Regioselectivity in [3 + 4] and [3 + 5] Annulation Reactions of Bis(trimethylsilyl) Enol Ethers with Acylsilane Dicarbonyl Dielectrophiles

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A number of 1,4- and 1,5-acylsilane dicarbonyl compounds were synthesized using Corey–Brook dithiane methods. These dicarbonyl substrates were annulated with the bis(trimethylsilyl) enol ether of methyl acetoacetate in the presence of TMSOTf, affording bicyclic ethers bearing silicon substituted at the bridgehead position. The annulation reactions proceeded with excellent regiochemical and good to excellent stereochemical control via a neighboring group participation mechanism. The silicon substituent was subsequently removed by treatment with fluoride ion. The overall transformation of annulation and desilylation represents a formal inversion of the regioselectivity normally exhibited with keto aldehyde dielectrophilic substrates in this process.

With increasing regularity, naturally occurring compounds containing functionalized seven-[1] and eight-membered ring systems[2] are being examined as potential therapeutic agents. Unfortunately, the synthesis of such medium-sized rings still presents many difficulties. Thus, while there are many general methods for the regiochemically and stereochemically controlled construction of five- and six-membered rings, seven-[3] and eight-membered ring syntheses[4] suffer from a lack of generally applicable methods.

In theory, the synthesis of seven- and eight-membered ring systems could be accomplished by reaction of a 1,3-dianionic synthon with a 1,4- or 1,5-dielectrophilic substrate, respectively.[5] However, there are considerable difficulties that must be overcome for this method to be practical. In addition to the inherent problem of generating medium-sized rings,[6] to insure high regioselectivity the two nucleophilic sites of the dianionic synthon and the two electrophilic sites of the dielectrophile must show differential reactivity. If new stereogenic centers are formed in the process, control of the relative stereochemistry must be addressed as well.

Lewis acid-promoted [3 + 4] and [3 + 5] annulation reactions were recently introduced as efficient processes for the construction of seven- and eight-membered carbocycles.[7] Highly functionalized bicyclic and tricyclic ethers were obtained in the coupling of 1,4- and 1,5-dicarbonyl electrophiles with bis(trimethylsilyl) enol

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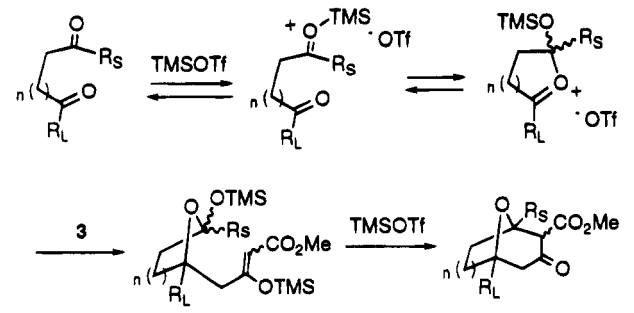
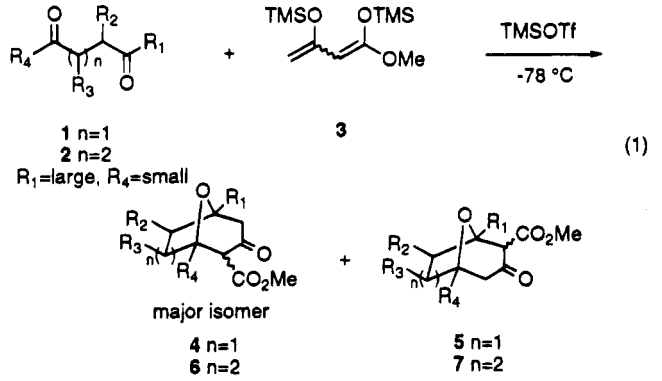
Scheme 1



ethers derived from β-keto esters and β-diketones (eq 1).



(1)

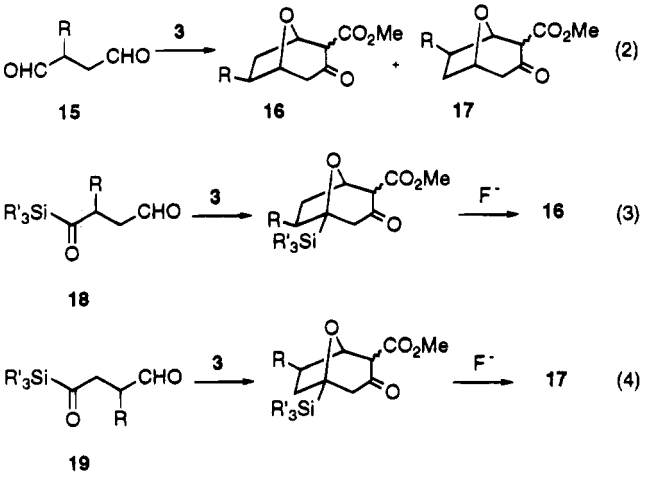
Extremely high levels of regiochemical control were achieved in this process. For example, when keto aldehydes (**1** and **2**, R_4 = H) were used in the annulation reaction, a single regioisomeric bicyclic ether was obtained. Even when diketone substrates were employed, good to very good regiochemical control was obtained depending on the ketone substituents. In all cases, the observed products **4** and **6** resulted from initial attack of the more nucleophilic carbon of the bis(trimethylsilyl) enol ether dinucleophile **3** (i.e., the terminal carbon) at the more hindered carbonyl carbon of the dielectrophile.[8]

These results were explained by a novel neighboring group participation mechanism (Scheme 1).[7,9] Trimethysilyl trifluoromethanesulfonate (TMSOTf) preferentially complexes the less hindered carbonyl of the dielectrophile, activating it toward intramolecular attack by the more hindered carbonyl group. The cyclic oxocarbenium ion thus formed in turn activated the more hindered carbonyl toward external nucleophilic attack. Subsequent reaction with **3** and TMSOTf-promoted ring closure via a second oxocarbenium ion provided the observed bicyclic product.[7]

The existence of a cyclic intermediate in this mechanism also provided the necessary basis for high levels of relative asymmetric induction in the annulation process. Conformational analysis of the proposed oxocarbenium ion intermediate allowed accurate prediction of the resultant stereochemical outcome in the bicyclic ether products.

To extend further the synthetic utility of this annulation process, a method was sought that would predictably invert the regiochemistry normally observed with keto aldehydes, thereby permitting access to the minor regioisomeric bicyclic ether products **5** and **7** (R_1 = alkyl or aryl, R_4 = H). The strategy decided upon involved the utilization of an acylsilane as a sterically demanding aldehyde equivalent (Scheme 2).[10] Replacement of the aldehyde carbonyl of the dielectrophile with the acylsilane group was reasoned to lead to initial activation of the ketone carbonyl by TMSOTf and formation of oxocarbenium ion **10**. Intermediate **10** would activate the acylsilane carbonyl carbon toward attack from **3**, ultimately leading to regioisomers **11** and **13**. Subsequent removal of the silyl group[11] would provide bicyclic ethers **5** and **7**, the minor regioisomers in the original annulation reactions.

An additional attractive feature of this method was that it would allow regioselective annulation of unsymmetrical dialdehyde substrates. For example, annulation of **15** with **3** in the presence of a Lewis acid would result in a mixture of regioisomers **16** and **17** (eq 2). However, regioselective annulation of **18** and desilylation would provide only **16** (eq 3). Similarly, annulation of **19** and desilylation would give only **17** (eq 4).



In order to explore the TMSOTf-promoted [3 + 4] and [3 + 5] annulation reactions of acylsilane dicarbonyl substrates with bis(trimethylsilyl) enol ether **3**, several 1,4- and 1,5-acylsilane dicarbonyl substrates were synthesized and subjected to the annulation process. The results of these studies are reported herein.

Results and Discussion

All of the acylsilane dicarbonyls were synthesized by application of the Corey–Brook dithiane method (Scheme

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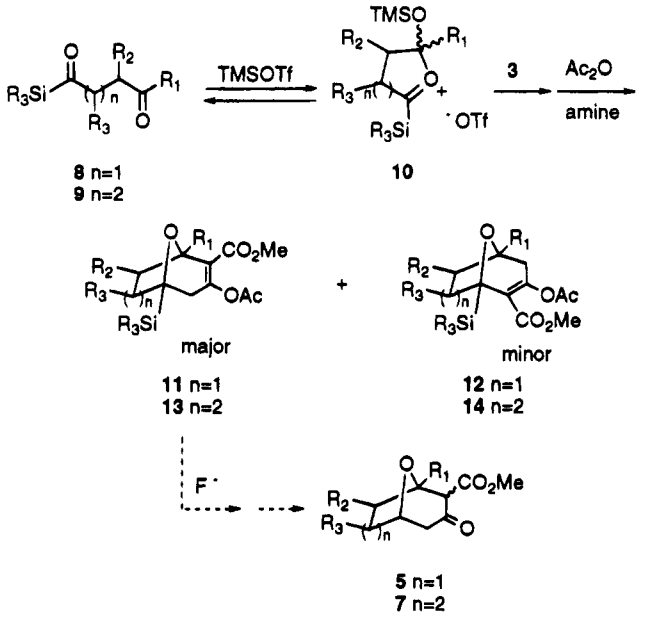
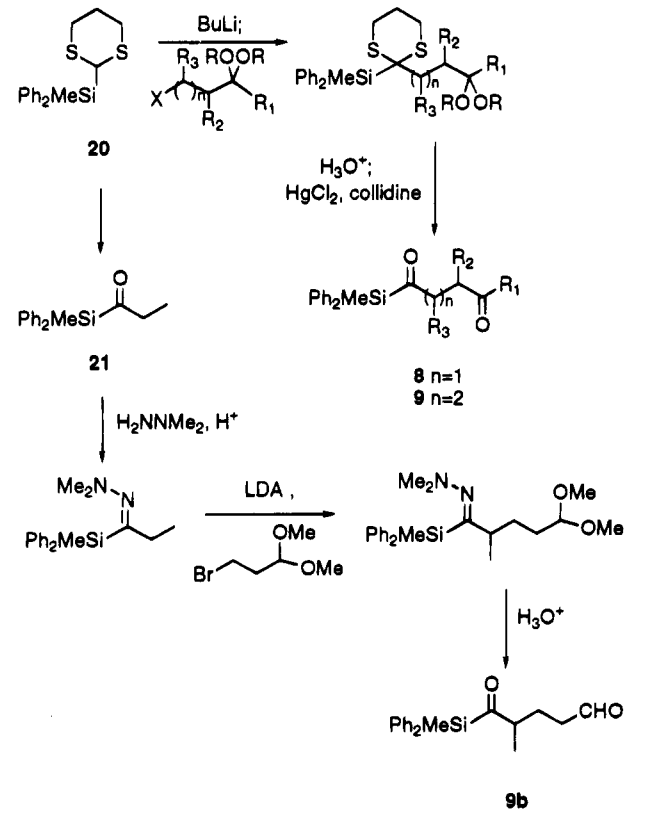
Scheme 2



Scheme 3



3).[12,13] Initially, the synthesis of dicarbonyl dielectrophiles containing acyltrimethylsilanes was undertaken. However, in each case it was not possible to isolate the final dicarbonyl compounds. Subsequently, acyldiphenylmethylsilanes were targeted for study and synthesized. Thus, alkylation of 2-silyl-1,3-dithiane **20**[14] with a halo acetal or halo ketal, followed by sequential acetal and dithiane hydrolysis, afforded 1,4- and 1,5-acylsilane dicarbonyls **8** and **9**. For the synthesis of **9b**, the dimethylhydrazone of **21** was alkylated,[15] and acidic hydrolysis of both the hydrazone and the acetal was accomplished in one step. Although hardier than the corresponding acyltrimethylsilanes, even the acyldiphenylmethylsilanes **8** and **9** are somewhat unstable, particularly toward acidic conditions. Polymerization and intramolecular cyclization occurs under these circumstances, producing furans and/or pyrans.[14] As such, the acylsilanes thus generated were normally employed in annulation reactions immediately after their purification.

Table 1. TMSOTf-Promoted Annulation of 1,4- and 1,5-Acylsilane Dicarbonyl Substrates 8 and 9 with 3

substrate	product	R_1	R_2	R_3	R_4	% yield[a]	diastereoselectivity[b] (regioselectivity)
8a	**11a**	H	H	H		82	(>200:1)
8b	**11b**	H	H	Me		58	3.5:1
8c	**11c**	H	H	Ph		68	51:1
8d	**11d**	H	Me	H		63	18.5:1
8e	**11e**	Me	H	H		70	(>200:1)
9a	**13a**	H	H	H	H	85	(>200:1)
9b	**13b**	H	H	H	Me	66	4.1:1
9c	**13c**	Me	H	H	H	83	(>28:1)

[a] Refers to isolated yields of purified product as a mixture of diastereomers. All of the above compounds have been fully characterized spectroscopically (^{1}H NMR, ^{13}C NMR, IR) and elemental composition has been established by combustion analysis and/or exact mass. [b] Diastereoselectivity and regioselectivity were determined by ^{1}H NMR after derivatization to the corresponding enol acetate.

Subjection of these substrates to the annulation reaction with bis(trimethylsilyl) enol ether **3** in the presence of catalytic TMSOTf afforded good to excellent yields of the expected bicyclic ether products. Because the acylsilane dicarbonyls themselves react with TMSOTf, the annulation conditions described in previous papers[7] were modified to suppress side reactions. Best yields occurred under dilute conditions at −78 °C, adding a 0.1 M solution of TMSOTf (20−40 mol %) in CH_2Cl_2 to a 0.045 M solution of the acylsilane dicarbonyl substrate in CH_2Cl_2 containing **3**.

Utilizing this protocol, the bicyclic ethers **11** and **13** were formed with extremely high regiochemical control in 58−85% isolated yields (Table 1). In every respect, the results obtained parallel the results of previous annulation reactions.[7] In all cases, initial attack of the dinucleophilic synthon occurred preferentially at the acylsilane carbonyl carbon. Acylsilane aldehydes were completely regioselective in their annulations, providing only bicyclic ethers **11** and **13**. Even the 1,5-acylsilane ketone **9c** was highly regioselective, and the 1,4-acylsilane ketone **8e** provided bicyclic ether **11e** with ≥200:1 regioselectivity. These results place the annulation of keto acylsilanes on a par with keto aldehydes in terms of their regioselectivity, while exhibiting even better regioselectivity than diketones.

All of the bicyclic ethers initally formed exist as a mixture of three isomers: the enol tautomer and both exo and endo β-keto ester diastereomers. To simplify spectral interpretation and the assessment of regioisomeric and diastereomeric ratios, the products were derivatized to their enol acetates. As in earlier reports,[7] the regiochemistry of the bicyclic ethers **11a−d** was assigned by examination of the bridgehead proton (H_1)

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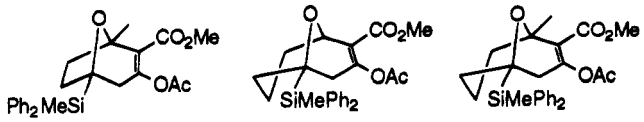
Table 2. NOE Data

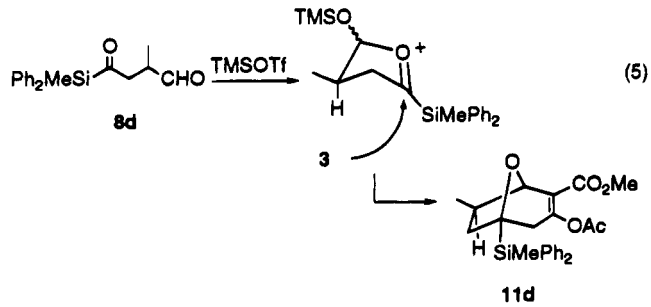


11e **13a** **13c**

		% NOE				
compd	irrad	C_1 subst	SiMe	SiPh	exo-H_4	endo-H_4
11e	CO_2Me	0.41				
11e	SiMe				1.01	1.13
11e	exo-H_4		1.41	1.94		
13a	CO_2Me	0.87				
13a	SiMe				1.54	
13c	CO_2Me	0.26				
13c	SiMe				1.50	1.02
13c	exo-H_4			2.11		

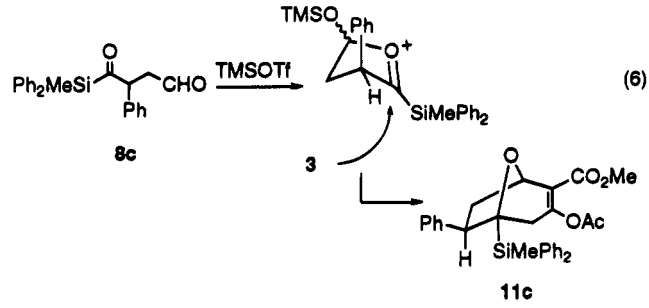
in the ^1H NMR spectrum (Table 2). This proton couples only to the exo hydrogens H_7 and H_2. Nuclear Overhauser enhancement (NOE) experiments were used to confirm the regiochemistry of bicyclic ethers **11e** and **13a–c**. For example, irradiation of the methoxycarbonyl singlet of **11e** resulted in enhancement of the bridgehead methyl proton resonance, and irradiation of H_4-exo gave an enhanced signal for the silylmethyl and silylphenyl groups. Likewise for **13c** methoxycarbonyl irradiation again produced enhancement of the bridgehead methyl protons, and irradiation at H_4-exo gave an enhanced signal for the silylphenyl group. For bicyclic ether **13a** irradiation at the methoxycarbonyl produced an enhanced signal for the bridgehead proton H_5, and irradiation at the silylmethyl group gave enhancement at H_4-exo and H_4-endo.

In addition to the high regioselectivities achieved, relative control of stereochemistry in this process was very good as well and exhibited the same trends as was found in previous substrates.[7] For instance, 1,3-relative asymmetric induction is generally greater than 1,2-asymmetric induction (**8d** vs **8b**). For each case, the major diastereomer could be predicted by conformational analysis of the respective oxocarbenium ion intermediates. Thus, substrate **8d** reacts with TMSOTf to form an oxocarbenium ion intermediate in which the methyl substituent is in a pseudoequatorial orientation (eq 5). Stereoelectronically favored pseudoaxial attack[16] of **3** on this cyclic intermediate provides the observed major diastereomer **11d**. The stereochemistry of **11d** was determined from the bridgehead resonance in the ^1H NMR spectrum, which was a singlet.[7]



8d **3** **11d** (5)

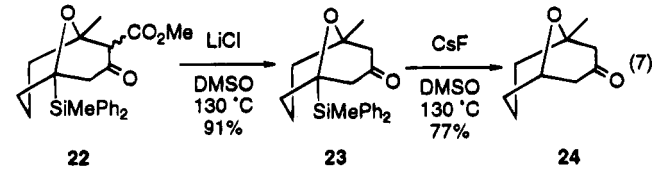
The preferred conformation of the oxocarbenium ion intermediate generated in the annulation of **8c** with bis-(trimethylsilyl) enol ether **3** is one in which the substituent is oriented in a pseudoaxial position (eq 6). Pseudoequatorial placement of the substituent is unfavorable because of $A^{1,2}$ strain,[17] with the silyl group and eclipsing interactions with the approaching nucleophile. For small



8c **3** **11c** (6)

substituents these negative interactions are attenuated and the two intermediates (pseudoequatorial and pseudoaxial) compete with each other, leading to lower levels of stereocontrol. For large substituents (particularly aryl groups, that are presumably locked into an orientation that facilitates conjugation of the aryl unit with the developing positive charge at the adjacent oxocarbenium ion center), pseudoequatorial placement is severely disfavored and excellent asymmetric induction from the axial conformer results. The stereochemical assignment for **11c** was made by analogy to similar systems not containing silicon[7] and by comparison of chemical shifts for H_6 and H_7 in **11c** relative to **11d.** For **11d** the chemical shift for H_7 in the major diastereomer (Me exo) is δ 2.57; the chemical shift for H_7 in the minor diastereomer (Me endo) is δ 2.52. For **11c** the chemical shift for H_6 in the major diastereomer (Ph exo) is δ 3.55; the chemical shift for H_6 in the minor diastereomer (Ph endo) is δ 3.35.

Once it had been established that the [3 + 4] and [3 + 5] annulation procedure could be applied successfully to acylsilane dicarbonyl systems, it remained only to demonstrate that the bridgehead silyl group could be removed from the bicyclic ether products to effect an apparent inversion of the normal regioselectivity of the process. It was hoped that a direct fluoride-promoted desilylation from the β-keto esters (e.g., **22**, eq 7) could be accomplished.[11] However, under standard desilylation conditions (using TBAF, KF, CsF, HF, or H_2SiF_6 under various conditions), none of the desired product was obtained. Only decarboxylated material could be isolated.



22 **23** **24** (7)

Consequently, the offending methoxycarbonyl group was first removed altogether under standard decarboxylation conditions (eq 7).[18] Thus, treatment of **22** with LiCl at 130 °C in wet DMSO afforded the decarboxylated

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(18) (a) Krapcho, P. A. *Synthesis* **1982**, 805. (b) Krapcho, P. A. *Synthesis* **1982**, 893.

bicyclic ketone **23** in excellent yield. Desilylation of **23** with excess CsF (10 equiv) in wet DMSO at 130 °C for 2 h proceeded smoothly, affording **24** in 77% yield.

Conclusions

The Lewis acid-promoted [3 + 4] and [3 + 5] annulation reaction of dicarbonyl substrates with bis(trimethylsilyl) enol ethers of 1,3-keto esters and 1,3-diketones has been further extended to include the use of 1,4- and 1,5-acylsilane dicarbonyl substrates. Regioselectivity and stereoselectivity are predictable, in accordance with the neighboring group participation mechanism. Removal of the bridgehead silicon substituent completes the process, allowing an inversion of the regiochemistry normally exhibited by keto aldehydes.

Experimental Section

Reagents. Tetrahydrofuran (THF) was distilled immediately prior to use from sodium benzophenone ketyl under Ar. CH_2Cl_2 was stirred over sulfuric acid, decanted, and stirred over K_2CO_3. It was distilled from CaH_2 onto 4-Å molecular sieves and stored over 4-Å molecular sieves. Standard benchtop techniques were employed for the handling of air-sensititve reagents,[19] and all reactions were carried out under argon.

(1,3-Dithian-2-yl)methyldiphenylsilane (20).[14] To a solution of 1,3-dithiane (20 g, 0.166 mol) in THF (250 mL) cooled to −25 °C was added dropwise with stirring *n*-butyllithium (1.6 M in hexanes, 114.4 mL, 183 mmol).[12] Stirring was continued for 2.5 h at −25 °C. The solution was cooled to −40 °C, and methyldiphenylsilyl chloride (45.5 mL, 0.216 mol) was added dropwise. The mixture was allowed to warm to room temperature overnight and then diluted with pentane, filtered, and concentrated *in vacuo*. Flash chromatography of the residue on silica gel (2% ether in petroleum ether) afforded **20** (47.17 g, 90%). Recrystallization from petroleum ether gave colorless prisms: mp 67.5−68.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (m, 4H), 7.49−7.39 (m, 6H), 4.25 (s, 1H), 2.93 (ddd, J = 13.9, 11.8, 3.2 Hz, 2H), 2.74 (ddd, J = 13.9, 3.7, 3.7 Hz, 2H), 2.17−1.98 (m, 2H), 0.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.14, 133.36, 129.93, 127.80, 32.75, 31.38, 25.84, −5.59.

General Procedure for the Alkylation of 20.[12] To a solution of **20** in THF cooled to −25 °C was added dropwise with stirring *n*-butyllithium (1.6 M in hexanes, 1.1 equiv). Stirring was continued for 2.5 h at −25 °C. The halo acetal or halo ketal was added dropwise either neat or as a solution in THF. After warming to room temperature, the reaction mixture was diluted with ether, washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. Flash chromatography of the residue on silica gel (ether in petroleum ether) afforded the silyldithiane acetal or ketal.

[2-(3,3-Diethoxypropyl)-1,3-dithian-2-yl]methyldiphenylsilane. 20 was alkylated with chloropropionaldehyde diethyl acetal (1.5 equiv) for 4 h at −25 °C to provide the title compound in 96% yield. Recrystallization from petroleum ether gave colorless prisms: mp 59.5−60 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (m, 4H), 7.45−7.39 (m, 6H), 4.38 (dd, J = 5.5, 5.5 Hz, 1H), 3.46−3.32 (m, 4H), 3.07 (ddd, J = 14.0, 12.9, 3.1 Hz, 2H), 2.46 (ddd, J = 14.0, 3.9, 3.9 Hz, 2H), 2.34 (m, 2H), 1.97 (m, 2H), 1.78 (m, 2H), 1.15 (t, J = 7.0 Hz, 6H), 0.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.72, 133.95, 129.47, 127.43, 102.30, 60.18, 38.58, 32.11, 30.83, 24.46, 23.58, 15.65, −4.23.

[2-[2-(1,3-Dioxolan-2-yl)-1-methylethyl]-1,3-dithian-2-yl]methyldiphenyl silane (2d). 20 was alkylated with 2-(2-iodo-1-methylethyl)-1,3-dioxolane[20] (1.2 equiv) for 2 h at −78 °C to provide the title compound in 83% yield. Recrystallization from petroleum ether gave colorless prisms: mp 84−86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, J = 6.4, 1.5 Hz, 4H), 7.43−7.35 (m, 6H), 4.69 (d, J = 2.9 Hz, 1H), 3.86−3.73 (m, 4H), 3.00 (ddd, J = 14.0, 10.3, 3.5 Hz, 1H), 2.95 (ddd, J = 14.2, 10.4, 3.4 Hz, 1H), 2.51 (dd, J = 14.8, 3.0 Hz, 1H), 2.45 (ddd, J = 14.0, 9.0, 5.0 Hz, 2H), 2.13 (m, 1H), 2.06 (dd, J = 14.8, 6.2 Hz, 1H), 1.97−1.81 (m, 2H), 0.90 (d, J = 6.7 Hz, 3H), 0.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.96, 135.94, 134.83, 134.72, 129.53, 129.49, 127.55, 127.51, 107.20, 65.06, 64.93, 39.07, 38.71, 34.70, 24.57, 24.42, 15.44, −4.10.

[2-[2-(2-Methyl-1,3-dioxolan-2-yl)ethyl]-1,3-dithian-2-yl]methyldiphenylsilane. 20 was alkylated with 2-methyl-2-(2-iodoethyl)-1,3-dioxolane[20] (1.5 equiv) for 4 h at −78 °C to provide the title compound in 74% yield. Recrystallization from petroleum ether gave colorless prisms: mp 113.5−114.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (m, 4H), 7.46−7.38 (m, 6H), 3.90−3.76 (m, 4H), 3.09 (ddd, J = 14.2, 11.9, 3.2 Hz, 2H), 2.44 (ddd, J = 14.2, 4.0, 3.8 Hz, 2H), 2.34 (m, 2H), 2.05−1.89 (m, 2H), 1.72 (m, 2H), 1.13 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.80, 134.01, 129.61, 127.52, 109.69, 64.33, 38.84, 36.00, 31.55, 24.67, 23.60, 23.49, −4.09.

[2-[2-(1,3-Dioxolan-2-yl)-2-methylethyl]-1,3-dithian-2-yl]methyldiphenylsilane. The general alkylation procedure described above was followed with the following exception: After formation of the 2-lithio-1,3-dithiane, HMPA (1 equiv) was added. Alkylation with 2-(2-iodo-2-methylethyl)-1,3-dioxolane[21] (1.5 equiv) for 4 h at −78 °C provided the title compound in 31% isolated yield (93% based on recovered **20**). Recrystallization from petroleum ether gave colorless prisms: mp 116−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 6.7 Hz, 4H), 7.42−7.34 (m, 6H), 4.81 (dd, J = 6.8, 3.3 Hz, 1H), 3.94−3.73 (m, 4H), 3.02 (ddd, J = 14.1, 10.8, 3.8 Hz, 1H), 2.89 (ddd, J = 14.1, 10.4, 3.8 Hz, 1H), 2.61 (m, 1H), 2.44−2.30 (m, 3H), 1.98−1.83 (m, 2H), 1.33 (ddd, J = 13.3, 11.1, 3.3 Hz, 1H), 1.11 (d, J = 6.9 Hz, 3H), 0.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.21, 136.16, 135.64, 135.58, 129.41, 129.38, 127.41, 127.40, 104.19, 64.66, 64.39, 44.92, 38.01, 36.75, 24.20, 23.97, 23.93, 18.04, −2.37.

[2-[2-(1,3-Dioxolan-2-yl)-2-phenylethyl]-1,3-dithian-2-yl]methyldiphenylsilane. The general alkylation procedure described above was followed with the following exception: After formation of the 2-lithio-1,3-dithiane, HMPA (1 equiv) was added. Alkylation with 2-(2-iodo-2-phenylethyl)-1,3-dioxolane[22] (1.5 equiv) for 2 h at −78 °C and warming to room temperature overnight provided the title compound as a mixture with cinnamaldehyde ethylene ketal. The byproduct was removed by Kugelrohr distillation to provide [2-[2-(1,3-dioxolan-2-yl)-2-phenylethyl]-1,3-dithian-2-yl]methyldiphenylsilane in 19% isolated yield (85% based on recovered **20**). Recrystallization from petroleum ether gave a white solid: mp 139−141 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (m, 2H), 7.80 (m, 2H), 7.41−7.28 (m, 8H), 7.18−7.11 (m, 3H), 4.31 (dd, J = 8.3, 2.1 Hz, 1H), 3.75−3.65 (m, 2H), 3.62−3.55 (m, 2H), 3.40 (dd, J = 12.4, 3.0 Hz, 1H), 2.47 (ddd, J = 13.5, 12.4, 2.1 Hz, 1H), 2.42 (m, 1H), 2.35 (ddd, J = 13.5, 8.3, 3.0 Hz, 1H), 2.21 (m, 2H), 2.12 (ddd, J = 13.8, 6.6, 4.7 Hz, 1H), 1.74−1.66 (m, 1H), 1.60−1.50 (m, 1H), 0.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.85, 136.28, 136.25, 136.03, 135.78, 129.32, 129.19, 127.52, 127.49, 127.33, 127.09, 103.25, 64.52, 64.47, 51.38, 41.83, 36.90, 25.81, 25.54, 22.53, −3.78.

[2-(3-Oxopropyl)-1,3-dithian-2-yl]methyldiphenylsilane. A solution of [2-(3,3-diethoxypropyl)-1,3-dithian-2-yl]-methyldiphenylsilane (11.5 g, 30.86 mmol) and wet Amberlyst-15 resin[23] (25 g) in acetone (350 mL) was stirred at room temperature for 3 h. The mixture was filtered, washed with aqueous saturated sodium bicarbonate and brine, dried (Mg-

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(20) Prepared by the method of Larson and Kleese from methacrolein: Larson, G. L.; Kleese, R. *J. Org. Chem.* **1985**, *50*, 3627.

(21) Prepared by the method of Larson and Kleese[20] from crotonaldehyde.

(22) Prepared by the method of Larson and Kleese[20] from cinnamaldehyde.

(23) Ballini, R.; Petrini, M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2563.

SO_4), and concentrated *in vacuo*. Flash chromatography of the residue on silica gel (12% ether in petroleum ether) and recrystallization from petroleum ether afforded the title compound (8.5 g, 92%) as colorless prisms: mp 85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1H), 7.85 (m, 4H), 7.47–7.39 (m, 6H), 2.99 (ddd, J = 14.3, 11.6, 3.1 Hz, 2H), 2.62–2.57 (m, 2H), 2.52–2.46 (m, 2H), 2.44 (ddd, J = 14.3, 4.3, 4.3 Hz, 2H), 2.04–1.88 (m, 2H), 0.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.32, 135.78, 133.62, 129.85, 127.71, 41.69, 38.27, 29.47, 24.21, 23.71, −4.45.

[2-(3-Oxobutyl)-1,3-dithian-2-yl]methyldiphenylsilane. A solution of [2-[2-(2-methyl-1,3-dioxolan-2-yl)ethyl]-1,3-dithian-2-yl]methyldiphenylsilane (590 mg, 1.37 mmol) and PPTS[24] (35 mg, 0.137 mmol) in acetone (25 mL) was heated at reflux for 6 h. The mixture was concentrated *in vacuo*, and the residue was filtered through a short column of silica gel (chloroform) to give the title compound (519 mg, 98%). Recrystallization from petroleum ether gave colorless prisms: mp 95–96 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (m, 4H), 7.46–7.38 (m, 6H), 3.02 (ddd, J = 14.4, 11.9, 3.0 Hz, 2H), 2.56 (m, 2H), 2.43 (m, 4H), 2.02–1.86 (m, 2H), 1.94 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.93, 135.80, 133.85, 129.76, 127.65, 41.13, 38.65, 30.66, 39.98, 24.43, 23.80, −4.39.

General Procedure for the Hydrolysis of Methyldiphenylsilyl Dithiane Acetals. A solution of the methyldiphenylsilyl dithiane acetal in THF/3 N HCl (1:2) was stirred at room temperature for 6–24 h. The mixture was diluted with ether, and the organic layer was separated, washed with water, saturated aqueous $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated *in vacuo*. Flash chromatography of the residue on silica gel (ether in petroleum ether) gave the silyl dithiane aldehyde.

[2-(1-Methyl-3-oxopropyl)-1,3-dithian-2-yl]methyldiphenylsilane: isolated in 95% yield from [2-[2-(1,3-dioxolan-2-yl)-2-methylethyl]-1,3-dithian-2-yl]methyldiphenylsilane; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (d, J = 1.9 Hz, 1H), 7.93 (dd, J = 7.9, 1.5 Hz, 2H), 7.89 (dd, J = 7.9, 1.5 Hz, 2H), 7.46–7.35 (m, 6H), 3.15–3.05 (m, 2H), 2.89 (ddd, J = 14.1, 11.3, 3.9 Hz, 1H), 2.86 (ddd, J = 14.1, 11.3, 3.9 Hz, 1H), 2.39 (ddd, J = 14.1, 4.7, 4.7 Hz, 1H), 2.34 (ddd, J = 14.1, 4.7, 4.7 Hz, 1H), 2.07–1.83 (m, 3H), 1.12 (d, J = 7.2 Hz, 3H), 0.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.54, 136.12, 135.19, 135.17, 129.69, 129.53, 127.64, 127.49, 48.82, 43.92, 35.68, 24.27, 24.18, 23.69, 18.85, −2.41.

[2-(3-Oxo-1-phenylpropyl)-1,3-dithian-2-yl]methyldiphenylsilane: isolated in 90% yield from [2-[2-(1,3-dioxolan-2-yl)-2-phenylethyl]-1,3-dithian-2-yl]methyldiphenylsilane; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.37 (dd, J = 2.4, 1.1 Hz, 1H), 7.86 (dd, J = 7.9, 1.4 Hz, 2H), 7.82 (dd, J = 7.9, 1.4 Hz, 2H), 7.46–7.31 (m, 6H), 7.24–7.13 (m, 5H), 3.82 (dd, J = 10.5, 4.4 Hz, 1H), 3.23 (ddd, J = 16.6, 4.4, 1.1 Hz, 1H), 3.12 (ddd, J = 16.6, 10.5, 2.4 Hz, 1H), 2.43 (ddd, J = 13.7, 8.6, 4.7 Hz, 1H), 2.32–2.20 (m, 2H), 2.13 (ddd, J = 13.7, 6.9, 4.6 Hz, 1H), 1.76–1.69 (m, 1H), 1.65–1.54 (m, 1H), 0.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.01, 139.50, 135.21, 135.89, 135.70, 135.24, 130.69, 129.58, 129.50, 127.74, 127.65, 127.53, 127.50, 49.30, 47.01, 41.52, 25.70, 25.49, 22.40, −3.90.

[2-(2-Methyl-3-oxopropyl)-1,3-dithian-2-yl]methyldiphenylsilane: isolated in 91% yield from [2-[2-(1,3-dioxolan-2-yl)-1-methylethyl]-1,3-dithian-2-yl]methyldiphenylsilane. Recrystallization from petroleum ether gave colorless prisms: mp 100–102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (d, J = 2.6 Hz, 1H), 7.86 (dd, J = 7.9, 1.5 Hz, 2H), 7.81 (dd, J = 7.9, 1.5 Hz, 2H), 7.48–7.36 (m, 6H), 3.12 (dd, J = 15.0, 9.4 Hz, 1H), 2.99 (ddd, J = 14.0, 11.4, 3.0 Hz, 1H), 2.82 (ddd, J = 14.0, 11.6, 3.2 Hz, 1H), 2.61 (m, 1H), 2.40 (m, 2H), 2.02–1.84 (m, 2H), 1.94 (dd, J = 15.0, 2.1 Hz, 1H), 0.86 (s, 3H), 0.81 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.42 (135.87), 135.78, 134.12, 133.48, 129.92, 129.80, 127.82, 127.63, 44.51, 40.82, 38.16, 24.34, 24.19, 23.98, 16.04, −4.00.

General Procedure for the Hydrolysis of Silyl Dithianes.[12] A solution of the silyl dithiane, mercuric chloride (7 equiv), and collidine (2 equiv) in 80% acetone was stirred in the dark at room temperature for 16–24 h. The mixture was diluted with ether, filtered through Celite/neutral alumina, washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. Rapid flash chromatography of the residue on silica gel (ether in hexanes or acetone in hexanes) afforded the acylsilane dicarbonyl compound.

(1,4-Dioxobutyl)methyldiphenylsilane (8a): isolated in 70% yield from [2-(3-oxopropyl)-1,3-dithian-2-yl]methyldiphenylsilane; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (s, 1H), 7.61 (m, 4H), 7.47–7.36 (m, 6H), 2.97 (t, J = 6.1 Hz, 2H), 2.65 (t, J = 6.1 Hz, 2H), 0.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.36, 196.75, 134.97, 132.27, 130.20, 128.22, 41.70, 36.09, −5.46.

(2-Methyl-1,4-dioxobutyl)methyldiphenylsilane (8b): isolated in 61% yield from [2-(1-methyl-3-oxopropyl)-1,3-dithian-2-yl]methyldiphenylsilane; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (s, 1H), 7.65–7.61 (m, 4H), 7.47–7.37 (m, 6H), 3.49 (m, 1H), 2.92 (dd, J = 18.2, 8.3 Hz, 1H), 2.32 (ddd, J = 18.2, 5.0, 0.6 Hz, 1H), 0.91 (d, J = 7.3 Hz, 3H), 0.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.45, 193.18, 135.03, 135.01, 133.91, 132.77, 130.09, 129.81, 128.15, 127.86, 45.67, 44.70, 14.67, −4.64.

(1,4-Dioxo-2-phenylbutyl)methyldiphenylsilane (8c): isolated in 83% yield from [2-(3-oxo-1-phenylpropyl)-1,3-dithian-2-yl]methyldiphenylsilane; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 7.46–7.29 (m, 10H), 7.21–7.17 (m, 3H), 6.81 (m, 2H), 4.64 (dd, J = 9.6, 4.3 Hz, 1H), 3.40 (dd, J = 18.3, 9.6 Hz, 1H), 2.56 (dd, J = 18.3, 4.3 Hz, 1H), 0.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.12, 198.51, 135.06, 134.80, 132.81, 132.39, 129.88, 129.52, 128.86, 127.95, 127.89, 127.48, 57.11, 46.04, −4.65.

(3-Methyl-1,4-dioxobutyl)methyldiphenylsilane (8d): isolated in 75% yield from [2-(2-methyl-3-oxopropyl)-1,3-dithian-2-yl]methyldiphenylsilane; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.64 (s, 1H), 7.61–7.57 (m, 4H), 7.48–7.36 (m, 6H), 3.12 (dd, J = 18.4, 6.7 Hz, 1H), 2.93 (m, 1H), 2.67 (dd, J = 18.4, 5.7 Hz, 1H), 1.04 (d, J = 7.3 Hz, 3H), 0.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.35, 196.26, 135.00, 132.20, 132.15, 130.28, 130.26, 128.30, 128.27, 50.09, 40.42, 13.41, −5.47.

(1,4-Dioxopentyl)methyldiphenylsilane (8e): isolated in 85% yield from [2-(3-oxobutyl)-1,3-dithian-2-yl]methyldiphenylsilane; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (m, 4H), 7.47–7.38 (m, 6H), 2.94 (t, J = 6.1 Hz, 2H), 2.64 (t, J = 6.1 Hz, 2H), 2.17 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.06, 195.84, 134.99, 132.46, 128.26, 43.10, 35.64, 29.85, −5.43.

[2-[3-(1,3-Dioxolan-2-yl)propyl]-1,3-dithian-2-yl]methyldiphenylsilane. The general alkylation procedure described above was followed with the following exception: After formation of the lithio-1,3-dithiane of **20**, HMPA (1 equiv) was added. Alkylation with 2-(3-chloropropyl)-1,3-dioxolane (1.4 equiv) for 2 h at −78 °C, warming to room temperature overnight, workup, and flash chromatography gave the title compound in 96% yield. Recrystallization from petroleum ether gave a white solid: mp 56–57 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (m, 4H), 7.44–7.36 (m, 6H), 4.68 (t, J = 4.1 Hz, 1H), 3.88–3.75 (m, 4H), 3.01 (ddd, J = 14.1, 11.6, 3.2 Hz, 2H), 2.44 (ddd, J = 14.1, 4.2, 4.0 Hz, 2H), 2.23 (m, 2H), 2.03–1.86 (m, 2H), 1.55–1.50 (m, 4H), 0.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.87, 134.22, 129.56, 127.52, 104.20, 64.74, 39.13, 37.70, 33.84, 24.64, 24.02, 21.81, −3.91.

[2-[3-(2-Methyl-1,3-dioxolan-2-yl)propyl]-1,3-dithian-2-yl]methyldiphenylsilane. The general alkylation procedure described above was followed with the following exception: After formation of the lithio-1,3-dithiane of **20**, HMPA (1 equiv) was added. Alkylation with 2-(3-chloropropyl)-2-methyl-1,3-dioxolane (1.5 equiv) for 1 h at −25 °C gave the title compound in 94% yield. Recrystallization from petroleum ether gave colorless prisms: mp 80–82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (br d, J = 7.5 Hz, 4H), 7.44–7.36 (m, 6H), 3.88–3.71 (m, 4H), 3.02 (ddd, J = 14.0, 13.0, 2.9 Hz, 2H), 2.44 (ddd, J = 14.0, 4.1, 3.7 Hz, 2H), 2.19 (m, 2H), 2.02–1.87 (m, 2H), 1.48 (m, 4H), 1.18 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.84, 134.30, 129.55, 127.52, 109.75, 64.56, 39.32, 39.18, 37.97, 24.68, 23.98, 23.88, 22.03, −4.00.

[2-(4-Oxobutyl)-1,3-dithian-2-yl]methyldiphenylsilane. Following the general procedure for acetal hydrolysis

(24) Sterzycki, R. *Synthesis* **1979**, 724.

described above, the title compound was isolated in 85% yield from [2-[3-(1,3-dioxolan-2-yl)propyl]-1,3-dithian-2-yl]methyldiphenylsilane. Recrystallization from petroleum ether gave white needles: mp 82–83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.52 (s, 1H), 7.81 (m, 4H), 7.44–7.36 (m, 6H), 3.01 (ddd, J = 14.1, 11.8, 3.0 Hz, 2H), 2.44 (ddd, J = 14.1, 4.2, 3.9 Hz, 2H), 2.26 (t, J = 6.9 Hz, 2H), 2.19 (m, 2H), 2.02–1.87 (m, 2H), 1.75–1.68 (m, 2H), 0.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.10, 135.79, 133.95, 129.71, 127.60, 43.65, 38.83, 37.21, 24.52, 23.94, 20.03, −4.00.

[2-(4-Oxopentyl)-1,3-dithian-2-yl]methyldiphenylsilane. A solution of [2-[3-(2-methyl-1,3-dioxolan-2-yl)propyl]-1,3-dithian-2-yl]methyldiphenylsilane (5.10 g, 11.47 mmol) and PPTS (300 mg, 1.14 mmol) in acetone (200 mL) was heated at reflux for 8 h. The mixture was concentrated *in vacuo*, and the residue was flash chromatographed on silica gel (20% ether in hexanes) to provide the title compound (4.59 g, 100%) as a white solid. Recrystallization from petroleum ether gave white crystals: mp 92–93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, J = 7.8, 1.4 Hz, 4H), 7.44–7.35 (m, 6H), 3.03 (ddd, J = 14.5, 11.9, 3.1 Hz, 2H), 2.43 (ddd, J = 14.5, 4.2, 3.9 Hz, 2H), 2.26 (t, J = 7.0 Hz, 2H), 2.16 (m, 2H), 2.03–1.86 (m, 2H), 1.98 (s, 3H), 1.66 (m, 2H), 0.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.51, 135.89, 134.19, 129.68, 127.61, 43.63, 39.00, 37.27, 29.55, 24.63, 24.00, 21.86, −3.99.

(1,5-Dioxopentyl)methyldiphenylsilane, 9a. Following the general procedure for dithiane hydrolysis described above, the title compound was isolated in 65% yield from [2-(4-oxobutyl)-1,3-dithian-2-yl]methyldiphenylsilane as a clear oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (t, J = 1.4 Hz, 2H), 7.58 (m, 4H), 7.47–7.38 (m, 6H), 2.71 (t, J = 6.9 Hz, 2H), 2.36 (td, J = 7.1, 1.4 Hz, 2H), 1.82 (br qt, J = 7.0 Hz, 2H), 0.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.93, 194.37, 134.96, 132.39, 130.22, 128.27, 48.23, 42.96, 14.64, −5.47.

(1,5-Dioxohexyl)methyldiphenylsilane (9c). Following the general procedure for dithiane hydrolysis described above, the title compound was isolated in 81% yield from [2-(4-oxopentyl)-1,3-dithian-2-yl]methyldiphenylsilane: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (m, 4H), 7.47–7.38 (m, 6H), 2.69 (t, J = 7.0 Hz, 2H), 2.34 (t, J = 7.0 Hz, 2H), 2.04 (s, 3H), 1.76 (q, J = 7.0 Hz, 2H), 0.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.45, 193.86, 134.93, 132.45, 130.14, 128.20, 48.35, 42.50, 29.76, 16.23, −5.47.

[2-(2-Ethyl)-1,3-dithian-2-yl]methyldiphenylsilane. Following the general alkylation procedure described above, (1,3-dithian-2-yl)methyldiphenylsilane was alkylated with ethyl bromide (1.2 equiv) for 1h at −78 °C to provide the title compound in 95% yield. Recrystallization from petroleum ether provided colorless prisms: mp 89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (m, 4H), 7.45–7.36 (m, 6H), 3.01 (br ddd, J = 14.1, 3.0 Hz, 2H), 2.44 (ddd, J = 14.1, 4.0, 3.9 Hz, 2H), 2.27 (q, J = 7.4 Hz, 2H), 2.02–1.87 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H), 0.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.87, 134.41, 129.57, 127.54, 40.03, 30.63, 24.69, 23.91, 12.08, −3.90.

(1-Oxopropyl)methyldiphenylsilane (21). To a stirred solution of [2-(2-ethyl)-1,3-dithian-2-yl]methyldiphenylsilane (4.60 g, 18.08 mmol) in acetone (150 mL) at room temperature was added dropwise from an addition funnel over 30 min chloramine-T hydrate[25] (12.15 g, 53.37 mmol). The mixture was poured into brine, extracted with ether, dried ($MgSO_4$), and concentrated *in vacuo*. Flash chromatography of the residue on silica gel (4% ether in petroleum ether) afforded the title compound (2.45 g, 72%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (m, 4H), 7.48–7.38 (m, 6H), 2.70 (q, J = 7.1 Hz, 2H), 0.95 (t, J = 7.1 Hz, 3H), 0.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.35, 134.96, 132.82, 130.05, 128.16, 42.97, 6.12, −5.33.

(1-Oxopropyl)methyldiphenylsilane Dimethylhydrazone. **21** (1.80 g, 7.07 mmol) and PPTS (180 mg, 0.71mmol) were stirred in dimethylhydrazine (30 mL) for 30 min at room temperature. Concentration *in vacuo* and flash chromatography of the residue on silica gel (17% ether in hexanes) afforded the title compound as a white solid (1.69 g, 81%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (m, 4H), 7.37 (m, 6H), 2.30 (q, J = 7.4 Hz, 2H), 2.07 (s, 6H), 0.99 (t, J = 7.4 Hz, 3H), 0.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.32, 137.29, 134.53, 128.77, 127.62, 46.91, 30.84, 11.71, −1.67.

(5,5-Dimethoxy-2-methyl-1-oxopentyl)methyldiphenylsilane Dimethylhydrazone. To a freshly prepared solution of LDA (7.14 mmol) in THF (40 mL) at 0 °C was added dropwise with stirring a solution of (1-oxopropyl)methyldiphenylsilane dimethylhydrazone (1.93 g, 6.51mmol) in THF (10 mL).[13] After 2 h at 0 °C, HMPA (2.5 mL) was added and stirring was continued for 10 min. The mixture was cooled to −78 °C and a solution of 3-bromopropionaldehyde dimethyl acetal (1.80 mL, 13.19 mmol) in THF (5 mL) was added dropwise. After reaction for 2 h at −78 °C, the mixture was warmed to room temperature, diluted with ether, washed with aqueous saturated $NaHCO_3$, dried (K_2CO_3), and concentrated *in vacuo*. Flash chromatography of the residue on silica gel (20% ether in hexanes containing 1% triethylamine) provided the title compound (2.15 g, 83%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (m, 4H), 7.34 (m, 6H), 4.27 (t, J = 5.7 Hz, 1H), 3.29 (s, 3H), 3.27 (s, 3H), 2.40 (sex, J = 6.8 Hz, 1H), 2.03 (s, 6H), 1.79–1.70 (m, 1H), 1.61–1.44 (m, 2H), 1.35–1.27 (m, 1H), 1.03 (d, J = 6.8 Hz, 3H), 0.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.40, 137.85, 137.59, 134.54, 128.67, 128.65, 127.60, 104.48, 52.74, 52.20, 46.93, 38.85, 30.44, 29.29, 18.55, −1.33.

(2-Methyl-1,5-dioxopentyl)methyldiphenylsilane (9b). To a stirred solution of (5,5-dimethoxy-2-methyl-1-oxopentyl)-methyldiphenylsilane dimethylhydrazone (1.10 g, 2.26 mmol) in acetone (100 mL) at 0 °C was added wet Amberlyst-15 (10.0 g) in portions over 5 min. The solution was warmed to room temperature over 20 min and then filtered through Celite, dried (K_2CO_3), and concentrated *in vacuo*. Rapid flash chromatography of the residue on a short column of silica gel (28% ether in hexanes) provided the title compound (330 mg, 41%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.54 (t, J = 1.3 Hz, 1H), 7.60 (m, 4H), 7.46–7.38 (m, 6H), 3.02 (br sex, J = 6.8 Hz, 1H), 2.28–2.14 (m, 2H), 1.91 (m, 1H), 1.48 (m, 1H), 0.90 (d, J = 7.0 Hz, 3H), 0.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.74, 191.35, 134.97, 133.93, 130.15, 128.21, 49.77, 41.25, 29.99, 14.60, −4.92.

General Procedure for the Annulation of Acylsilane Dicarbonyl Substrates.[7] A stirred solution of the 1,4- or 1,5-dicarbonyl substrate in CH_2Cl_2 (0.045 M) containing **3** (1.2 equiv) was cooled to −78 °C. A 0.1 M solution of TMSOTf (0.2 equiv) in CH_2Cl_2 was added dropwise via cannula, and stirring was continued for 2–6 h at −78 °C. The reaction was quenched by the addition of pH 7.0 phosphate buffer, and the mixture was warmed to room temperature, extracted with CH_2Cl_2, dried (Na_2SO_4), and concentrated *in vacuo*. Flash chromatography of the residue on silica gel (ether in hexanes) provided the bicyclic ethers as a mixture of isomers (C_2 epimers and enol).

To a stirred solution of bicyclic ether in CH_2Cl_2 (10 mL) at room temperature were added pyridine (0.5 mL), acetic anhydride (1.0 mL), and DMAP (cat.), and stirring was continued for 3–16 h. The mixture was concentrated *in vacuo*. Flash chromatography of the residue on silica gel followed by Kugelrohr distillation provided the bicyclic enol acetates.

(1*R,5*R**)-3-Acetoxy-2-(methoxycarbonyl)-5-(methyldiphenylsilyl)-8-oxabicyclo[3.2.1]oct-2-ene (11a).** Isolated in 82% yield from **8a**; oven temperature (ot) 130–140 °C/0.07 mmHg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (m, 4H), 7.45–7.34 (m, 6H), 5.11 (d, J = 5.5 Hz, 1H), 3.71 (s, 3H), 2.81 (d, J = 18.0 Hz, 1H), 2.24–2.13 (m, 2H), 2.15 (s, 3H), 1.98–1.84 (m, 2H), 1.89 (d, J = 18.0 Hz, 1H), 0.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.37, 163.58, 154.61, 135.23, 135.14, 134.03, 133.53, 129.73, 129.68, 127.96, 127.90, 122.58, 74.62, 73.56, 51.60, 40.02, 37.29, 32.98, 20.91, −6.82; IR (neat) 2952, 1766, 1723, 1662, 1429, 1359, 1266, 1195, 1170, 1116, 787, 728, 701 cm^{-1}; LRMS (EI$^+$) m/z 379 (66), 347 (9), 320 (8), 197 (100), 137 (17), 105 (20), 83 (12), 43 (70). Anal. Calcd for $C_{24}H_{26}O_5Si$: C, 68.20; H, 6.21. Found: C, 68.05; H, 6.26.

(1*R,5*R**,6*S**)-3-Acetoxy-2-(methoxycarbonyl)-6-methyl-5-(methyldiphenylsilyl)-8-oxabicyclo[3.2.1]oct-2-ene**

(25) Huurdeman, W. F. J.; Wynberg, H.; Emerson, D. W. *Tetrahedron Lett.* **1971**, 3449.

(11b): isolated in 58% yield from **8b** as a 3.5:1 mixture of diastereomers; ot 140 −150 °C/0.07 mmHg; ^{1}H NMR (400 MHz, $CDCl_3$) (major diastereomer) δ 7.69 (m, 4H), 7.41−7.33 (m, 6H), 5.12 (d, J = 6.2 Hz, 1H), 3.72 (s, 3H), 2.82 (d, J = 18.1 Hz, 1H), 2.61−2.52 (m, 1H), 2.48 (dd, J = 11.5, 8.0 Hz, 1H), 2.15 (s, 3H), 2.07 (d, J = 18.1 Hz, 1H), 1.73−1.64 (m, 1H), 0.96 (d, J = 7.0 Hz, 3H), 0.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (major diastereomer) δ 168.47, 163.55, 155.04, 135.87, 135.40, 135.20, 135.10, 129.42, 129.33, 127.87, 127.83, 122.64, 78.79, 73.31, 51.57, 47.69, 42.86, 41.07, 20.90, 20.41, −4.71; IR (neat) 2958, 1766, 1722, 1662, 1429, 1359, 1263, 1194, 1171, 787, 728, 701 cm^{-1}; LRMS (EI$^+$) m/z 393 (48), 320 (13), 197 (100), 165 (8), 137 (16), 105 (11), 43 (22). Anal. Calcd for $C_{25}H_{28}O_5Si$: C, 68.78; H, 6.47. Found: C, 68.30; H, 6.52.

(1*R,5*R**,6*R**)-3-Acetoxy-2-(methoxycarbonyl)-5-(methyldiphenylsilyl)-6-phenyl-8-oxabicyclo[3.2.1]oct-2-ene (11c)**: isolated in 68% yield from **8c** as a 51:1 mixture of diastereomers; ot 160 −165 °C/0.07 mmHg; ^{1}H NMR (400 MHz, $CDCl_3$) (major diastereomer) δ 7.43−7.38 (m, 4H), 7.34−7.19 (m, 6H), 7.02 (m, 1H), 6.88 (br t, 2H), 6.83 (br d, 2H), 5.38 (d, J = 6.3 Hz, 1H), 3.74 (s, 3H), 3.55 (br t, J = 8.5, 8.0 Hz, 1H), 2.93 (d, J = 18.3 Hz, 1H), 2.63 (dd, J = 12.5, 8.3 Hz, 1H), 2.41 (br ddd, J = 12.5, 8.0, 6.3 Hz, 1H), 2.24 (d, J = 18.3 Hz, 1H), 2.16 (s, 3H), 0.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (major diastereomer) δ 168.51, 163.49, 154.17, 141.29, 135.98, 135.02, 134.83, 134.79, 129.87, 129.17, 129.01, 127.67, 127.54, 127.46, 126.43, 123.08, 80.70, 73.91, 55.23, 51.69, 46.79, 41.66, 20.94, −5.84; IR (neat) 3070, 2951, 1768, 1722, 1664, 1429, 1357, 1257, 1163, 1123, 785, 731, 701 cm^{-1}; LRMS (EI$^+$) m/z 498 (1), 427 (13), 351 (12), 197 (100), 155 (11), 105 (11), 91 (9), 43 (24). Anal. Calcd for $C_{30}H_{30}O_5Si$: C, 72.26; H, 6.07. Found: C, 72.55; H, 6.31.

(1*R,5*R**,7*R**)-3-Acetoxy-2-(methoxycarbonyl)-7-methyl-5-(methyldiphenylsilyl)-8-oxabicyclo[3.2.1]oct-2-ene (11d)**: isolated in 63% yield from **8d** as an 18.5:1 mixture of diastereomers; ot 140−150 °C/0.07 mmHg; ^{1}H NMR (400 MHz, $CDCl_3$) (major diastereomer) δ 7.68−7.65 (m, 4H), 7.44−7.35 (m, 6H), 4.61 (s, 1H), 3.71 (s, 3H), 2.79 (br d, J = 18.1 Hz, 1H), 2.57 (m, 1H), 2.14 (s, 3H), 2.12 (dd, J = 12.7, 8.3 Hz, 1H), 1.87 (d, J = 18.1 Hz, 1H), 1.67 (br d, J = 12.7 Hz, 1H), 0.74 (d, J = 7.0 Hz, 3H), 0.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (major diastereomer) δ 168.37, 163.69, 154.16, 135.40, 135.29, 133.74, 133.39, 129.71, 127.89, 122.58, 79.40, 75.13, 51.62, 44.78, 41.66, 39.45, 20.89, 20.56, −6.92; IR (neat) 2957, 1770, 1723, 1661, 1429, 1360, 1265, 987, 787, 728, 701 cm^{-1}; LRMS (EI$^+$) m/z 436 (2), 393 (42), 320 (10), 197 (100), 165 (9), 137 (17), 105 (12), 43 (38). Anal. Calcd for $C_{25}H_{28}O_5Si$: C, 68.78; H, 6.47. Found: C, 68.61; H, 6.59.

(1*R,5*R**)-3-Acetoxy-2-(methoxycarbonyl)-1-methyl-5-(methyldiphenylsilyl)-8-oxabicyclo[3.2.1]oct-2-ene (11e).** The general annulation procedure described above was followed except that 1.5 equiv of **3** and 0.4 equiv of TMSOTf were used. For formation of the enol acetate a stirred solution of the bicyclic ether in THF (10 mL) was heated at reflux for 24 h with pyridine (25 equiv), acetic anhydride (25 equiv), and DMAP (cat.). After aqueous workup, flash chromatography, and Kugelrohr distillation, the title compound was isolated in 70% yield from **8e**: ot 140−150 °C/0.07 mmHg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (dd, J = 7.7, 1.5 Hz, 2H), 7.63 (dd, J = 7.8, 1.4 Hz, 2H), 7.43−7.33 (m, 6H), 3.73 (s, 3H), 2.87 (d, J = 17.4 Hz, 1H), 2.57 (m, 1H), 2.19 (br t, 1H), 2.08 (s, 3H), 1.90 (ddd, J = 12.6, 8.5, 8.5 Hz, 1H), 1.80 (d, J = 17.4 Hz, 1H), 1.56 (m, 1H), 1.56 (s, 3H), 0.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.28, 165.44, 150.54, 135.26, 135.19, 134.32, 133.74, 129.64, 129.58, 127.87, 127.80, 126.59, 80.49, 74.33, 51.52, 43.91, 38.81, 34.23, 21.52, 20.81, −6.86; IR (neat) 2951, 1762, 1718, 1654, 1428, 1342, 1288, 1234, 1199, 1170, 1112, 1072, 1049, 792, 728, 703 cm^{-1}; HRMS calcd for $C_{25}H_{28}O_5Si$ 436.1706, found 436.1688; LRMS (EI$^+$) m/z 436 (2), 393 (13), 361 (12), 333 (8), 197 (100), 165 (13), 137 (15), 105 (14), 43 (42).

(1*R,5*R**)-3-Acetoxy-2-(methoxycarbonyl)-5-(methyldiphenylsilyl)-9-oxabicyclo[3.3.1]non-2-ene (13a)**: isolated in 85% yield from **9a**; ot 150−160 °C/0.07 mmHg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (m, 4H), 7.43−7.34 (m, 6H), 4.94 (br s, 1H), 3.72 (s, 3H), 2.82 (d, J = 19.2 Hz, 1H), 2.20 (s, 3H), 2.03−1.88 (m, 3H), 1.98 (d, J = 19.2 Hz, 1H), 1.68−1.60 (m, 1H), 1.55 (m, 1H), 1.43 (br d, J = 10.7 Hz, 1H), 0.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.60, 163.52, 157.10, 135.55, 135.43, 133.97, 129.52, 127.80, 119.29, 67.81, 67.61, 51.57, 34.91, 32.93, 28.08, 20.89, 24.36, −7.09; IR (neat) 2948, 1766, 1722, 1669, 1429, 1364, 1254, 1200, 1137, 1088, 790, 729, 701 cm^{-1}; LRMS (EI$^+$) m/z 436 (1), 379 (22), 298 (17), 238 (13), 197 (100), 148 (37), 105 (24), 77 (8), 43 (95). Anal. Calcd for $C_{25}H_{28}O_5Si$: C, 68.78; H, 6.47. Found: C, 69.20; H, 6.64.

(1*R,5*R**,8*R**)-3-Acetoxy-2-(methoxycarbonyl)-8-methyl-5-(methyldiphenylsilyl)-9-oxabicyclo[3.3.1]non-2-ene (13b)**: isolated in 66% yield from **9b** as a 4:1 mixture of diastereomers; ot 150−160 °C/0.07 mmHg; ^{1}H NMR (400 MHz, $CDCl_3$) (major diastereomer) δ 7.60 (m, 4H), 7.40−7.29 (m, 6H), 4.96 (d, J = 2.7 Hz, 1H), 3.73 (s, 3H), 2.89 (d, J = 19.4 Hz, 1H), 2.20 (m, 1H), 2.17 (s, 3H), 2.14 (d, J = 19.4 Hz, 1H), 1.63 (m, 1H), 1.41 (m, 1H), 1.24 (m, 1H), 1.07 (d, J = 7.0 Hz, 3H), 0.83 (m, 1H), 0.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (major diastereomer) δ 168.54, 163.54, 156.61, 135.74, 135.54, 134.98, 134.85, 129.41, 129.16, 127.78, 127.70, 119.30, 71.76, 67.63, 51.55, 37.17, 36.77, 23.06, 21.75, 20.87, 18.51, −5.01; IR (neat) 2951, 1772, 1670, 1429, 1363, 1259, 1199, 1171, 1136, 1089, 1022, 789, 727, 701 cm^{-1}; LRMS (CI$^+$(NH$_3$)) m/z 468 (100), 451 (14), 331 (15), 299 (12), 214 (17), 154 (7), 78 (9). Anal. Calcd for $C_{26}H_{30}O_5Si$: C, 69.30; H, 6.72. Found: C, 69.18; H, 6.86.

(1*R,5*R**)-3-Acetoxy-2-(methoxycarbonyl)-1-methyl-5-(methyldiphenylsilyl)-9-oxabicyclo[3.3.1]non-2-ene (13c)**: prepared according to the general procedure for **8e** to provide the title compound in 83% yield from **9c** as a ≥28:1 mixture of regioisomers; ot 155−165 °C/0.07 mmHg; ^{1}H NMR (400 MHz, $CDCl_3$) (major regioisomer) δ 7.68 (m, 4H), 7.43−7.33 (m, 6H), 3.73 (s, 3H), 2.85 (d, J = 18.5 Hz, 1H), 2.13 (s, 3H), 2.10 (m, 1H), 1.96−1.83 (m, 2H), 1.87 (d, J = 18.5 Hz, 1H), 1.60−1.50 (m, 2H), 1.43 (s, 3H), 1.40 (br d, J = 11.1 Hz, 1H), 0.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (major regioisomer) δ 168.33, 165.57, 152.53, 135.57, 135.45, 134.25, 134.19, 129.45, 127.75, 123.79, 71.80, 67.51, 51.47, 34.73, 33.64, 33.20, 26.46, 20.79, 16.50, −7.28; IR (neat) 2935, 1761, 1721, 1429, 1337, 1253, 1204, 1162, 1111, 1075, 1043, 792, 726, 701 cm^{-1}; LRMS (EI$^+$) m/z 408 (10), 390 (22), 330(16), 253 (17), 197 (100), 165 (8), 137 (19), 105 (12), 67 (10), 43 (15). Anal. Calcd for $C_{26}H_{30}O_5Si$: C, 69.30; H, 6.72. Found: C, 69.21; H, 6.83.

2-(Methoxycarbonyl)-1-methyl-5-(methyldiphenylsilyl)-9-oxabicyclo[3.3.1] nonan-3-one (22). The general annulation procedure described above was followed except that the enol acetate was not prepared: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 0.18H), 7.76−7.62 (m, 4H), 7.47−7.28 (m, 6H), 3.74 (s, 0.54H), 3.73 (s, 0.54H), 3.56 (s, 1.92H), 3.36 (s, 0.18H), 3.27 (s, 0.64H), 3.20 (d, J = 16.3 Hz, 0.64H), 2.89 (d, J = 19.2 Hz, 0.18H), 2.65 (d, J = 16.3 Hz, 0.18H), 2.41 (m, 0.18H), 2.26 (d, J = 16.3 Hz, 0.18H), 2.16 (d, J = 16.3 Hz, 0.64H), 1.96 (d, J = 19.2 Hz, 0.18H), 1.91−1.73 (m, 0.82H), 1.69−1.40 (m, 5H), 1.51 (s, 0.54H), 1.36 (s, 0.54H), 1.31 (s, 1.92H), 0.64 (s, 1.92H), 0.60 (s, 0.54H), 0.57 (s, 0.54H).

1-Methyl-5-(methyldiphenylsilyl)-9-oxabicyclo[3.3.1]-nonan-3-one (23). A stirred solution of **22** (660 mg, 1.617 mmol) and lithium chloride (143 mg, 3.373 mmol) in DMSO (15 mL) containing 2% water was heated at 130 °C for 2 h[25] and then cooled to room temperature, diluted with CH_2Cl_2, washed with water and brine, dried (Na_2SO_4), and concentrated *in vacuo*. Flash chromatography of the residue on silica gel (14% ether in hexanes) provided the title compound (515 mg, 91%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (m, 4H), 7.44−7.35 (m, 6H), 2.62 (d, J = 15.7 Hz, 1H), 2.40 (dd, J = 15.6, 1.5 Hz, 1H), 2.32 (d, J = 15.6 Hz, 1H), 2.21 (dd, J = 15.7, 1.5 Hz, 1H), 1.94−1.89 (m, 1H), 1.64−1.46 (m, 5H), 1.37 (s, 3H), 0.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.41, 135.54, 135.50, 134.00, 133.91, 129.52, 129.51, 127.76, 127.74, 73.51, 71.06, 52.07, 45.93, 36.82, 31.13, 30.46, 17.19, −7.35; IR (neat) 2932, 1709, 1428, 1293, 1247, 1110, 803, 726, 700 cm^{-1}; HRMS calcd for $C_{22}H_{26}O_2Si$ 350.1702, found 350.1694; LRMS (EI$^+$) m/z 350 (3), 335 (7), 292 (37), 239 (13), 197 (100), 165 (7), 137 (42), 105 (15), 43 (12).

1-Methyl-9-oxabicyclo[3.3.1]nonan-3-one (24). A stirred solution of **23** (515 mg, 1.47 mmol) and cesium fluoride (2.20 g, 14.48 mmol) in DMSO containing 2% water was heated at

130 °C for 3 h. The mixture was cooled to room temperature, diluted with ether, washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. Flash chromatography of the residue on silica gel (33% ether in pentane) provided the title compound (175 mg, 77%): ^1H NMR (400 MHz, $CDCl_3$) δ 4.45 (br t, 1H), 2.63 (dd, J = 15.8, 7.5 Hz, 1H), 2.31 (s, 2H), 2.24 (d, J = 15.8 Hz, 1H), 1.86–1.77 (m, 1H), 1.56–1.46 (m, 5H), 1.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.88, 62.96, 69.98, 51.81, 44.93, 36.70, 30.64, 29.75, 16.64; IR (neat) 2934, 1715, 1292, 1236, 1200, 1151, 1028, 851, 776 cm^{-1}; HRMS calcd for $C_9H_{14}O_2$ 154.0994, found 154.0983; LRMS (EI^+) m/z 154 (13), 96 (19), 84 (40), 68 (11), 58 (15), 43 (100), 35 (7).

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Supplementary Material Available: Copies of ^1H and ^{13}C NMR spectra of compounds for which no elemental analysis was obtained (61 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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