Diastereoselective Nucleophilic Substitution Reactions of Oxasilacyclopentane Acetals: Application of the "Inside Attack" Model for Reactions of Five-Membered Ring Oxocarbenium Ions

Teresa J. Bear, Jared T. Shaw, and K. A. Woerpel*

Department of Chemistry, University of California, Irvine, California 92697-2025

kwoerpel@uci.edu

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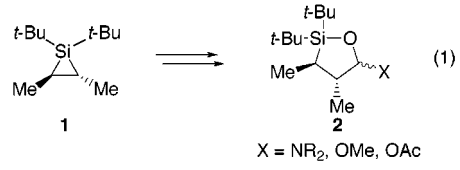
The additions of nucleophiles to oxocarbenium ions derived from oxasilacyclopentane acetates proceeded with high diastereoselectivity in most cases. Sterically demanding nucleophiles such as the silyl enol ether of diethyl ketone add to the face opposite the C-2 substituent. These reactions establish the syn stereochemistry about the newly formed carbon−carbon bond. Small nucleophiles such as allyltrimethylsilane do not show this same stereochemical preference: they add from the same face as the substituent in C-2-substituted oxocarbenium ions. The stereoselectivities exhibited by both small and large nucleophiles can be understood by application of the "inside attack" model for five-membered ring oxocarbenium ions developed previously for tetrahydrofuran-derived cations. This stereoelectronic model requires attack of the nucleophile from the face of the cation that provides the products in their lower energy staggered conformations. Small nucleophiles add to the "inside" of the lower energy ground-state conformer of the oxocarbenium ion. In contrast, sterically demanding nucleophiles add to the inside of the envelope conformer where approach is anti to the C-2 substituent of the oxocarbenium ion, regardless of the ground-state conformer population.

Introduction

In the course of research aimed at developing the reactions of silacyclopropanes as methods for stereoselective organic synthesis,[1] we developed procedures for converting silacyclopropanes such as **1** to oxasilacyclopentane acetals **2** in high yield and with a high degree of stereochemical control (eq 1). We envisioned that these acetals would be useful synthetic intermediates, because Lewis acid-mediated nucleophilic substitution reactions employing allylic silanes or silyl enol ethers should afford oxasilacyclopentanes **3**. The configuration at the newly formed stereogenic center would be established by attack on the intermediate oxocarbenium ion from the face opposite the substituent at C-2. The resulting product could be converted to diol **4** by oxidation of the carbon−silicon bond (eq 2).[2−6]



In this paper, we report full details of the diastereoselective reactions of oxasilacyclopentane acetals such as **2** with carbon nucleophiles. We evaluated the reactions of a range of oxasilacyclopentane acetals with various substituents at both C-2 and C-3 with various nucleophiles to determine the generality and limitations of the idea described in eq 2. Reactions of the *trans*-2,3-dimethyl acetal **2** provided products where the nucleophile had indeed approached the putative oxocarbenium ion intermediate from the face opposite the methyl group at C-2 as anticipated.[7] In several cases, however, the stereoselectivities were high, but the sense of selectivity was opposite what might be predicted on the basis of a cursory examination of the substrate.[8] These seemingly contrasteric results, as well as the less surprising selectivities, can be accommodated by application of our recently reported "inside attack" model to explain stereoselective reactions of tetrahydrofuran-derived oxocarbenium ions.[9] The results and analysis in this paper demonstrate that the inside attack model[9] can be applied with success to systems that differ significantly from those for which the model was originally derived.[10] Furthermore, the experiments described here suggest that oxasilacyclopentane acetals are useful synthetic intermediates.

(1) Franz, A. K.; Woerpel, K. A. *Acc. Chem. Res.* **2000**, *33*, 813−820.
(2) Tamao, K.; Ishida, N.; Tanaka, T.; Kumada, M. *Organometallics* **1983**, *2*, 1694−1696.
(3) Fleming, I. *Chemtracts: Org. Chem.* **1996**, *9*, 1−64.
(4) Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599−7662.
(5) Tamao, K. *Advances in Silicon Chemistry*; JAI: Greenwich, CT, 1996; Vol. 3; pp 1−62.
(6) Smitrovich, J. H.; Woerpel, K. A. *J. Org. Chem.* **1996**, *61*, 6044−6046.
(7) Shaw, J. T.; Woerpel, K. A. *Tetrahedron* **1997**, *53*, 16597−16606.
(8) Shaw, J. T.; Woerpel, K. A. *J. Org. Chem.* **1997**, *62*, 6706−6707.
(9) Larsen, C. H.; Ridgway, B. H.; Shaw, J. T.; Woerpel, K. A. *J. Am. Chem. Soc.* **1999**, *121*, 12208−12209.
(10) Iminium ions are believed to undergo nucleophilic attack by transition structures similar to those for oxocarbenium ions: Bur, S. K.; Martin, S. F. *Org. Lett.* **2000**, *2*, 3445−3447.

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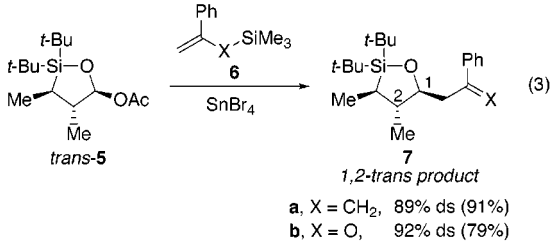
Nucleophilic Substitution Reactions

Oxasilacyclopentane acetals were prepared by stereospecific and regioselective insertion reactions of carbonyl compounds into silacyclopropanes.[7,11,12] In earlier publications of these reactions,[7,11,12] we isolated and purified the products of insertion. We have found that it is operationally easier to carry the insertion products through subsequent steps without purification and only purify the desired oxasilacyclopentane acetal that would be used for the nucleophilic substitution reaction. The details of the syntheses of these substrates are included as Supporting Information. In early experiments, the acetate derivatives provided the highest yields of nucleophilic substitution products with the fewest side products, so we focused on these substrates.

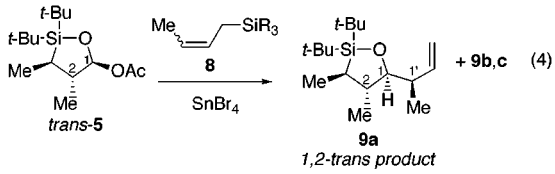
2,3-Dimethyl-Substituted Oxasilacyclopentane Acetals. The acetate *trans*-**5**[13] underwent stereoselective nucleophilic substitution reactions with both (2-phenylallyl)trimethylsilane[14,15] (**6a**) and 1-(trimethylsilyloxy)styrene[16] (**6b**; eq 3).[17] These reactions proceeded with



(3)

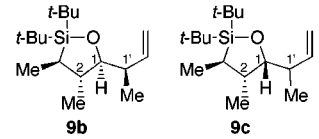
high 1,2-trans diastereoselectivity,[18] indicating that the nature of the nucleophilic alkene does not determine the stereoselectivity of its reactions.[19] A variety of Lewis acids, solvents, and temperatures were investigated for these reactions to develop optimal conditions.[7] The optimized conditions employed $SnBr_4$ as the Lewis acid and CH_2Cl_2 as the solvent. Conducting the reactions at low temperatures (−78 °C) minimized competing side reactions such as overadditions in the case of silyl enol ethers. These conditions were used for all nucleophilic substitution reactions reported here.

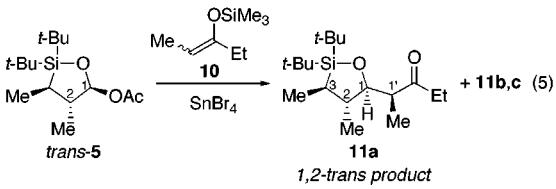
Reactions with internal alkenes allowed for stereochemical control at the exocyclic stereocenter as well as the ring junction. Substitutions by various (*E*)- and (*Z*)-crotylsilanes **8**[20−25] were not highly stereoselective (eq 4), but the 1,2-trans products **9a** and **9b** predominated in all cases just as they had with the other nucleophiles (eq 3). The newly formed carbon−carbon bond (C-1−C-1′) was formed with syn diastereoselectivity (up to 86%). When the (*E*)-silyl[26] and (*Z*)-silyl[27] enol ethers of 3-pentanone (**10**) were employed as the nucleophiles (eq 5), the



(4)

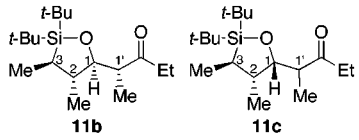
E:*Z* Ratio of **8**	Diastereomer Ratio **9a** : **9b** : **9c**	Yield
5 : >95 (R = Me)	75 : 11 : 14	91%
>95 : 5 (R = Me)	78 : 21 : 1	-
5 : >95 (R = Ph)	37 : 25 : 38	-
90 : 10 (R = Ph)	68 : 28 : 4	-





(5)

E:*Z* Ratio of **10**	Diastereomer Ratio **11a** : **11b** : **11c**	Yield
97 : 3	92 : 5 : 3	100%
10 : 90	80 : 13 : 7	94%

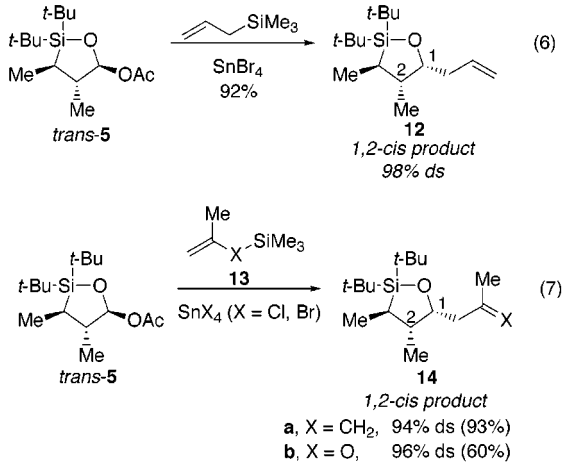


nucleophilic substitution reactions were significantly more stereoselective. The major diastereomer **11a**, whose structure was proven by X-ray crystallography,[28] was formed with high 1,2-trans selectivity, and the new carbon−carbon bond was established with high syn selectivity. The configurations of the minor products **9b**,**c** and **11b**,**c** was assigned by chemical correlation.[7,28] Although the structure of the major products did not depend on the stereochemistry of the silyl enol ether, the (*E*)-isomer proved to be more selective.

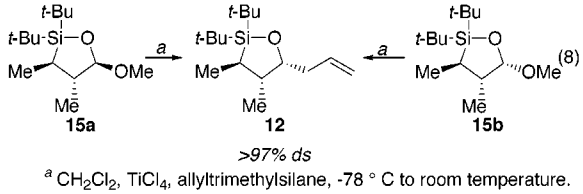
In sharp contrast to the results with the styrene nucleophiles and the internal alkenes, 1,2-cis products were formed preferentially with smaller, unhindered

(11) Franz, A. K.; Woerpel, K. A. *Angew. Chem., Int. Ed.* **2000**, *39*, 4295−4299.
(12) Franz, A. K.; Woerpel, K. A. *J. Am. Chem. Soc.* **1999**, *121*, 949−957.
(13) X-ray crystallography was used to prove the stereochemistry of this compound. The details are provided as Supporting Information.
(14) Narayanan, B. A.; Bunnelle, W. H. *Tetrahedron Lett.* **1987**, *28*, 6261−6264.
(15) For a review of the methods for the synthesis of allylsilanes, see: Sarkar, T. K. *Synthesis* **1990**, 969−983, 1101−1111.
(16) Walshe, N.; Goodwin, G.; Smith, G.; Woodward, F. *Org. Synth.* **1986**, *65*, 1−5.
(17) In all cases, stereoselectivities were determined by GC or GC−MS analysis of unpurified reaction mixtures. These selectivities were corroborated by ^1H and ^{13}C NMR spectroscopy. The yields are reported for purified products.
(18) The configuration of **7b** was determined by protection of the ketone, oxidation of the carbon−silicon bond to provide the diol, and analysis of the ^{13}C chemical shifts of the derived acetonides (Rychnovsky, S. D.; Rogers, B. N.; Richardson, T. I. *Acc. Chem. Res.* **1998**, *31*, 9−17). The structure of **7a** was proven by chemical correlation to **7b**.
(19) Mayr, H.; Patz, M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 938−957.
(20) Wrighton, M. S.; Schroeder, M. A. *J. Am. Chem. Soc.* **1974**, *96*, 6235−6237.
(21) Hayashi, T.; Kabeta, K.; Hamachi, I.; Kumada, M. *Tetrahedron Lett.* **1983**, *24*, 2865−2868.
(22) Matarasso-Tchiroukhine, E.; Cadiot, P. *J. Organomet. Chem.* **1976**, *121*, 155−168.
(23) Abel, E. W.; Rowley, R. J. *J. Organomet. Chem.* **1975**, *84*, 199−229.
(24) Leboutet, L.; Courtois, G.; Miginiac, L. *J. Organomet. Chem.* **1991**, *420*, 155−161.
(25) Rajagopalan, S.; Zweiffel, G. *Synthesis* **1984**, 113−115.
(26) Hall, P. L.; Gilchrist, J. H.; Collum, D. B. *J. Am. Chem. Soc.* **1991**, *113*, 9571−9574.
(27) Cazeau, P.; Duboudin, F.; Moulines, F.; Babot, O.; Dunogues, J. *Tetrahedron* **1987**, *43*, 2075−2088.
(28) The details are provided as Supporting Information.

terminal alkene nucleophiles. Allyltrimethylsilane underwent substitution to give the 1,2-cis product **12** with 98% diastereoselectivity (eq 6).[29] Similarly, methallyltrimethylsilane (**13a**)[30] and 2-((trimethylsilyl)oxy)propene (**13b**)[16] underwent highly selective reactions, favoring the 1,2-cis products **14a** and **14b**, respectively (eq 7).[29]

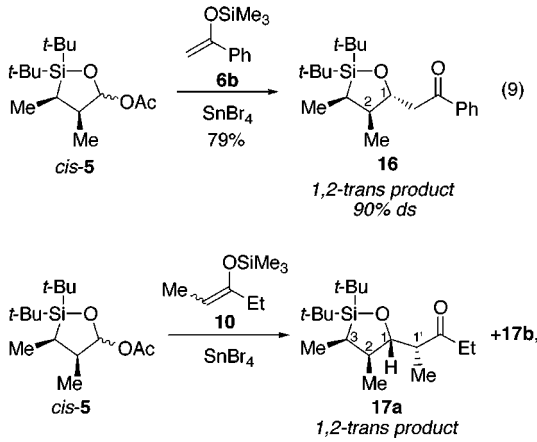


A control experiment (eq 8) suggested that an oxocarbenium ion was the reactive intermediate in the substitution reaction with allyltrimethylsilane.[31−33] The methyl



acetals **15a**,**b** were prepared separately,[34] and each epimer was independently treated with allyltrimethylsilane and $TiCl_4$ (eq 8).[35] The selectivities of these substitution reactions were within experimental error of the selectivity observed in the reaction with the acetate *trans*-**5** (eq 6). Because the stereoselectivity was independent of both the leaving group and the configuration of the acetal, we propose that these reactions proceed via a common oxocarbenium ion intermediate. If isomerization of the acetal epimers occurred during the reaction, however, a direct nucleophilic substitution reaction (S_N2) would also account for this stereochemical convergence. The control experiments shown in eq 8 cannot discount such a mechanism.

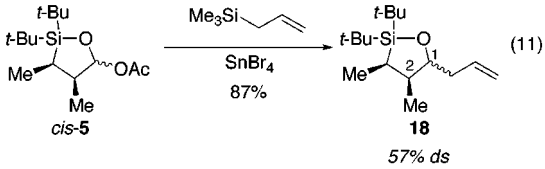
The cis-disubstituted acetate *cis*-**5**, like *trans*-**5**, underwent highly 1,2-trans-selective reactions with large nucleophiles. Substitution of *cis*-**5** with silyl enol ether **6b** provided the 1,2-trans product **16** (eq 9).[36] Substitution with the silyl enol ethers of diethyl ketone (**10**) gave the expected trans product **17a** with high diastereoselectivity (eq 10). The configuration of **17a** was proven by X-ray



E:*Z* Ratio of **10**	Diastereomer Ratio **17a** : **17b** : **17c**	Yield
5 : 95	93 : 5 : 2	79%
97 : 3	94 : 5 : 1	83%

crystallography of its 2,4-dinitrophenylhydrazone derivative.[28] As observed for *trans*-**5**, syn diastereoselectivity about the C-1−C-1′ bond was favored, and the configuration of the major product was independent of the alkene isomer of the enol silane.

The reaction of *cis*-**5** with the small nucleophile allyltrimethylsilane proceeded with low selectivity (eq 11). This behavior of *cis*-**5** is surprising when compared to the reaction with *trans*-**5** (eq 6). In defiance of intuition, when



the two methyl groups are on opposite sides of the ring (as in *trans*-**5**), attack occurs overwhelmingly from one face, but when they are on the same side (as in *cis*-**5**), the nucleophile cannot differentiate the two faces of the ring.

2- and 3-Alkyl-Substituted Oxasilacyclopentane Acetals. To elucidate the role of each alkyl substituent in the 2,3-dimethyl systems, substitution reactions on monosubstituted oxasilacyclopentane acetals were performed. Both small (methyl) and large (isopropyl) substituents were placed at both C-2 and C-3, and the reactions with both small and large nucleophiles were examined.

Nucleophilic substitution reactions of the 2-alkyloxasilacyclopentane acetates with the large nucleophile (*E*)-**10** proceeded with high 1,2-trans selectivity. The reaction

(29) The stereochemistry was proven by oxidation to the diol and conversion to the derived acetonide. The details are provided as Supporting Information.

(30) Ishihara, K.; Mouri, M.; Gao, Q.; Maruyama, T.; Furuta, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 11490−11495.

(31) There has been much discussion of the mechanism of Lewis acid-promoted acetal substitution in the literature. See, for example: (a) Mori, I.; Ishihara, K.; Flippin, L. A.; Nozaki, K.; Yamamoto, H.; Bartlett, P. A.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 6107−6115. (b) Denmark, S. E.; Almstead, N. G. *J. Org. Chem.* **1991**, *56*, 6458−6467.

(32) Sammakia has demonstrated that the $SnCl_4$-mediated reaction of dimethyl acetals proceeds through an oxonium ion intermediate: Sammakia, T.; Smith, R. S. *J. Am. Chem. Soc.* **1994**, *116*, 7915−7916.

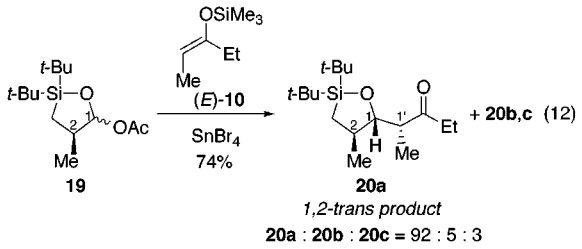
(33) Acyclic alkoxyalkyl acetates undergo substitution reactions with nucleophilic alkenes via oxonium ion intermediates: Matsutani, H.; Ichikawa, S.; Yaruva, J.; Kusumoto, T.; Hiyama, T. *J. Am. Chem. Soc.* **1997**, *119*, 4541−4542.

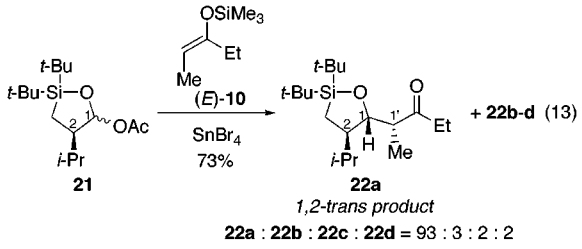
(34) We do not know the stereochemistry of the two acetals, but that knowledge is not important since we have both stereoisomers.

(35) $TiCl_4$ was used as the Lewis acid since $SnBr_4$ was not acidic enough to promote the reaction with the methyl acetals.

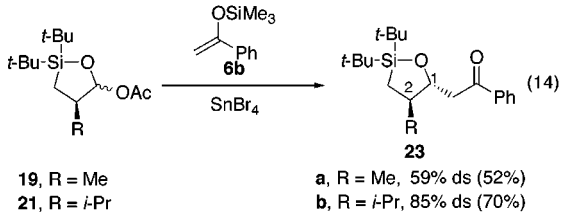
(36) The configuration of **16** was proven by conversion to the 1,3-diol acetonide. The details are provided as Supporting Information.

of the 2-methyl acetate **19** afforded predominately **20a**, which possessed 1,2-trans stereochemistry as well as high selectivity about the C-1−C-1′ bond (eq 12).[37] A similar major product (**22a**) was observed with the more hindered 2-isopropyl acetate **21** (eq 13).[38]

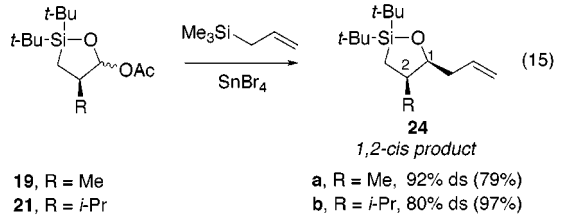




Nucleophilic substitution on the mono-alkyl-substituted acetates **19** and **21** with the alkene **6b** occurred with only modest diastereoselectivity (eq 14). In the case of the 2-isopropyl substrate **21**, the reaction was somewhat more selective, favoring the 1,2-trans product **23b**.[39]

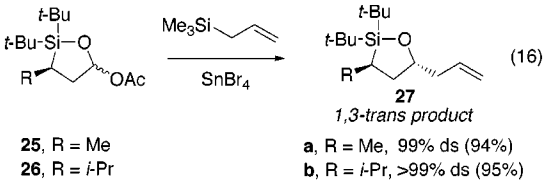


In contrast to the reactions with the larger nucleophiles **10** and **6b** (eqs 12−14), substitution by allyltrimethylsilane gave 1,2-cis products **24** (eq 15).[40] These results are



inconsistent not only with intuition but also with studies of simple 2-methyltetrahydrofuran acetals.[41,42] Although the 2-methyl-substituted acetate **19** showed high 1,2-trans selectivity with large nucleophiles (eqs 12 and 13) as Reissig observed,[41,42] in that study it was reported that reactions with allyltrimethylsilane proceeded with 1,2-trans selectivity as well (albeit of lower magnitude).[41,42] We have previously demonstrated that a 2-methyltetrahydrofuran acetal with geminal substitution at C-4 (i.e., the carbon analogue of **19**) reacts with 1,2-cis selectivity comparable to the acetate **19**.[43] The attenuated 1,2-cis selectivity for the isopropyl-substituted acetal **21** suggests that developing steric interactions between the nucleophile and the resident substituent can influence the selectivity. Taken together, these experiments show that the unusual selectivities observed for acetates **19** and **21** are not due to the presence of the silicon atom, but are caused by the geminal substitution on the silicon.

Nucleophilic substitution reactions of the 3-alkyloxasilacyclopentane acetals **25** and **26** proceeded with high 1,3-trans diastereoselectivity even for small nucleophiles. With both the 3-methyl and the 3-isopropyl groups, 1,3-trans products were observed with allyltrimethylsilane (eq 16).[44] Similar selectivities were observed by Reissig for the analogous tetrahydrofuran acetals.[41,42]



Explanation for the Observed Stereoselectivities

The selectivities exhibited by oxasilacyclopentane acetates cannot be rationalized by examining the dispositions of the substituents on the five-membered ring. For example, the allylations of some systems showed preferential allylation cis to the substituent at C-2, even in the absence of other stereocenters in the molecule (eq 15). At the stage when we had examined a relatively small collection of five-membered ring oxocarbenium ion systems, we proposed a tentative explanation.[8] The selectivities of additions to oxasilacyclopentane oxocarbenium ions derived from *cis*-**5**, **19**, and **21** were not consistent with that model, however.

Concurrent with the oxasilacyclopentane oxocarbenium ion studies, we developed the inside attack model that correctly predicts additions of allyltrimethylsilane to oxocarbenium ions derived from tetrahydrofurans.[5] The inside attack model proposes that approach of a nucleophile to a five-membered ring oxocarbenium ion occurs to the "inside" face of the envelope conformer adopted by the cation (transition structures **28a**,**b**, eq 17). Attack to the inside of the envelope leads to an all-staggered, lower energy conformer (**29a**,**b**). Attack from the "outside" is disfavored because it leads to a higher energy product (**31a**,**b**) that experiences eclipsing interactions between substituents at C-1 and C-2 (eq 18). Extrapolation of this stereoelectronic model can explain the selectivities observed in the oxasilacyclopentane oxocarbenium ions reported here. It should be noted that in the course of his observations of five-membered ring oxocarbenium ion

(37) The configuration of this product was assigned by an NMR chemical shift correlation. The details are provided as Supporting Information.

(38) The configuration of the ring junction was proven by NOE measurements, and the stereochemistry at C-1′ was assigned by analogy to the examples proven by X-ray crystallography. The details are provided as Supporting Information.

(39) The configuration of **23a** was not proven. The stereochemistry of **23b** was proven by an NMR shift correlation. The details are provided as Supporting Information.

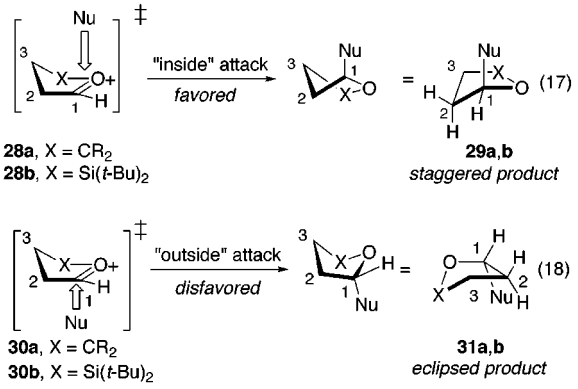
(40) The configuration of **24a** was determined by conversion to a known compound. The structure of **24b** was assigned by conversion to a cyclic acetal and examination of coupling constants. The details are provided as Supporting Information.

(41) Schmitt, A.; Reissig, H.-U. *Synlett* **1990**, 40−42.

(42) Schmitt, A.; Reissig, H.-U. *Eur. J. Org. Chem.* **2000**, 3893−3901.

(43) Shaw, J. T.; Woerpel, K. A. *Tetrahedron* **1999**, *55*, 8747−8756.

(44) The configuration of **27a** was determined by conversion to a known compound. The silane **27b** was converted to the diol acetonide. The details are provided as Supporting Information.



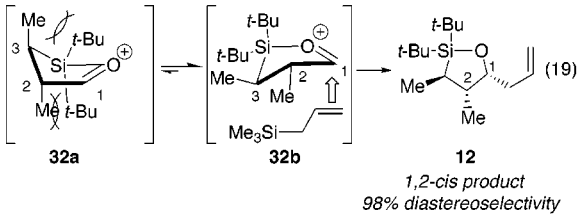
reactivities, Reissig proposed a modified Felkin−Anh model to explain the reactions of these intermediates.[41,42]

To understand the selectivities exhibited by substituted oxasilacyclopentane acetates, the transition structures for nucleophilic attack must be analyzed to determine their relative energies. Because attack of the silyl enol ether or allylic silane on the oxocarbenium ion is irreversible,[45,46] this step determines the stereochemical course of the reaction. Although interconversion between the conformers of the oxocarbenium ions is likely to be rapid relative to nucleophilic attack,[47−49] the transition structures for nucleophilic attack bear some resemblance to the starting carbocations. Consequently, the relative energies of the oxocarbenium ion conformers will be reflected in the energies of the transition structures. Developing steric interactions in the products will also influence the energies of the transition structures.

The magnitude of the steric interactions that develop upon nucleophilic attack (such as *gauche*- or *syn*-pentane interactions) will depend on the size of the nucleophile. Attack by a small nucleophile will engender less destabilization in the transition state than attack by a large nucleophile would. Consequently, when diastereomeric transition states involving a small nucleophile are considered, developing destabilizing interactions will not play as large a role in determining diastereoselectivity as it would with a larger nucleophile.

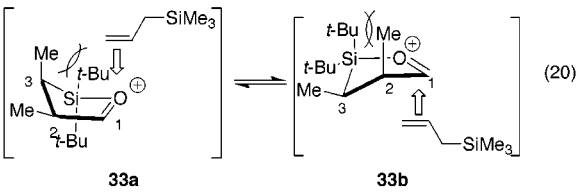
The idea that the stereoselective reactions involving small nucleophiles should be more dependent upon interactions in the reactant than in the product is consistent with the experiments reported here. For small nucleophiles such as allyltrimethylsilane, the relative configuration of the product can be explained by nucleophilic attack to the inside of the lower energy envelope conformer of the cation, because minimal steric interactions develop in the transition state. The additions of larger nucleophiles, on the other hand, are controlled by developing steric interactions. For these nucleophiles, addition occurs to the inside of the envelope conformer that provides fewer steric interactions in the transition state regardless of the relative energies of the oxocarbenium ion conformers.

For small nucleophiles such as allyltrimethylsilane, methallyltrimethylsilane, and 2-((trimethylsilyl)oxy)propene, the major products are obtained by inside attack on the lower energy conformers of the oxocarbenium ions. This point is demonstrated by the analysis of the high 1,2-cis selectivity (98:2) observed for the addition of allyltrimethylsilane to the oxocarbenium ion derived from *trans*-**5** (eq 6). Semiempirical (AM-1) calculations indicate that **32b** is the preferred conformer for the oxocarbenium ion generated from *trans*-**5** (eq 19). These calculations



indicate that the dihedral angle for the C-3 axial substituent and the pseudoequatorial *tert*-butyl is approximately 0°. Therefore, in addition to the pseudo-1,3-diaxial interaction between the C-2 methyl and the pseudoaxial *tert*-butyl group in **32a,** the axial C-3 methyl group of **32a** experiences an eclipsing interaction with the pseudoequatorial *tert*-butyl group. Consequently, the more populated conformer is **32b**, and allyltrimethylsilane adds to the inside to generate the observed 1,2-cis adduct **12** with high diastereoselectivity.

This model can also be used to understand the lack of selectivity observed for the cis analogue (*cis*-**5,** eq 11) with allyltrimethylsilane. Considering the interactions described for the trans-substituted case (vide supra), the two ground-state conformers of the oxocarbenium ion (**33a**,**b**) do not differ much in energy, because each conformer experiences an unfavorable interaction (eq 20). Because the two conformers are similarly populated, allyltrimethylsilane adds to the inside of both **33a** and **33b** to give a 57:43 mixture of diastereomeric products.



As the size of the nucleophiles increases, destabilizing steric interactions between the nucleophile and the C-2 substituent develop in the transition structure. As a result, knowledge of the ground-state conformer populations alone is insufficient to understand the selectivities that are observed. The magnitudes of the interactions between the nucleophile and the substituent depend on the size of the nucleophile and the size of the substituent with which it interacts. With nucleophiles of moderate size, such as 2-((trimethylsilyl)oxy)styrene (**6b**), the destabilizing interactions can be either modest or significant depending on the size of the substituent (methyl or isopropyl) at C-2 (eq 14). With the largest nucleophile examined, silyl enol ether **10**, however, the steric interactions between the nucleophile and the C-2 substituent in the transition state dominate the stereoselectivity, thereby leading to 1,2-trans stereochemistry in all cases (eqs 5, 10, 12, and 13). Nucleophilic addition still occurs to the inside of the envelope conformation, but approach occurs onto the higher energy conformer of the oxocar-

(45) Burfeindt, J.; Patz, M.; Müller, M.; Mayr, H. *J. Am. Chem. Soc.* **1998**, *120*, 3629−3634.
(46) Hagen, G.; Mayr, H. *J. Am. Chem. Soc.* **1991**, *113*, 4954−4961.
(47) Seeman, J. I. *J. Chem. Educ.* **1986**, *63*, 42−48.
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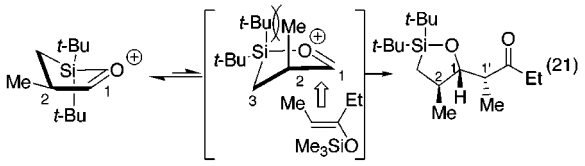
benium ion to avoid development of steric interactions, in accord with the Curtin−Hammett principle.[47−49]

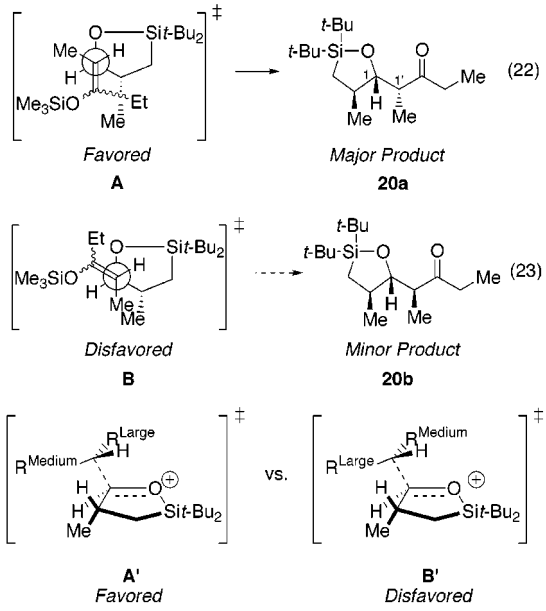
The stereoselective reaction of 2-methyl acetate **19** with (*E*)-**10** (eq 12) illustrates the role of destabilizing interactions on stereoselectivity. The preferred conformer of the derived oxocarbenium ion is **34a** with the methyl group in the equatorial position (eq 21), but inside attack



of the sterically demanding nucleophile **10** on this conformer would develop a severe steric interaction between the methyl group and the approaching nucleophile. Because the two conformers **34a** and **34b** are in rapid equilibrium, the lower energy transition state can be accessed by the addition of the large nucleophile to the higher energy conformer **34b** (eq 21). Addition to the inside of the less populated conformer **34b** affords the observed 1,2-trans product **20a** with high (≥92%) diastereoselectivity.

The reactions of internal alkenes such as crotylsilanes **8** and silyl enol ethers **10** not only control the stereochemical relationships on the five-membered ring, but also establish the syn configuration about the C-1−C-1′ bond. This stereochemical result is independent of the nucleophile configuration (*E* or *Z*) or the nature of the nucleophile (allylic silane or silyl enol ether). These observations contrast with other work in the literature.[50] For example, Scolastico has shown that nucleophilic additions to a cyclic oxocarbenium ion proceed with either syn or anti stereochemistry depending upon whether silyl enol ethers[51] or crotylstannanes[52] were employed.

In the case of the oxocarbenium ions derived from oxasilacyclopentanes, the configuration of the exocyclic stereogenic center is most likely established by an anti transition structure. A priori, two possible staggered transition structures can be considered for the addition: **A**, in which the orientation of the alkene nucleophile to the oxygen atom of the electrophile is antiperiplanar (eq 22), or **B**, in which it is synclinal (eq 23).[53] In both structures, the hydrogen atom is directed toward the inside of the ring, which is the most sterically demanding position. The configuration of the silyl enol ether **10** would not greatly influence the preferences for these two reaction pathways. As the prochiral sp^2-hybridized nucleophile approaches the oxocarbenium ion along the Bürgi−Dunitz trajectory, the position antiperiplanar to the oxygen is more sterically crowded than the synclinal position.[54,55] We believe that transition structures resembling **A** are favored because the smaller sp^2-hybridized carbon (R^{medium}) adopts the more sterically demanding antiperiplanar position (**A′**) as compared to the methyl group (R^{large}) in this position (transition structure **B′**).



Conclusion

The additions of nucleophiles to oxocarbenium ions derived from oxasilacyclopentane acetates occurred with high diastereoselectivity in most cases. These stereoselectivities can be understood by application of our inside attack model[9] for five-membered ring oxocarbenium ions. These results demonstrate that small nucleophiles add to the inside of the lower energy ground-state conformer of the oxocarbenium ion. In contrast, sterically demanding nucleophiles add to the inside of the envelope conformer where approach is anti to the C-2 substituent of the oxocarbenium ion, regardless of the ground-state conformer population. The products generated from these substitution reactions provide access to 1,3-diols with high diastereoselectivity. Future studies will investigate the use of this methodology for the synthesis of polyoxygenated structures such as those embedded in natural products.

Experimental Section

General Procedures. General experimental details are provided as Supporting Information. Microanalyses were performed by Atlantic Microlab, Atlanta, GA. All reactions were carried out under a stream of nitrogen in glassware that had been flame-dried. Solvents were dried and distilled prior to use.

1-Oxa-3,4-dimethyl-5-(3-(2-phenyl-1-propenyl))-2-di-(*tert*-butyl)silacyclopentane (7a). To a stirred solution of acetate *trans*-**5** (0.070 g, 0.25 mmol) in 3 mL of CH_2Cl_2 at −78

(50) Other systems show varying degrees of dependence upon these two variables. For example, see: (a) Danishefsky, S. J.; DeNinno, S.; Lartey, P. *J. Am. Chem. Soc.* **1987**, *109*, 2082−2089. (b) Murata, S.; Suzuki, M.; Noyori, R. *Tetrahedron* **1988**, *44*, 4259−4270. (c) Panek, J. S.; Schaus, J. V. *Tetrahedron* **1997**, *53*, 10971-10982. (d) Rychnovsky, S. D.; Sinz, C. J. *Tetrahedron Lett.* **1998**, *39*, 6811−6814. (e) Comins, D. L.; Kuethe, J. T.; Hong, H.; Lakner, F. J.; Concolino, T. E.; Rheingold, A. L. *J. Am. Chem. Soc.* **1999**, *121*, 2651−2652. (f) Matsumura, Y.; Kanda, Y.; Shirai, K.; Onomura, O.; Maki, T. *Org. Lett.* **1999**, *1*, 175−178. (g) Pilli, R. A.; Riatto, V. B.; Vencato, I. *Org. Lett.* **2000**, *2*, 53−56.

(51) Bernardi, A.; Cardani, S.; Carugo, O.; Columbo, L.; Scolastico, C.; Villa, R. *Tetrahedron Lett.* **1990**, *31*, 2779−2782.

(52) Pasquarello, A.; Poli, G.; Scolastico, C. *Tetrahedron: Asymmetry* **1990**, *1*, 429−432.

(53) Intramolecular additions of silyl enol ethers to aldehydes in the presence of Lewis acids exhibit only a modest preference for antiperiplanar transition states: Denmark, S. E.; Lee, W. *J. Org. Chem.* **1994**, *59*, 707−709.

(54) Seebach, D.; Golinski, J. *Helv. Chim. Acta* **1981**, *64*, 1413−1423.

(55) Bassindale, A. R.; Ellis, R. J.; Lau, J. C.-Y.; Taylor, P. G. *J. Chem. Soc., Chem. Commun.* **1986**, 98−100.

°C was added $SnBr_4$ (0.246 mL, 1 M, CH_2Cl_2) followed by 2-phenyl-3-(trimethylsilyl)-1-propene[14] (0.104 mL, 0.492 mmol, density of 0.9 assumed). The reaction was stirred for 0.5 h and then quenched by the addition of MeOH/triethylamine (0.5 mL, 2:1). The mixture was diluted in 10 mL of CH_2Cl_2 and poured into 40 mL of saturated aqueous $NaHCO_3$. The organic layer was recovered, and the aqueous layer was extracted with 2 × 10 mL of CH_2Cl_2. The combined organic layers were filtered through a cotton plug and reduced in vacuo. Purification by flash chromatography (10:90 to 30:70 CH_2Cl_2/hexanes) yielded the product as a clear oil (0.079 g, 93%). Analysis by GC indicated an 89:11 mixture of diastereomers: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.40 (m, 2H), 7.32 (m, 2H), 7.25 (m, 1H), 5.28 (d, J = 0.8, 1H), 5.22 (d, J = 1.5, 1H), 4.28 (m, 1H), 2.66 (dd, J = 4.3, 15.1, 1H), 2.43 (dd, J = 9.0, 15.2, 1H), 2.15 (m, 1H), 1.17 (d, J = 7.3, 3H), 1.05 (s, 9H), 1.01 (s, 9H), 0.97 (d, J = 6.8, 3H, overlapped with m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 146.7, 142.4, 128.1, 126.5, 114.3, 78.24, 78.17, 43.3, 38.4, 28.8, 28.4, 22.3, 21.9, 20.1, 15.3, 12.8; IR (neat) 3081, 1731, 1630, 1473, 1364, 1075 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{18}H_{27}OSi$ (M − t-Bu)$^+$ 287.1831, found 287.1831. Anal. Calcd for $C_{22}H_{36}OSi$: C, 76.68; H, 10.53. Found: C, 76.76; H, 10.60.

1-Oxa-3,4-dimethyl-5-(3-(1-butenyl))-2-di(*tert*-butyl)silacyclopentane (9). To a stirred solution of acetate *trans*-**5** (1.654 g, 5.773 mmol) in 60 mL of CH_2Cl_2 at −78 °C was added $SnBr_4$ (5.8 mL, 1 M, CH_2Cl_2) followed by (*Z*)-crotyltrimethylsilane[20] (1.50 mL, 11.6 mmol, >99:1 *Z*/*E*). The reaction mixture was stirred at −78 °C for 0.5 h and then warmed to room temperature over 0.5 h. The reaction mixture was poured into 40 mL of saturated aqueous $NaHCO_3$ and diluted in 10 mL of CH_2Cl_2. The organic layer was saved and the aqueous layer extracted with 2 × 20 mL of CH_2Cl_2. The combined organic layers were washed once with brine, filtered through a pad of Na_2SO_4, and reduced in vacuo. Purification by flash chromatography (2:98 to 4:96 to 10:90 to 20:80 to 30:70 CH_2Cl_2/hexanes) yielded the product as a clear oil (1.49 g, 91%) in a 75:11:14 mixture of **9a**/**9b**/**9c** by GC. The isomers were sufficiently resolved by flash chromatography to allow individual characterization.

Data for 9a: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.02 (m, 1H) 5.04 (m, 1H), 4.94 (m, 1H), 3.29 (dd, J = 7.8, 10.0, 1H), 2.33 (m, 1H), 1.51 (m, 1H), 1.19 (d, J = 7.5, 3H), 1.04 (s, 9H), 1.01 (d, J = 7.0, 3H), 1.00 (s, 9H), 0.93 (d, J = 6.1, 3H), 0.85 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 143.9, 112.6, 86.6, 43.2, 41.0, 27.9, 25.8, 21.3, 15.9, 13.8, 12.8; IR (neat) 3074, 1640, 1473, 1386, 1097, 1000 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{17}H_{34}OSi$ (M + H)$^+$ 283.2457, found 283.2457. Anal. Calcd for $C_{17}H_{34}OOSi$: C, 72.27; H, 12.13. Found: C, 72.35; H, 12.10.

Data for 9b: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.88 (m, 1H) 4.99 (m, 1H), 4.96 (m, 1H), 3.19 (dd, J = 2.0, 10.0, 1H), 2.34 (m, 1H); 1.47 (m, 1H), 1.16 (d, J = 6.8, 3H), 1.15 (d, J = 6.7, 3H), 1.02 (s, 9H), 1.00 (s, 9H), 0.89 (d, J = 6.1, 3H), 0.85 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 140.6, 114.4, 87.4, 43.2, 41.2, 27.9, 25.5, 21.3, 18.7, 15.3, 12.6; IR (neat) 3072,1642, 1473, 1387, 1096, cm^{-1}; HRMS (EI) m/z calcd for $C_{17}H_{34}OSi$ (M)$^+$ 282.2379, found 282.2386.

Data for 9c: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.79 (m, 1H) 4.96 (m, 1H), 4.90 (m, 1H), 3.91 (dd, J = 7.4, 8.9, 1H), 2.26 (m, 1H), 2.14 (m, 1H), 1.16 (d, J = 7.6, 3H), 1.09 (d, J = 6.4, 3H), 1.06 (s, 18H), 0.97 (d, J = 6.8, 3H overlapped with m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 143.9, 113.0, 83.5, 44.2, 41.2, 28.8, 28.7, 23.0, 22.2, 20.3, 19.7, 16.6, 13.6; IR (neat) 3076, 1639, 1473, 1386, 1085, 907 cm^{-1}. Anal. Calcd for $C_{17}H_{34}OSi$: C, 72.27; H, 12.13. Found: C, 72.31; H, 12.10.

1-Oxa-3-methyl-5-(3-propenyl)-2-di(*tert*-butyl)silacyclopentane (12). To a stirred solution of acetate *trans*-**5** (0.260 g, 0.904 mmol) in 3 mL of CH_2Cl_2 at −78 °C was added $SnBr_4$ (0.913 mL, 1 M, CH_2Cl_2) followed by methallyltrimethylsilane[30] (0.327 mL, 1.83 mmol). The reaction was stirred for 0.5 h and then quenched by the addition of MeOH/triethylamine (0.5 mL, 2:1). Then the mixture was diluted in 10 mL of CH_2Cl_2 and poured into 40 mL of saturated aqueous $NaHCO_3$. The organic layer was recovered, and the aqueous layer was extracted with 2 × 10 mL of CH_2Cl_2. The combined organic layers were filtered through a cotton plug and reduced in vacuo. Purification by flash chromatography (15:85 to 20:80 CH_2Cl_2/hexanes) yielded the product as a clear oil (0.279 g, 93%). Analysis by GC indicated a 99:1 mixture of diastereomers: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.83 (m, 1H), 5.04 (m, 2H), 4.16 (m, 1H), 2.36 (m, 1H), 2.14 (m, 1H), 1.87 (m, 1H), 1.75 (m, 1H), 1.42 (m, 1H), 1.24 (d, J = 7.6, 3H), 1.06 (s, 9H), 1.04 (s, 9H overlapped with m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 135.8, 116.5, 76.5, 42.5, 39.5, 28.4, 28.2, 22.0, 20.0, 15.5, 15.0; IR (neat) 3076, 1642, 1474, 1388, 1023 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{12}H_{25}OSi$ (M − C_3H_5)$^+$ 213.1675, found 213.1674. Anal. Calcd for $C_{15}H_{30}OSi$: C, 71.57; H, 12.01. Found: C, 71.49; H, 12.02.

1-Oxa-3,4-dimethyl-5-(3-(2-methyl-1-propenyl))-2-di(*tert*-butyl)silacyclopentane (14a). To a stirred solution of acetate *trans*-**5** (0.302 g, 1.06 mmol) in 3 mL of CH_2Cl_2 at −78 °C was added $SnBr_4$ (1.06 mL, 1 M, CH_2Cl_2) followed by methallyltrimethylsilane[30] (0.380 mL, 2.12 mmol). The reaction was stirred for 0.5 h and then quenched by the addition of MeOH/triethylamine (0.5 mL, 2:1). Then the mixture was diluted in 10 mL of CH_2Cl_2 and poured into 40 mL of saturated aqueous $NaHCO_3$. The organic layer was recovered, and the aqueous layer was extracted with 2 × 10 mL of CH_2Cl_2. The combined organic layers were filtered through a cotton plug and reduced in vacuo. Purification by flash chromatography (15:85 to 20:80 CH_2Cl_2/hexanes) yielded the product as a clear oil (0.279 g, 93%). Analysis by GC indicated a 94:6 mixture of diastereomers: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.79 (s, 1H), 4.75 (s, 1H), 4.33 (m, 1H), 2.18 (m, 1H), 2.10 (m, 1H), 2.01 (m, 1H), 1.80 (s, 3H), 1.17 (d, J = 7.2, 3H), 1.04 (s, 18H), 0.93 (d, J = 6.8, 3H, overlapped with m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 144.1, 111.8, 78.5, 43.1, 40.4, 28.7, 28.4, 22.6, 22.1, 21.9, 20.0, 15.1, 12.9; IR (neat) 3075, 1651, 1474, 1363, 1078, 1030 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{13}H_{27}OSi$ (M − t-Bu)$^+$ 227.1831, found 227.1834. Anal. Calcd for $C_{17}H_{34}OSi$: C, 72.27; H, 12.13. Found: C, 72.37; H, 12.14.

1-Oxa-3,4-dimethyl-5-(3-(2-oxopropyl))-2-di(*tert*-butyl)-silacyclopentane (14b). To a stirred solution of acetate *trans*-**5** (0.069 g, 0.24 mmol) in 3 mL of CH_2Cl_2 at −78 °C was added $SnCl_4$ (0.240 mL, 1 M, CH_2Cl_2) followed by 2-(trimethylsiloxy)propene[16] (0.052 mL, 0.32 mmol). The reaction was stirred for 0.5 h and then quenched by the addition of MeOH/triethylamine (0.5 mL, 2:1). The mixture was diluted in 10 mL of CH_2Cl_2 and poured into 40 mL of saturated aqueous $NaHCO_3$. The organic layer was recovered, and the aqueous layer was extracted with 2 × 10 mL of CH_2Cl_2. The combined organic layers were filtered through a cotton plug and reduced in vacuo. Purification by flash chromatography (3:97 to 5:95 EtOAc/hexanes) yielded the product as a clear oil (0.031 g, 60%). Analysis by GC indicated a 94:6 mixture of diastereomers: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.70 (td, J = 5.7, 8.1, 1H), 2.43 (d, J = 4.8, 1H), 2.41 (d, J = 2.0, 1H), 2.22 (s, 3H), 1.17 (d, J = 7.5, 3H), 1.038 (s, 9H), 1.035 (s, 9H), 0.89 (d, J = 6.8, 3H, overlapped with m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 208.2, 77.3 (overlapped with $CDCl_3$), 47.5, 42.6, 30.0, 28.6, 28.3, 22.1, 21.9, 20.0, 14.8, 12.7; ^{13}C NMR (CD_2Cl_2, 125 MHz) 208.2, 77.7, 47.4, 42.9, 30.3, 28.8, 28.4, 22.4, 22.1, 20.2, 14.9, 12.8; IR (neat) 2934, 2892, 1716, 1474, 1364, 1079 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{12}H_{23}O_2Si$ (M − t-Bu)$^+$ 227.1467, found 227.1464. Anal. Calcd for $C_{16}H_{32}O_2Si$: C, 67.55; H, 11.25. Found: C, 67.45; H, 11.30.

1-Oxa-3,4-dimethyl-5-(2-phenyl-2-oxoethyl)-2,2-di(*tert*-butyl)silacyclopentane (16). To a cooled (−78 °C) solution of *cis*-**5** (1.00 g, 3.49 mmol) in 35 mL of CH_2Cl_2 was added $SnBr_4$ (3.80 mL, 0.93 M, CH_2Cl_2) followed by 1-phenyl-1-((trimethylsilyl)oxy)ethylene[10] (0.671 g, 3.49 mmol). After 10 min at −78 °C, the reaction mixture was poured into 200 mL of saturated aqueous $NaHCO_3$ and diluted in 200 mL of CH_2Cl_2. The aqueous layer was extracted with 2 × 50 mL of CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Analysis of the unpurified product by GC−MS indicated a pair of diastereomers in a ratio of 90:10. Purification by flash chromatography (1:99 to 2:98 EtOAc/hexanes) yielded the product (as an inseparable mixture of diastereomers) as a colorless oil (0.94 g, 79%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 7.4, 2H),

7.51 (t, J = 7.9, 1H), 7.42 (t, J = 7.7, 2H), 4.06 (ddd, J = 10.3, 7.4, 2.9, 1H), 3.15 (dd, J = 14.5, 7.9, 1H), 3.00 (dd, J = 14.5, 3.4, 1H), 1.99 (m, 1H), 1.41 (quintet, J = 8.2, 1H), 1.19 (d, J = 7.9, 3H), 1.02 (s, 9H), 0.96 (d, J = 7.2, 3H), 0.95 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.3, 138.5, 133.0, 129.0, 128.7, 79.3, 45.5, 42.9, 29.0, 28.5, 22.4, 20.7, 20.3, 13.2, 11.4; IR (thin film) 2932, 2858, 1716, 1473, 1364 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{17}H_{25}O_2Si$ $(M - C_4H_9)^+$ 289.1624, found 289.1621. Anal. Calcd for $C_{21}H_{34}O_2Si$: C, 72.78; H, 9.89. Found: C, 72.55; H, 9.87.

1-Oxa-3,4-dimethyl-5-(2-(3-oxopentyl))-2,2-di(*tert*-butyl)-silacyclopentane (17). To a cooled (−78 °C) solution of acetate *cis*-**5** (0.150 g, 0.524 mmol) in 5.7 mL of CH_2Cl_2 was added $SnBr_4$ (0.56 mL, 0.93 M, CH_2Cl_2) followed by (*E*)-3-((trimethylsilyl)oxy)-2-pentene[26] (0.493 g, 3.11 mmol). After 10 min at −78 °C, the reaction mixture was poured into 50 mL of saturated aqueous $NaHCO_3$ and diluted in 25 mL of CH_2Cl_2. The aqueous layer was extracted with 2 × 10 mL of CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Analysis of the unpurified reaction mixture by GC showed a 94:5:1 mixture of diastereomers. Purification by flash chromatography (1:99 to 2:98 EtOAc/hexanes) yielded the product as a colorless oil (0.129 g, 79%) as a 93:5:2 mixture of diastereomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.86 (dd, J = 10.5, 2.8, 1H), 2.56 (q, J = 7.2, 2H), 2.48 (dq, J = 7.0, 2.8, 1H), 1.98 (m, 1H), 1.41 (q, J = 8.1, 1H), 1.08 (d, J = 6.9, 3H), 1.07 (d, J = 8.2, 3H), 1.04 (t, J = 7.2, 3H), 1.03 (s, 9H), 0.97 (s, 9H), 0.87 (d, J = 6.9, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 214.0, 81.0, 49.2, 38.5, 33.1, 28.5, 28.0, 22.1, 20.5, 19.8, 12.3, 10.8, 8.3, 7.8; IR (thin film) 2936, 2850, 1716, 1472, 1388, 980 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{18}H_{37}O_2Si$ $(M + H)^+$ 313.2563, found 313.2562. Anal. Calcd for $C_{18}H_{36}O_2Si$: C, 69.17; H, 11.61. Found C, 69.26; H, 11.54.

1-Oxa-3,4-dimethyl-5-(2-propenyl)-2-di(*tert*-butyl)silacyclopentane (18). The procedure used for the preparation of **14a** was employed. An experiment starting with acetate *cis*-**5** (0.200 g, 0.696 mmol) provided an impure oil that GC analysis showed was a pair of diastereomers in a 57:43 ratio as well as 5% of the trans isomer (**12**), which presumably arose from small quantities of acetate *trans*-**5** in acetate *cis*-**5**. Purification by flash chromatography (0:100 to 1:99 EtOAc/hexanes) yielded the product **18** as a colorless oil (0.161 g, 87% combined) as an inseparable mixture of diastereomers. The resonances for each isomer were identifiable in the NMR spectra. Combustion analysis, HRMS, and IR data were obtained for the mixture of diastereomers: IR (thin film): 3075, 2857, 1642, 1473, 1388, 1364 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{16}H_{33}OSi$ $(M + H)^+$ 269.2300, found 269.2295. Anal. Calcd for $C_{16}H_{32}OSi$: C, 71.57; H, 12.01. Found: C, 71.28; H, 12.03.

NMR Data for the Major Isomer of 18: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.01 (m, 1H), 5.08 (m, 2H), 3.56 (ddd, J = 10.0, 5.9, 3.7, 1H), 2.49 (m, 1H), 2.15 (m, 1H), 1.90 (m, 1H), 1.38 (quintet, J = 8.2, 1H), 1.09 (s, 9H), 1.07 (d, J = 8.1, 3H), 0.99 (s, 9H), 0.87 (d, J = 7.0, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 135.6, 116.1, 81.0, 43.0, 39.1, 28.7, 28.1, 22.1, 20.5, 20.0, 12.7, 11.0.

NMR Data for the Minor Isomer of 18: ^{1}H NMR (500 MHz, $CDCl_3$, not all signals were sufficiently resolved) δ 5.89 (m, 1H), 3.91 (dt, J = 7.1, 4.8, 1H), 2.38 (m, 1H), 1.63 (m, 1H), 1.08 (s, 9H), 1.03 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.2, 115.9, 80.1, 40.3, 38.1, 29.0, 28.5, 21.9, 20.5, 20.4, 12.3, 9.6.

1-Oxa-4-methyl-5-(2-(3-oxopentyl))-2,2-di(*tert*-butyl)silacyclopentane (20). The procedure used for the preparation of **17** was employed. An experiment starting with acetate **19** (0.214 g, 0.786 mmol) provided an impure oil that GC−MS analysis showed was a 92:5:3 mixture of diastereomers. Purification by flash chromatography (1:99 to 2:98 EtOAc/hexanes) yielded the product as a colorless oil (0.23 g, 74%) as an inseparable mixture of diastereomers in a 92:5:3 ratio: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.71 (dd, J = 10.2, 2.7, 1H), 2.55 (m, 3H), 1.86 (m, 1H), 1.10 (d, J = 7.0, 3H), 1.04 (t, J = 7.3, 3H), 1.01 (d, J = 6.5, 3H), 0.98 (s, 9H), 0.97 (s, 9H and m, 1H), 0.47 (dd, J = 14.8, 11.6, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.8, 88.1, 49.4, 36.0, 33.2, 27.6, 27.5, 20.7, 19.9, 19.4, 16.0, 8.9, 7.9; IR (thin film) 2932, 2858, 1716, 1473, 1364 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{17}H_{35}O_2Si$ $(M + H)^+$ 299.2406, found 299.2405. Anal. Calcd for $C_{17}H_{34}O_2Si$: C, 68.39; H, 11.48. Found: C, 68.11; H, 11.48.

1-Oxa-4-(2-propyl)-5-(2-(3-oxopentyl))-2,2-di(*tert*-butyl)-silacyclopentane (22). The procedure used for the preparation of **17** was employed. An experiment starting with acetate **21** (0.100 g, 0.333 mmol) provided an impure oil that by GC analysis was a 93:3:2:2 mixture of diastereomers. Purification by flash chromatography (1:99 to 2:98 EtOAc/hexanes) yielded the product as a colorless oil (0.079 g, 73%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.00 (dd, J = 10.6, 2.6, 1H), 2.54 (m, 3H), 1.77 (m, 2H), 1.09 (d, J = 6.9, 3H), 1.06 (t, J = 7.3, 3H), 0.99 (s, 9H), 0.98 (s, 9H), 0.96 (d, J = 6.7, 3H), 0.84 (d, J = 6.7, 3H), 0.69 (dd, J = 14.6, 7.4, 1H), 0.58 (dd, J = 14.6, 12.0, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.8, 79.7, 49.2, 46.3, 33.0, 27.7, 27.5, 27.2, 22.6, 21.0, 20.1, 15.3, 8.4, 7.9, 4.6; IR (thin film) 2958, 2857, 1716, 1472, 1387, 1365 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{19}H_{39}O_2Si$ $(M + H)^+$ 327.2719, found 327.2712. Anal. Calcd for $C_{19}H_{38}O_2Si$: C, 69.88; H, 11.73. Found: C, 69.95; H, 11.61.

1-Oxa-4-methyl-5-(2-phenyl-2-oxoethyl)-2,2-di(*tert*-butyl)silacyclopentane (23a). The procedure used for the preparation of **16** was employed. An experiment starting with acetate **19** (0.116 g, 0.426 mmol) provided an impure oil that by GC−MS analysis was a pair of diastereomers in a 59:41 ratio. Purification by flash chromatography (2:98 to 4:96 EtOAc/hexanes) yielded the major diastereomer and an enriched sample of the minor diastereomer, both as colorless oils (0.072 g, 52% combined). HRMS and IR data were obtained for the mixture of diastereomers: IR (thin film) 3061, 2963, 2859, 1747, 1598, 1471 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{20}H_{33}O_2Si$ $(M + H)^+$ 333.2250, found 333.2255.

NMR Data for the Major Isomer of 23a: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00−8.02 (m, 2H), 7.52−7.56 (m, 1H), 7.41−7.46 (m, 2H), 3.93 (ddd, J = 10.5, 8.0, 3.2, 1H), 3.18 (dd, J = 14.5, 8.0, 1H), 3.00 (dd, J = 14.5, 3.2, 1H), 1.83 (m, 1H), 1.09 (d, J = 6.5, 3H), 1.05 (dd, J = 15.0, 7.6, 1H), 0.95 (s, 18H), 0.50 (dd, J = 15.0, 11.8, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.9, 138.0, 132.7, 128.6, 128.3, 81.7, 45.1, 39.8, 29.7, 27.6, 27.5, 20.5, 19.7, 15.9.

NMR Data for the Minor Isomer of 23a: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94−7.96 (m, 2H), 7.53−7.56 (m 1H), 7.44−7.47 (m, 2H), 4.80 (q, J = 6.7, 1H), 3.14 (dd, J = 16.2, 6.8, 1H), 3.04 (dd, J = 16.2, 6.4, 1H), 2.56 (m, 1H), 1.04 (s, 9H and m, 1H), 1.00 (s, 9H), 0.98 (d, J = 7.0, 3H), 0.54 (dd, J = 15.1, 9.0, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.0, 137.5, 132.8, 128.5, 128.1, 77.5, 42.4, 35.0, 29.7, 28.5, 28.0, 20.9, 18.5, 13.8.

1-Oxa-4-(2-propyl)-5-(2-phenyl-2-oxoethyl)-2,2-di(*tert*-butyl)silacyclopentane (23b). The procedure used for the preparation of **16** was employed. An experiment starting with acetate **21** (0.200 g, 0.666 mmol) provided an impure oil that by GC analysis was the product as a pair of diastereomers in a ratio of 85:15. Purification by flash chromatography (1:99 to 2:98 EtOAc/hexanes) yielded the major diastereomer and a sample enriched with the minor diastereomer, both as colorless oils (0.177 g, 70% combined). Combustion analysis, HRMS, and IR data were obtained for the mixture of diastereomers: IR (thin film): 3060, 2958, 2857, 1690, 1598, 1471 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{22}H_{37}O_2Si$ $(M + H)^+$ 361.2562, found 361.2555. Anal. Calcd for $C_{22}H_{36}O_2Si$: C, 73.28; H, 10.06. Found: C, 73.11; H, 10.22.

NMR Data for the Major Isomer of 23b: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 7.4, 2H), 7.53 (t, J = 7.4, 1H), 7.43 (t, J = 7.7, 2H), 4.19 (ddd, J = 10.2, 8.2, 3.0, 1H), 3.18 (dd, J = 8.0, 14.6, 1H), 3.01 (dd, J = 14.6, 3.0, 1H), 1.83 (m, 1H), 1.74 (m, 1H), 0.97 (d, J = 8.7, 3H), 0.96 (s, 9H), 0.95 (s, 9H), 0.85 (d, J = 6.7, 3H), 0.70 (dd, J = 14.8, 8.0, 1H), 0.62 (dd, J = 14.8, 12.1, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.9, 138.0, 132.6, 128.5, 128.2, 77.8, 50.7, 45.7, 28.0, 27.7, 27.4, 22.6, 20.8, 19.7, 15.9, 5.0.

NMR Data for the Minor Isomer of 23b: ^{1}H NMR (500 MHz, $CDCl_3$, not all signals were sufficiently resolved) δ 7.93 (m, 2H), 7.53−7.56 (m, 1H), 7.44−7.48 (m, 2H), 4.90 (ddd, J

= 10.0, 7.1, 3.0, 1H), 3.08 (dd, J = 15.6, 10.0, 1H), 2.90 (dd, J = 15.6, 3.0, 1H), 2.01 (m, 1H), 1.43 (m, 1H), 1.01 (d, J = 6.5, 1H), 0.99 (s, 9H), 0.98 (s, 9H), 0.94 (d, J = 6.4, 3H), 0.48 (t, J = 14.2, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.9, 137.7, 132.7, 128.5, 128.1, 76.2, 49.8, 41.0, 31.4, 28.5, 28.2, 22.6, 21.9, 20.7, 19.5, 9.6.

1-Oxa-4-methyl-5-(3-propenyl)-2-di(*tert*-butyl)silacyclopentane (24a). The procedure used for the preparation of **14a** was employed. An experiment starting with acetate **19** (0.349 g, 1.28 mmol) yielded 0.256 g (79%) of the product as a colorless oil in a 94:6 ratio by GC analysis: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.95 (m, 1H), 5.06 (m, 2H), 4.09 (q, J = 7.2, 1H), 2.42 (m, 1H), 2.12 (m, 2H), 1.04 (s, 9H), 1.02 (s, 9H), 1.01 (d, J = 6.0, 3H), 0.93 (dd, J = 7.4, 14.9, 1H), 0.50 (dd, J = 11.3, 14.9, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 136.8, 116.0, 81.1, 36.9, 35.9, 28.4, 28.1, 20.7, 19.4, 18.5, 13.5; IR (neat) 2858, 1474, 1364, 1039, 824, 628 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{12}H_{25}OSi$ $(M - C_3H_5)^+$ 213.1675, found, 213.1674. Anal. Calcd for $C_{15}H_{30}OSi$: C, 70.80; H, 11.88. Found: C, 70.50; H, 11.78.

1-Oxa-4-(2-propyl)-5-(3-propenyl)-2-di(*tert*-butyl)silacyclopentane (24b). The procedure used for the preparation of **14a** was employed. An experiment starting with acetate **21** (0.391 g, 1.30 mmol) yielded 0.358 g (97%) of the product as a colorless oil in an 80:20 mixture by GC analysis: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.01 (m, 1H), 5.09 (s, 1H), 5.07 (d, J = 10.2, 1H), 4.22 (m, 1H), 2.14 (m, 1H), 2.05 (m, 1H), 1.88 (m, 1H), 1.42 (m, 1H), 1.04 (s, 9H), 1.02 (s, 9H), 0.97 (d, J = 6.4, 3H), 0.91 (d, J = 6.4, 3H overlapped with m, 1H), 0.42 (t, J = 14.2, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 137.1, 116.0, 80.1, 50.1, 35.7, 31.0, 28.5, 28.3, 22.6, 21.7, 20.7, 19.6, 9.3; IR (neat) 3075, 2859, 1472, 1365, 1021 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{14}H_{29}OSi$ $(M - C_3H_5)^+$ 241.1988, found 241.1988. Anal. Calcd for $C_{17}H_{34}OSi$: C, 72.27; H, 12.13. Found: C, 72.16; H, 12.17.

1-Oxa-3-methyl-5-(3-propenyl)-2-di(*tert*-butyl)silacyclopentane (27a). The procedure used for the preparation of **14a** was employed. An experiment starting with acetate **25** (0.260 g, 0.955 mmol) yielded 0.228 g (94%) of the product as a 99:1 mixture of diastereomers as indicated by GC analysis: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.83 (m, 1H), 5.04 (m, 2H), 4.16 (m, 1H), 2.36 (m, 1H), 2.14 (m, 1H), 1.87 (m, 1H), 1.75 (m, 1H), 1.42 (m, 1H), 1.24 (d, J = 7.6, 3H), 1.06 (s, 9H), 1.04 (s, 9H overlapped with m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 135.8, 116.5, 76.5, 42.5, 39.5, 28.4, 28.2, 22.0, 20.0, 15.5, 15.0; IR (neat) 3076, 2858, 1642, 1474, 1388, 1023, 822 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{12}H_{25}OSi$ $(M - C_3H_5)^+$ 213.1675, found 213.1674. Anal. Calcd for $C_{15}H_{30}OSi$: C, 71.57; H, 12.01. Found: C, 71.49; H, 12.02.

1-Oxa-3-(2-propyl)-5-(2-propenyl)-2-di(*tert*-butyl)silacyclopentane (27b). The procedure used for the preparation of **14a** was employed. A reaction employing acetate **26** (0.516 g, 1.72 mmol) yielded an impure oil that GC analysis indicated was a single diastereomer. Purification by flash chromatography (1:99 to 2:98 EtOAc/hexanes) yielded the product as a colorless oil (0.461 g, 95%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.82 (m, 1H), 5.04 (m, 2H), 4.19 (q, J = 7.3, 1H), 2.31 (ddd, J = 13.8, 7.2, 6.5, 1H), 2.08 (ddd, J = 14.0, 7.2, 7.0, 1H), 1.93 (dd, J = 12.9, 8.4, 1H), 1.83 (m, 2H), 1.14 (m, 1H), 1.06 (s, 9H), 1.04 (s, 9H and m, 3H), 0.94 (d, J = 6.4, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.0, 116.6, 75.8, 43.0, 36.3, 31.7, 29.1, 28.7, 28.3, 26.7, 23.9, 22.7, 19.7; IR (neat) 3076, 2858, 1642, 1474, 1386, 1034, 821 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{17}H_{35}OSi$ $(M + H)^+$ 283.2457, found 283.2464. Anal. Calcd for $C_{17}H_{34}OSi$: C, 72.27; H, 12.13. Found: C, 71.95; H, 12.00.

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Supporting Information Available: General experimental details, description of the preparation of oxasilacyclopentane acetates *trans*-**5**, *cis*-**5**, **19**, **21**, **25**, and **26**, stereochemical proofs for compounds **7a,b**, **9a**−**c**, **11a**−**c**, **12**, **14a,b**, **16**, **17a**, **20a**, **22a**, **23b**, **24a,b**, and **27a,b**, X-ray crystal structure data for *trans*-**5**, **S8**, and **S16**, and NMR spectra and GC traces for compounds **16**, **17a**, **20a**, **22a**, and **27b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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