Allyldimethyltritylsilane. Synthesis of Cyclopentanols, Oxetanes, and Tetrahydrofurans by Reaction with Electron Deficient Olefins

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Allyldimethyltritylsilane (ADTS, **1**) has been employed to access a variety of cyclopentanols via Lewis acid mediated annulation to electron deficient olefins. The intermediate silylcyclopentanes were converted to their respective cyclopentanols under mild, nonepimerizing oxidative conditions. In addition, ADTS undergoes efficient annulation onto aldehydes to provide oxetanes and tetrahydrofurans. Some preliminary investigations of this annulation to chiral nonracemic bicyclic lactams are presented.

The Lewis acid mediated 1,2- and 1,4-additions of allylsilanes to aldehydes and electron deficient olefins has become a very powerful tool in synthesis since allylsilanes are relatively stable compared to other allylmetalloid species and they are easily accessible by conventional synthetic methods.[1−3] In addition to simple 1,2- and 1,4-additions, allylsilanes have demonstrated that they may be utilized to annulate olefins and carbonyls to a variety of four- and five-membered rings ranging from carbocycles to tetrahydrofurans, oxetanes, azetidines, and pyrrolidines.[4,5] A notable feature of these annulations is the high propensity for a *trans* configuration in the cyclic product, **2** (Scheme 1). This stereoselectivity can be attributed to the preference of the electron-withdrawing group and the silicon to align themselves to produce a *syn*-clinal transition state.[6] Although there are four possible *syn*-clinal transition states that can be written for this reaction, the carbonyl group prefers to adopt an *endo* (A) rather than the *exo* orientation with respect to the silane moiety in order to minimize charge separation in the dipolar transition state. Furthermore, the initial adduct, B, can also close to a four-membered ring under certain conditions, as previously reported.[7] This annulation process provides a potentially powerful tool for the construction of carbo- and heterocycles with predictable and highly selective stereocenters.

Another important feature of allylsilanes is the ability of silicon to act as a hydroxyl surrogate.[8] It has been demonstrated that any silane containing a nucleofugal group such as a halogen, oxygen, or nitrogen can be oxidized to a hydroxyl group with retention of stereochemistry at the silicon-bearing carbon. This, in combination with the allylsilane addition to electron deficient olefins or carbonyls augers well for the development of these reagents as valuable additions to current synthetic methods. For example, allylmethyldiphenylsilane **1a** has been shown by Knölker[9] to undergo annulation (Table 1) with 1-acetylcyclohexene **3** followed by oxidative conversion to the alcohol **5**. This interesting and useful transformation, however, suffered from a modest yield (26−38%) in the annulation to **4**, while the oxidative removal via the Tamao[10] method proceeded well (80%) to give **5**. We found that allyltriisopropylsilane **1b** underwent similar annulations with excellent yields but we were unable to convert the silyl adduct to the carbinol, **4**. On the other hand, allyltriphenylsilane **1c** underwent annulations to **3** with very poor yields but was converted to the carbinol **5** quantitatively (Table 1).

It is apparent that at least two alkyl groups on the silicon atom are required to effect efficient addition−

Scheme 1

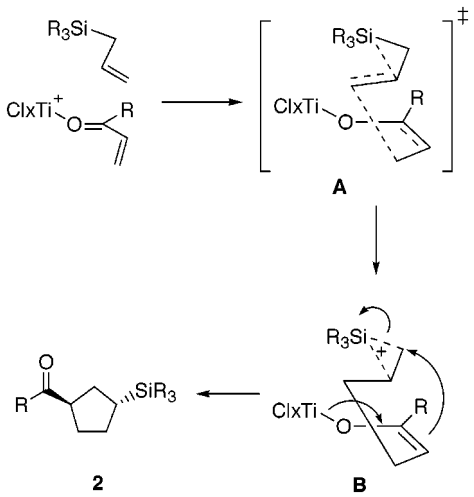

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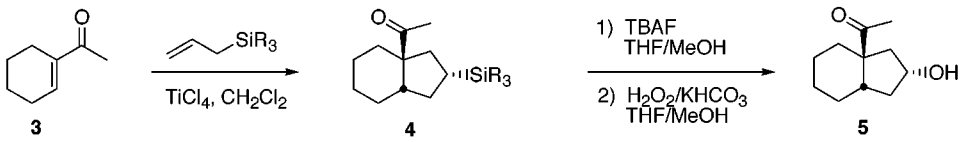
Table 1. Allyl Silane Annulations−Oxidation to Fused Cyclopentanols



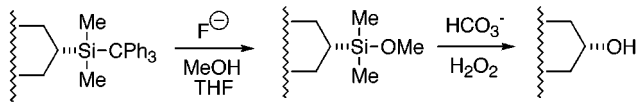
3 4 5

Silane, R_3	%4	%5
1a, $SiMePh_2$	38[a]	80[a]
1b, Si (*i*-Pr)$_3$	94	0
1c, $SiPh_3$	51	97
1d, $SiMe_2CPh_3$	80	70

[a] See reference 9.

annulation and a readily F-labile group is necessary for efficient oxidation. This delicate balance between reactivity and oxidative silicon removal was fortunately achieved by use of allyldimethyltritylsilane, **1d**. We recently reported our preliminary results on the use of allyldimethyltritylsilane (ADTS) to annulate several enone systems.[5a] When enone **3** was treated with ADTS under Lewis acid conditions, the annulation occurred in 80% yield and more importantly, the oxidative disilylation proceeded in 67−70% yields. The large trityl group, the necessary alkyl groups, and ease of oxidative removal of the silicon all contributed to a successful solution to the problem at hand. The further versatility of this reagent in annulation and subsequent oxidative silicon removal is the subject of this report.

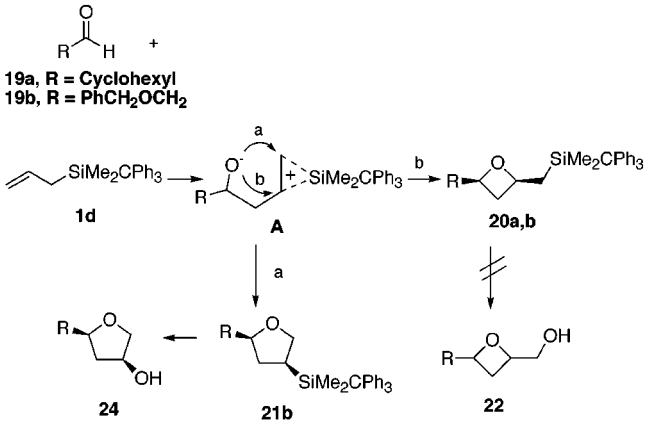
Synthesis of 3-Substituted, 3,3-Disubstituted, and 3,4-Disubstituted Cyclopentanols. When 1.5 equiv of allyldimethyltritylsilane (ADTS) **1d** was added to a premixed solution of the electron deficient olefin (Table 2) and titanium(IV) chloride in dichloromethane at −78 °C, the cyclopentyldimethyltritylsilanes were obtained in moderate to high yield (40−85%). The various olefins annulated in Table 2 exhibit the versatility of the silane addition as well as the diastereoselectivity of the process. In almost every case, except in entry f, we were unable to observe any other stereoisomer. The silylcyclopentanes were subsequently converted to their respective cyclopentanol derivatives by a modified Tamao oxidation.[10] The tritylsilane was first converted to the methoxysilane **18** by reaction with tetrabutylammonium fluoride or cesium fluoride in a MeOH−THF solution.



18

Treatment of the crude methoxysilane **18** with basic hydrogen peroxide in a MeOH−THF solution furnished the cyclopentanols in consistently good yields (67−93%) (Table 2). It is noteworthy that little or no epimerization occurred during the transformation of the silyl group to the hydroxyl. The stereochemical assignments are based on comparison to spectral data of known or analogous compounds. It is also important to mention that the mild oxidation conditions showed only a slight loss of the diastereomeric integrity in only two cases (entries b and c). In the cases where epimerization was not a concern, Tamao oxidation could be achieved in one pot by a combination of tetrabutylammonium hydroxide and hydrogen peroxide in THF. The examples depicted in Table 2 demonstrate the advantages of ADTS when compared to earlier allylsilanes utilized in annulations.

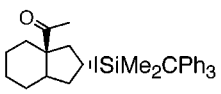
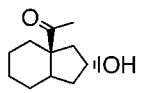
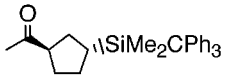
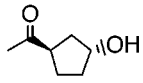
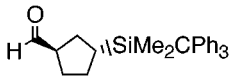
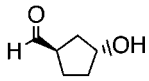
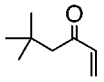
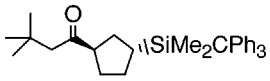
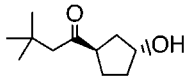
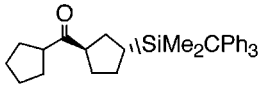
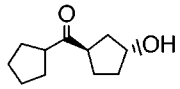
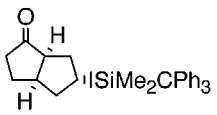
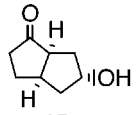
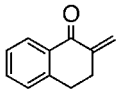
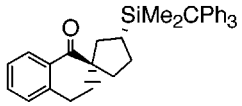
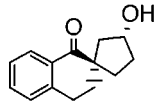
Synthesis of 2,4-Disubstituted Oxetanes and Tetrahydrofurans. In addition to the carbocycle formation seen above, ADTS was found to smoothly cycloadd to aldehydes **19**. There are two reaction pathways which may occur and therefore offer the option to form oxetane **20** or tetrahydrofuran **21**. For example, if the intermediate alkoxide **A** undergoes a *4-endo* mode of attack (path b), the oxetane is formed, whereas *5-exo* attack (path a) leads to the tetrahydrofuran.



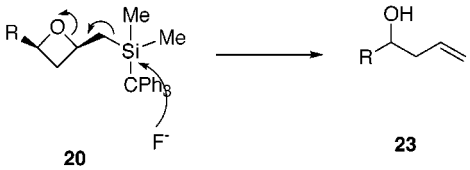
In contrast to the carbocycle formation where temperature dictates whether a four- or a five-membered ring will form,[7] changing the nature of the Lewis acid affects ring size in the heterocycle formation. Thus, when benzyloxyacetaldehyde **19b** is added to a mixture of ADTS and zirconium(IV) chloride at −20 °C, oxetane **20b** is obtained exclusively in 88% yield after 30 min. In contrast, when benzyloxyacetaldehyde is added to a solution of $BF_3{\cdot}OEt_2$ and ADTS at −78 °C, the tetrahydrofuran **21b** is the only product obtained in 72% yield after 12 h. The stereochemistry of **20b** and **21b** was assigned on the basis of literature precedent for similar annulations with other allylsilanes.

To demonstrate that ADTS may serve as a hydroxyl equivalent, attempts were made to convert the silylmethyl oxetanes **13a** to the hydroxymethyl oxetanes **22**. However, after some effort no oxetane product was obtained. This failure was attributed to the facile β-cleavage of the oxetane during the Tamao oxidation. In an attempt to determine which step in the oxidation was causing the ring opening, an effort was made to isolate the intermediate fluoro or methoxy silane from **20**.

Table 2. Stereoselective Cyclopentanol Synthesis Using ADTS, 1d

Entry	Olefin	Silylcyclopentane	% Yield (*d.r.*)[a]	Cyclopentanol	% Yield (*d.r.*)
a)		 **4**	85 (*>97:3*)	 **5**	67 (*>97:3*)
b)		 **6**	78 (*>97:3*)	 **7**	69 (*8:1*)
c)		 **8**	40 (*>97:3*)	 **9**	78 (*7:1*)
d)		 **10**	55 (*>97:3*)	 **11**	82 (*>97:3*)
e)		 **12**	63 (*>97:3*)	 **13**	73 (*>97:3*)
f)		 **14**	46 (*9:1*)	 **15**	93 (*9:1*)
g)		 **16**	68 (*>97:3*)	 **17**	85 (*>97:3*)

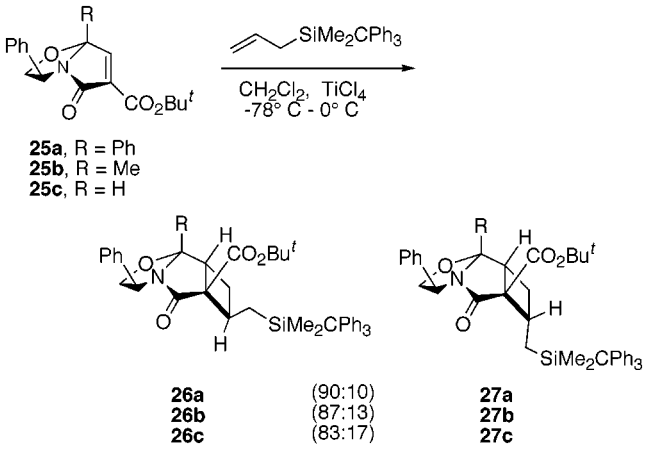
[a] Diastereomeric ratios were determined by 300 MHz ^{1}H NMR of the crude reaction mixture.



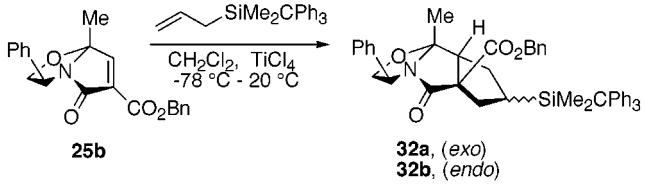
20 **23**

A solution of the silylmethyl oxetane **20** was added to a solution of tetrabutylammonium fluoride in THF at −20 °C. After 45 min the oxetane was completely converted to the homoallylic alcohol **23**. Solvolysis of **20** with tetrabutylammonium hydroxide and protodesilylation were both unsuccessful as well. However, in the case of the silyl tetrahydrofurans **21**, the ring cleavage should not be a competing pathway, and their corresponding hydroxytetrahydrofurans **24** were expected to form. In the event, the conversion of the 4-silyltetrahydrofuran **20b** to the 4-hydroxytetrahydrofuran **24b** proceeded cleanly in 86% yield.

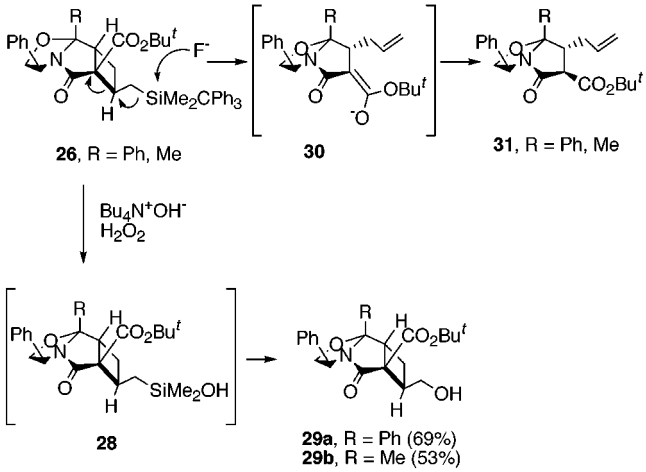
Annulations to α,β-Unsaturated Chiral Bicyclic Lactams. To assess the versatility and scope of the annulations above, a study to determine whether the chiral bicyclic lactams **25**, reported earlier[7] to give either four- or five-membered ring annulation, would respond to the allyltritylsilane. These annulations were previously performed using triisopropylallyl silanes (TIPS), but these products were obviously incapable of generating the alcohols. When the bicyclic lactams **25** were treated with $TiCl_4$ in CH_2Cl_2 at −78 °C and the reaction mixture was allowed to warm to 0 °C, a 50−75% yield the cyclobutane adducts **26** and **27** was exclusively obtained as a mixture of *exo*−*endo* silyl substituent. The major products in each instance were the *exo* products **26a**−**c**. It is noteworthy that no cyclopentane products **32** were observed as was previously observed[7] when warming the triisopropyl adducts to 0 °C in the presence of $TiCl_4$. Furthermore, the rates of reaction were qualitatively slower with ADTS when compared to those exhibited by



allyl TIPS additions, presumably due to slightly less inductive stabilization by the methyl and trityl groups. $TiCl_4$-mediated rearrangement[7] of the initially formed cyclobutane from **25b** to cyclopentane products **32** were attempted by warming the reaction mixture to 20−25 °C, but thermal decomposition of both the product and starting materials became quite noticeable and the cyclopentane was indeed formed in poor yield and with loss of stereochemical integrity. Thus, **32a** was obtained in 33% yield, but with only a diastereomeric ratio of 78:22, indicating that rearrangement took place with poor stereoconservation. The details of this rearrangement have already been discussed.[7]



Attempts to oxidize the silane **26** to the corresponding carbinol using standard Tamao conditions[10] resulted in formation of the Sakurai product,[11] **31**. This was considered to be a result of nucleophilic attack on the silicon by the fluoride ion and subsequent elimination to the alkene **30**. If fluoride ion is indeed responsible for this



fragmentation, then omitting it from the silyl−trityl solvolysis should avoid the problem. Thus, treating the cyclobutanes **26** with only tetrabutylammonium hydroxide in the presence of hydrogen peroxide produced the solvolyzed intermediate **28** which was readily oxidized to the primary alcohols **29a** and **b** in moderate yields.

In summary, allyldimethyltritylsilane (ADTS) has proven to be a potentially useful and convenient reagent for the construction of a variety of hydroxy carbo- and heterocycles via annulation of simple enones and aldehydes. Annulations with this silyl reagent on chiral nonracemic bicyclic lactams have also been demonstrated and appear to show promise in their application toward the synthesis of enantiopure carbo- and heterocycles. Further studies in this area will be reported soon.

Experimental[12] Section

Allyldimethyltritylsilane (ADTS) (1). To a solution of bromodimethyl(triphenylmethyl)silane[13] (6.06 g, 15.9 mmol) in dry THF (110 mL) was added a solution of allylmagnesium chloride (2.0 M in THF, 47.7 mmol, 24 mL). The resulting mixture was brought to reflux and stirred for 12 h. After being cooled to room temperature, the reaction mixture was slowly poured into a separatory funnel containing cold saturated aqueous NH_4Cl and Et_2O. The layers were separated, and the aqueous layer was washed with Et_2O. The organic layers were combined, washed with brine, and dried over $MgSO_4$. Filtration and rotary evaporation then gave a crude brown solid which was purified via flash chromatography (elution with hexane) to afford the allylsilane as a colorless solid (4.22 g, 77% yield), mp 86−89 °C: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.14 (s, 6H), 1.58 (d, J = 8.2 Hz, 2H), 4.74−4.83 (m, 2H), 5.58−5.72 (m, 1H), 7.00−7.04 (m, 6H), 7.14−7.28 (m, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −0.7, 24.8, 53.9, 113.7, 125.5, 127.9, 130.1, 135.1, 146.3; IR (neat) 3052, 700 cm^{-1}; HRMS (EI), (M^+) calcd for $C_{24}H_{26}Si$ 342.1804, found 342.1806.

General Method for Cyclopentannulation. To a solution of the electron deficient olefin (0.30 mmol) in CH_2Cl_2 (3 mL) at −78 °C was added titanium(IV) chloride (0.36 mmol, 1.0 M solution in dichloromethane) dropwise via syringe. After 5 min of vigorous stirring, allyltrityldimethylsilane (0.12 g, 0.36 mmol) was added dropwise as a solution in CH_2Cl_2. The reaction temperature was slowly allowed to reach 0 °C (approximately 4 h). The reaction was monitored via TLC (1:4 EtOAc/Hex) and quenched by the addition of saturated aqueous NH_4Cl, resulting in a colorless mixture. The layers were separated, and the aqueous layer was washed with CH_2Cl_2. The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated via rotary evaporation to yield the crude product which was purified via flash chromatography (9:1 Hex/EtOAc) and analyzed as shown below.

***trans*-1-Acetyl-8-(dimethyltritylsilyl)bicyclo[4.3.0]-nonane (4):** colorless solid (0.11 g, 85% yield), mp 152−153 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.17 (s, 3H), 0.21 (s, 3H), 1.09−1.60 (m, 12H), 1.69−1.76 (m, 1H), 1.93 (s, 3H), 2.21−2.29 (m, 1H), 7.01−7.27 (m, 15H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −1.8, −0.7, 22.0, 23.3, 24.2, 25.3, 26.6, 31.4, 33.6, 38.6, 40.7, 54.1, 58.0, 125.5, 127.9, 130.2, 146.4, 212.9; IR (neat) 1698 cm^{-1}; HRMS (FAB), (M^+) calcd for $C_{32}H_{38}OSi$ 466.2692, found 466.2676.

***trans*-1-Acetyl-3-(dimethyltritylsilyl)cyclopentane (6):** colorless oil (80 mg, 78% yield); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.16 (s, 3H), 0.18 (s, 3H), 1.01−1.25 (m, 2H), 1.71−1.79 (m, 1H), 1.98 (s, 3H), 2.73−2.76 (m, 1H), 7.04−7.06 (m, 6H), 7.13−7.26 (m, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −1.7, −1.0, 27.1, 28.4, 29.4, 30.6, 31.7, 52.3, 54.1, 125.5, 127.9, 130.2, 146.4, 210.7; IR (neat) 1707 cm^{-1}.

2-Oxo-7-(dimethyltritylsilyl)bicyclo[3.3.0]octane (14): colorless oil (70 mg, 46% yield); ^{1}H NMR ($CDCl_3$, 300 MHz) δ

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0.31 (s, 3H), 0.32 (s, 3H), 0.86−1.13 (m, 1H), 1.15−1.32 (m, 1H), 1.60−1.72 (m, 1H), 1.94 (app q, J = 8.1 Hz, 1H), 2.09−2.23 (m, 2H), 2.28−2.41 (m, 2H), 2.64 (app t, J = 10.1 Hz, 1H), 2.85−2.88 (m, 1H), 7.17−7.48 (m, 15H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −1.8, −0.7, 25.6, 27.3, 34.3, 38.1, 39.5, 40.3, 52.0, 54.3, 125.5, 127.9, 130.2, 146.3, 223.1; IR (neat) 1651 cm^{-1}.

Spiro silyl ketone 16: colorless oil (50 mg, 68% yield); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.31 (s, 3H), 0.32 (s, 3H), 0.86−1.13 (m, 1H), 1.15−1.32 (m, 1H), 1.60−1.72 (m, 1H), 1.94 (app q, J = 8.1 Hz, 1H), 2.09−2.23 (m, 2H), 2.28−2.41 (m, 2H), 2.64 (app t J = 10.1 Hz, 1H), 2.85−2.88 (m, 1H), 7.17−7.48 (m, 15H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −1.8, −0.7, 25.6, 27.3, 34.3, 38.1, 39.5, 40.3, 52.0, 54.3, 125.5, 127.9, 130.2, 146.3, 223.1; IR (neat) 1651 cm^{-1}; HRMS (EI), (M^+) calcd for $C_{35}H_{36}OSi$ 500.2535, found 500.2537.

General Procedure for Annulation to Aldehydes. To a solution of aldehyde (0.18 mmol) and **1d** (0.27 mmol) in toluene (1.0 mL) was added zirconium(IV) chloride (0.19 mmol) at −20 °C. After being stirred at −20 °C for 30 min, the reaction mixture was treated with saturated aqueous NH_4Cl. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The crude products were purified via flash chromatography eluting with EtOAc/Hex (1:9).

***cis*-2-Cyclohexyl-4-(dimethyltritylsilyl)methyloxetane (20a):** colorless oil (110 mg, 55% yield); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.39 (s, 3H), 0.41 (s, 3H), 1.18−2.1 (m, 13H), 3.58−3.82 (m, 1H), 4.22−4.35 (m, 1H), 6.95−7.05 (d, J = 9 Hz, 6H), 7.12 (m, 9H), ^{13}C NMR ($CDCl_3$, 75 MHz) δ −0.1, 1.3, 24.2, 25.1, 26.2, 27.8, 28.9, 29.2, 39.8, 46.5, 54.1, 59.8, 72.6, 125.6, 128.0, 130.1, 146.3; IR (neat) 3051, 850 cm^{-1}.

***cis*-2-Benzyloxymethyl-4-(dimethyltritylsilyl)methyloxetane (20b):** colorless oil (220 mg, 88% yield); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.16 (s, 3H), 0.19 (s, 3H), 1.03−1.28 (m, 2H), 1.46−1.68 (m, 2H), 3.14−3.24 (m, 1H), 3.29−3.38 (m, 1H), 3.91−4.04 (m, 1H), 4.16−4.28 (m, 1H), 4.42 (app t, J = 9 Hz, 2H), 6.86−6.91 (m, 6H), 7.02−7.28 (m, 14H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −0.1, 1.3, 29.2, 39.8, 42.5, 54.1, 59.8, 68.7, 72.6, 74.4, 125.6, 126.9, 128.0, 130.1, 137.5, 146.3; IR (neat) 3063, 845 cm^{-1}; HRMS (CI), (MNH_4^+) calcd for $C_{33}H_{40}O_2NSi$ 510.2828, found 510.2828.

***cis*-2-Benzyloxymethyl-4-(dimethyltritylsilyl)tetrahydrofuran (21b).** To a solution of aldehyde (0.18 mmol) and allylsilane (0.27 mmol) in toluene (1.0 mL) was added BF_3·OEt_2 (0.19 mmol) at −78 °C. After being stirred at −78 °C for 12 h, the reaction mixture was allowed to warm to room temperature and was treated with saturated aqueous NH_4Cl. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The crude product was purified by flash chromatography eluting with EtOAc/Hex (1:9) to afford the oxetane as a colorless oil (200 mg, 83% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.16 (s, 3H), 0.19 (s, 3H), 1.03−1.28 (m, 2H), 1.46−1.68 (m, 2H), 3.14−3.24 (m, 1H), 3.29−3.38 (m, 1H), 3.91−4.04 (m, 1H), 4.16−4.28 (m, 1H), 4.42 (app t, J = 9 Hz, 2H), 6.86−6.91 (m, 6H), 7.02−7.28 (m, 14H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −0.1, 1.3, 25.2, 40.8, 43.5, 53.1, 60.8, 68.7, 72.6, 74.4, 125.6, 125.9, 128.0, 130.1, 137.5, 146.3; IR (neat) 3041, 863 cm^{-1}; HRMS (CI), (MNH_4^+) calcd for $C_{33}H_{40}O_2NSi$ 510.2828, found 510.2825.

Homoallylic Alcohol 23. Colorless oil (120 mg, 89% yield). The spectral data were identical with those reported.[14]

General Procedure for Oxidative Removal of Silicon. A single-neck, round-bottomed flask, equipped with a Teflon stirbar, was charged with cesium fluoride (0.13 g, 0.87 mmol), and the flask was heated under vacuum with a heat gun. After being cooled to room temperature, the flask was filled with argon. Anhydrous MeOH (0.5 mL) and THF (2.5 mL) were added to the flask, and the silyl adduct (0.17 mmol) was added as a solution in THF (1.0 mL) via syringe. The reaction was stirred at room temperature for 4 h, then was partitioned between water and CH_2Cl_2, the layers were separated, and the aqueous layer was washed with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was dissolved in THF (2.5 mL) and MeOH (1.0 mL) and sequentially treated with $KHCO_3$ (30 mg, 0.29 mmol), 30% H_2O_2 (9.79 M in H_2O, 3.92 mmol, 0.40 mL), and tetrabutylammonium fluoride (1.0 M in THF, 0.25 mmol, 0.25 mL). The reaction mixture was vigorously stirred at room temperature for 5 h and then partitioned between water and CH_2Cl_2. The layers were separated, and the aqueous layer was washed with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude products were purified by flash chromatography eluting with EtOAc/Hex (1:9).

***trans*-1-Acetyl-8-hydroxybicyclo[4.3.0]nonane (5):** colorless oil (30 mg, 67% yield): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.15−1.23 (m, 1H), 1.33−1.77 (m, 8H), 1.82−1.89 (m, 1H), 1.98−2.16 (m, 2H), 2.09 (s, 3H), 2.31−2.36 (m, 1H), 4.29−4.37 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.7, 22.9, 25.4, 26.1, 30.0, 38.2, 39.3, 44.4, 57.7, 71.2, 212.7; IR (neat) 3420 cm^{-1}; HRMS (FAB), (M^+) calcd for $C_{11}H_{18}O_2$ 183.1385, found 183.1387.

***trans*-1-Acetyl-3-hydroxycyclopentane (7):** colorless oil (34 mg, 69% yield); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.57−2.10 (m, 6H), 2.15 (s, 3H), 3.16 (dddd, J = 9.5, 7.0, 5.5, 4.2 Hz, 1H), 4.38 (dddd, J = 8.5, 7.0, 3.5, 3.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.1, 29.1, 34.9, 37.8, 49.8, 73.6, 210.7; IR (neat) 3390 cm^{-1}.

Hydroxy ketone 15: colorless oil (71 mg, 93% yield); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.17−1.29 (m, 1H), 1.34−1.80 (m, 7H), 1.82−1.92 (m, 1H), 2.01−2.14 (m, 2H), 2.29−2.33 (m, 1H), 4.24−4.31 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.1, 31.3, 39.2, 40.3, 44.4, 56.7, 73.2, 192.7; IR (neat) 3392 cm^{-1}.

Spiro hydroxy ketone 17: colorless oil (61 mg, 78% yield); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.15−1.32 (m, 1H), 1.60−1.72 (m, 1H), 1.94 (app q, J = 8.1 Hz, 1H), 2.09−2.23 (m, 2H), 2.28−2.41 (m, 2H), 2.64 (app t, J = 10.1 Hz, 1H), 2.85−2.88 (m, 1H), 7.17−7.48 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.6, 29.7, 32.8, 34.9, 36.4, 44.0, 52.5, 74.1, 126.6, 128.1, 128.6, 131.3, 133.1, 143.7, 201.7; IR (neat) 3399 cm^{-1}. Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.83; H, 7.52.

Hydroxytetrahydrofuran 24: colorless oil (81 mg, 86% yield). Spectral data were identical with those reported.[15]

General Method for Cyclopentannulation onto Bicyclic Lactam (25). To a solution of the bicyclic lactam **25** (1.2 mmol) in CH_2Cl_2 (10 mL) at −78 °C was added titanium(IV) chloride (1.2 mmol, 1.0 M solution in CH_2Cl_2) dropwise via syringe. After 5 min of vigorous stirring, allyltrityldimethylsilane (600 mg, 1.75 mmol) was added as a solution in CH_2Cl_2 dropwise. The reaction temperature was allowed to rise to 0 °C over 4 h. The reaction was monitored via TLC (4:1 Hex/EtOAc) and then treated with saturated aqueous NH_4Cl, resulting in a colorless mixture. The layers were separated, and the aqueous layer was washed with CH_2Cl_2. The organic layers were combined, dried (Na_2SO_4), filtered, and concentrated under reduced pressure to afford the crude products **26a**−**c**. The crude products were purified by flash chromatography on SiO_2 eluting with EtOAc/Hex (1:1).

Bicyclic lactam 26a: colorless solid (0.59 g, 68% yield), mp 240 °C (dec); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.11 (s, 3H), 0.14 (s, 3H), 0.83 (app t, J = 14.1 Hz, 1H), 1.10 (dd, J = 13.9, 3.0, Hz, 1H), 1.19 (s, 9H), 1.68 (ddd, J = 12.6, 9.0, 3.5, Hz, 1H), 2.55−2.65 (m, 1H), 2.74−2.82 (m, 1H), 3.23 (dd, J = 8.8, 7.3 Hz, 1H), 3.95 (app t, J = 9.1 Hz, 1H), 4.73 (dd, J = 8.8, 7.7 Hz, 1H), 5.12 (app t, J = 8.3, 1H), 6.95−7.34 (m, 25H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −0.4, 1.3, 19.9, 25.0, 27.8, 37.9, 44.5, 53.8, 59.5, 64.4, 75.2, 81.8, 100.1, 125.5, 127.2, 127.6, 128.0, 128.2, 128.4, 129.9, 138.0, 142.2, 165.8, 176.1; IR (neat) 1736, 1717 cm^{-1}; $[\alpha]^{23}_D$ = − 11.5 (c = 0.80, CH_2Cl_2).

Bicyclic lactam 26b: colorless solid (0.15 g, 75% yield), mp 140−143 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.13 (s, 6H), 0.81

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(app t, $J = 14.2$ Hz, 1H), 1.22−1.26 (m, 1H), 1.30 (s, 9H), 1.48 (s, 3H), 1.49−1.60 (m, 1 H), 2.28−2.38 (m, 1H), 2.64−2.71 (m, 1H), 3.23 (app t, $J = 8.2$ Hz, 1H), 4.18 (dd, $J = 8.7$, 7.8 Hz, 1H), 4.74 (app t, $J = 8.7$ Hz, 1H), 5.13 (app t, $J = 7.8$ Hz, 1H), 6.98−7.35 (m, 20H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −0.4, 1.5, 19.8, 24.0, 24.8, 28.0, 37.7, 43.5, 54.0, 57.6, 65.1, 75.2, 82.0, 98.1, 125.6, 125.7, 127.6, 128.1, 128.8, 130.0, 139.4, 146.3, 166.7, 174.5; IR (neat) 1735, 1712 cm^{-1}; $[\alpha]^{23}_D = +32.3$ ($c = 0.86$, CH_2Cl_2). Anal. Calcd for $C_{39}H_{53}NO_4Si$: C, 76.67, H, 7.20. Found: C, 76.70, H, 7.24.

Bicyclic lactam 26c: colorless solid (100 mg, 50% yield), mp 82−85 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.11 (s, 3H), 0.14, (s, 3H), 0.83 (app t, $J = 14.1$ Hz, 1H), 1.30 (s, 9H), 1.40 (dd, $J = 14.2$, 2.7 Hz, 1H), 2.00−2.18 (m, 2H), 2.74−2.83 (m, 1H), 3.18 (dd, $J = 9.9$, 4.5 Hz, 1H), 3.78 (dd, $J = 8.6$, 7.1 Hz, 1H), 4.47 (app t, $J = 8.3$ Hz, 1H), 4.92 (s, 1H), 5.14 (app t, $J = 7.5$ Hz, 1H), 6.96−7.36 (m, 20H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −0.3, 1.2, 21.7, 28.0, 30.4 35.7, 40.6, 53.7, 58.9, 60.8, 73.0, 82.0, 96.1, 125.6, 126.1, 127.7, 128.0, 128.8, 129.9, 139.8, 146.1, 166.4, 177.9; IR (neat) 1744, 1712 cm^{-1}; $[\alpha]^{23}_D = +90.6$ ($c = 0.64$, CH_2Cl_2). Anal. Calcd for $C_{41}H_{45}NO_4Si$: C, 76.48, H, 7.04. Found: C, 76.30; H, 7.09.

Bicyclic lactam 32: colorless oil (80 mg, 50% yield) as an inseparable mixture of diastereomers. Major diastereomer: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.13 (s, 6H), 0.79−0.88 (m, 1H), 1.28 (s, 3H), 1.39−1.50 (m, 1H), 1.89 (dd, $J = 9.3$ Hz, 1H), 2.28−2.38 (m, 1H), 2.41−2.48 (m, 1H), 2.83 (d, $J = 8.2$ Hz, 1H), 3.9 (dd, $J = 8.7$, 7.8 Hz, 1H), 4.24 (app t, $J = 8.7$ Hz, 1H), 4.73 (app t, $J = 7.8$ Hz, 1H), 5.1 (s, 2H), 6.98−7.35 (m, 25H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −0.4, 1.3, 19.9, 25.0, 27.8, 37.9, 44.5, 53.8, 59.5, 64.4, 75.2, 81.8, 100.1, 126.5, 127.2, 127.6, 128.0, 128.2, 128.4, 131.9, 138.0, 142.2, 165.8, 176.1; IR (neat) 1748, 1716 cm^{-1}.

General Procedure for the Oxidative Removal of Silicon. To a solution of the silylcyclobutane **26** (0.47 mmol) in 10 mL of THF at 0 °C was added tetrabutylammonium hydroxide (0.94 mL, 1.0 M in MeOH). Hydrogen peroxide (1.40 mL, 30% solution in water) was added, and the reaction was stirred vigorously for 24 h and then diluted with CH_2Cl_2 and water. The layers were separated, and the aqueous layer was washed with CH_2Cl_2. The combined layers were dried over Na_2SO_4, filtered, and concentrated in vacuo to yield a crude oil. The crude products were purified by flash chromoatography eluting with EtOAc/Hex (1:1) to yield the hydroxymethylcyclobutane **29**.

Bicyclic lactam 29a: viscous oil/foam (50 mg, 63% yield); ^{1}H NMR ($CDCl_3$, D_2O wash, 300 MHz) δ 1.40 (s, 9 H), 2.03 (ddd, $J = 13.2$, 9.3, 4.1 Hz, 1H), 2.58 (ddd, $J = 12.9$, 9.4, 6.8 Hz, 1H), 2.80 (m, 1H), 3.27 (dd, $J = 9.3$, 6.9 Hz, 1H), 3.72 (dd, $J = 12.1$, 6.0 Hz, 1H), 3.85 (dd, $J = 12.0$, 3.8 Hz, 1H), 3.96 (app t, $J = 9.0$ Hz, 1H), 4.73 (br, s, HOD), 4.78 (dd, $J = 9.0$, 7.8 Hz, 1H), 5.17 (app t, $J = 8.1$ Hz, 1H), 7.09−7.41 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.8, 27.8, 41.7, 47.5, 59.1, 62.0, 63.0, 74.7, 83.3, 100.6, 125.8, 126.9, 127.6, 128.3, 128.5, 138.0, 141.9, 168.1, 176.6; IR (neat) 1731 cm^{-1}; HRMS: (FAB); (M + H) calcd for $C_{26}H_{29}NO_5$ 436.2124, found 436.2130; $[\alpha]^{23}_D = +19.1$ ($c = 0.68$, CH_2Cl_2).

Bicyclic lactam 29b: viscous oil/foam (33 mg, 53% yield); ^{1}H NMR ($CDCl_3$, D_2O wash, 300 MHz) δ 1.48 (s, 3H), 1.51 (s, 9H), 1.80 (ddd, $J = 13.0$, 9.3, 3.6 Hz, 1H), 2.33 (ddd, $J = 13.1$, 9.5, 7.2 Hz, 1H), 2.70 (m, 1H), 3.20 (dd, $J = 9.2$, 7.4 Hz, 1H), 3.78 (dd, $J = 11.8$, 6.3 Hz, 1H), 3.88 (dd, $J = 11.7$, 3.8 Hz, 1H), 4.22 (dd, $J = 8.8$, 7.3 Hz, 1H), 4.76 (br s, HOD), 4.81 (app t, $J = 8.7$ Hz, 1H), 5.18 (app t, $J = 7.6$ Hz, 1H), 7.20−7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.0, 24.6, 28.0, 41.1, 46.6, 56.9, 62.5, 63.4, 75.3, 83.1, 98.4, 125.3, 127.5, 128.7, 168.6, 174.4; IR (film) 3478, 1734, 1710 cm^{-1}; HRMS (FAB), (M + H) Calcd for $C_{21}H_{27}NO_5$ 374.1967, found 374.1969; $[\alpha]^{23}_D = +103.1$ ($c = 1.3$, CH_2Cl_2).

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for all products and characterization data for compounds, **8**−**13** (36 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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