-methyl-5-(diphenylmethylsilyl)-2-(2-phenylethyl)cyclopentanone (4f). Following the general procedure, 0.69 g (1.3 mmol) of **3f** in 13 mL of CH_2Cl_2 was reacted with 1.56 mL (1.56 mmol) of 1.0 M $TiCl_4$ in CH_2Cl_2 and the resulting mixture stirred for 2.75 h. After low-temperature flash chromatography (ethyl acetate/pentane (20:80–50:50)), 0.43 g (70%) of **4f** was obtained as a 75:13:12 mixture of isomers: IR (neat) 3459, 1713, 1250 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.57 (m, 4 H), 7.32 (m, 6 H), 7.19 (m, 2 H), 7.10 (m, 3 H), 3.49 (br s, 2 H), 3.17 (m, 2 H), 2.70 (t, J = 8.6 Hz, 1 H), 2.68 (m, 1 H), 2.57 (m, 1 H), 2.11 (m, 1 H), 2.15–1.95 (m, variable on dilution, 1 H), 2.02 (m, 1 H), 1.99 (m, 1 H), 1.68 (m, 1 H), 1.42 (m, 1 H), 1.22 (s, 3 H), 0.65 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 217.9, 141.7, 135.8, 134.4, 134.1, 133.9, 134.9, 134.8, 134.7, 129.6, 129.5, 129.3, 129.0, 128.4, 128.3, 129.0, 127.7, 127.6, 127.4, 125.5, 80.6, 63.3, 61.8, 59.0, 37.8, 35.0, 33.2, 25.0, 23.0, -4.6; ^{13}C-NMR (diagnostic signals for minor isomers) δ 217.6, 215.6, 142.0, 142.0, 125.8, 81.8, 81.7, 63.0, 62.7, 60.1, 59.9, 57.3, 38.7, 36.6, 34.0, 33.4, 32.8, 25.3, 24.0, 20.9, 19.1, -4.8, -4.9. Anal. Calcd for $C_{29}H_{34}O_3Si$: C, 75.94; H, 7.47. Found: C, 75.68; H, 7.52.

2-Ethyl-3-(2-hydroxyethoxy)-3-methylcyclohexanone (11). Following the general procedure, 0.66 g (1.4 mmol) of **10** in 14.0 mL of CH_2Cl_2 was reacted with 1.68 mL (1.68 mmol) of 1.0 M $TiCl_4$ in CH_2Cl_2 and the resulting mixture stirred for 1.5 h. After low-temperature flash chromatography (ethyl acetate/pentane (30:70)), 0.14 g (51%) of **11** was obtained as a 93:7 mixture of isomers: IR (neat) 3444, 1714 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.67 (t, J = 4.6 Hz, 2 H), 3.51 (m, 1 H), 3.41 (m, 1 H), 2.41–2.29 (m, 1 H, variable on dilution), 2.38 (m, 1 H), 2.36 (m, 1 H), 2.25 (m, 1 H), 1.93 (m, 1 H), 1.84 (m, 2 H), 1.72 (m, 1 H), 1.59 (m, 2 H), 1.13 (s, 3 H), 0.86 (t, J = 7.4 Hz, 3 H); ^{13}C-NMR ($CDCl_3$) δ 212.8, 80.2, 61.7, 62.1, 61.9, 38.2, 32.2, 21.2, 20.9, 19.5, 12.4; ^{13}C-NMR (diagnostic signals for minor isomer) δ 62.8, 40.5, 33.6, 22.9, 21.4, 16.7, 13.3. Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07. Found: C, 66.07; H, 10.06.

3-Methyl-5-methylene-2-(2-phenylethyl)-2-cyclopenten-1-one (12). The standard apparatus was charged with 0.07 g (2.4 mmol) of an 80% sodium hydride dispersion in mineral oil and washed with dry hexane (3 × 2 mL). Then, 6.0 mL of dry THF was added, the system cooled (dry ice/acetone) for 10 min, and 0.26 g (0.6 mmol) of **4f** in 2 mL of dry THF added dropwise. After 15 min, 2 mL (1.5 mmol) of a freshly prepared solution of monomeric formaldehyde in diethyl ether[27] was added dropwise. The reaction mixture was allowed to reach rt overnight, and then it was quenched with a saturated aqueous solution of NH_4Cl. After extraction with ether (3 × 20 mL), the combined organic layers were dried over anhyd sodium sulfate and filtered, and the solvent was evaporated at reduced pressure. The product, which was contaminated with diphenylmethylsilanol, was treated with 3.0 equiv of triethylamine and a catalytic amount DMAP in 8.0 mL of dry THF during 1 h. Then, 2.0 equiv of chlorotrimethylsilane was added. After 0.5 h the same workup was done yielding 0.09 g (73%) of **12**: mp 69–71 °C; IR (neat) 1680, 1650, 1618 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.22–7.02 (m, 5 H), 6.01 (d, J = 0.9 Hz, 1 H), 5.28 (d, J = 1.1 Hz, 1 H), 2.98 (br s, 2 H), 2.69 (t, J = 7.5 Hz, 2 H), 2.50 (t, J = 7.5 Hz, 2 H), 1.71 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 195.7, 165.2, 141.7, 141.1, 128.6, 128.2, 125.8, 114.9, 36.9, 34.1, 25.6, 16.3; MS m/z (relative intensity) 212 (M^+, 74), 211 (5), 199 (5), 197 (28), 122 (5), 121 (56), 115 (5), 93 (7), 92 (15), 91 (100), 78 (7).

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Supplementary Material Available: ^{1}H and ^{13}C NMR spectra of **3a–f**, **10**, and **12** and NOESY spectra of **4a**, **4c**, and **4e** (21 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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