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Allyldimethyltritylsilane: construction of enantiomerically pure cyclobutano[*c*]fused pyrrolidines

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Dedicated to Professor Henri Kagan for his outstanding contributions to asymmetric reactions and his well-deserved recognition in the form of the Tetrahedron Prize

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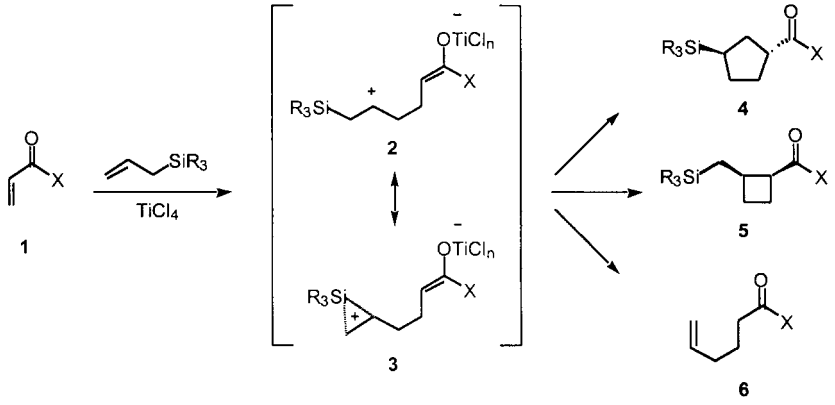
Abstract—Cyclobutannulation of the bicyclic lactam with allyldimethyltritylsilane is accomplished in high yield with good diastereoselectivity. The resulting tricyclic system is converted to a enantiomerically pure cyclobutane-fused pyrrolidine.

In the past 25 years, allylsilanes have become ubiquitous reagents in organic synthesis with a wide variety of applications.[1–3] Analogues of this reagent ranging from allenylsilane[4] to propargylsilanes[5] have also been investigated. One of the unique properties of these allylic silanes is the ability to behave as a 1,3-dipole and a '[2+2]' cycloaddition reaction partner. The three reaction manifolds proceed through a common intermediate shown as **2** and **3**. Addition of the terminal carbon of the allylsilane to the β-carbon of the enone system results in the β-silicon-stabilized carbenium species (**2**). The latter may also be represented by the non-classical 'siliranium' intermediate (**3**). At this juncture, the process may advance through three possible pathways. First, halide from the Lewis acid (usually titanium(IV) tetrachloride) may add to the silicon resulting in its displacement effecting net allyl transfer (**6**). Second, the intermediate metalloenolate may add intramolecularly to the siliranium intermediate (**3**) through a 4-*endo* process to afford the cyclobutane adduct (**5**). Finally, this same metalloenolate intermediate may add *via* a 5-*exo* pathway to yield the cyclopentane (**4**). The initial two pathways are usually predominant when the R group on silicon is larger than methyl (e.g. *i*-propyl, phenyl, *t*-butyl, etc.). Majetich[6] took advantage of the annulation manifold by performing the conjugate addition in an *intramolecular* sense wherein the allylsilane was tethered to the enone system. Despite the extensive investigation[7] of *intermolecular* annulation of allenylsilanes to produce cyclopentene products by



Scheme 1.

Keywords: cyclobutannulation; allyldimethyltritylsilane; '[2+2]' cycloaddition.
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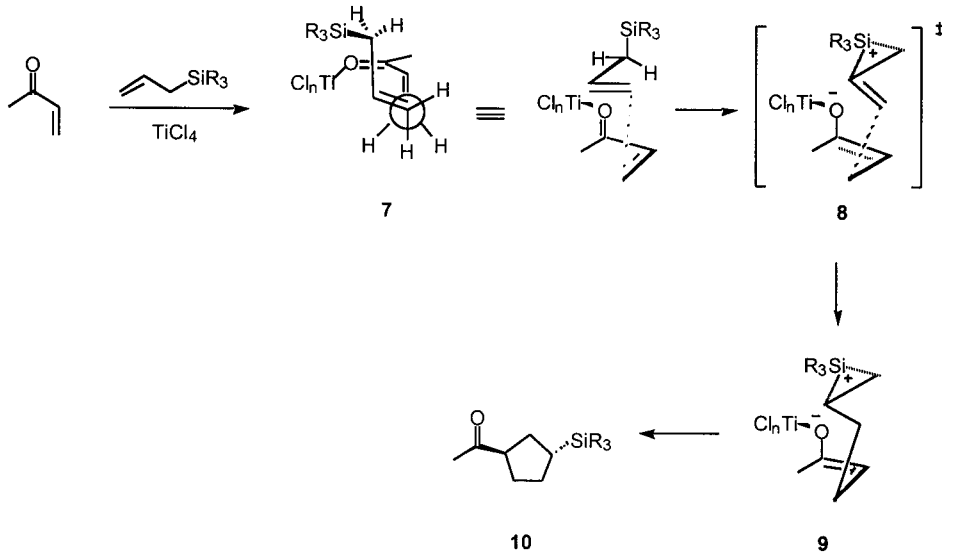
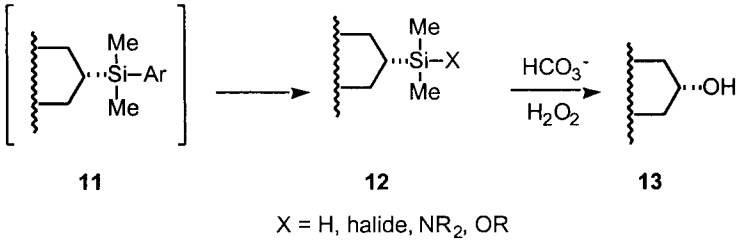


Scheme 2.



Scheme 3.

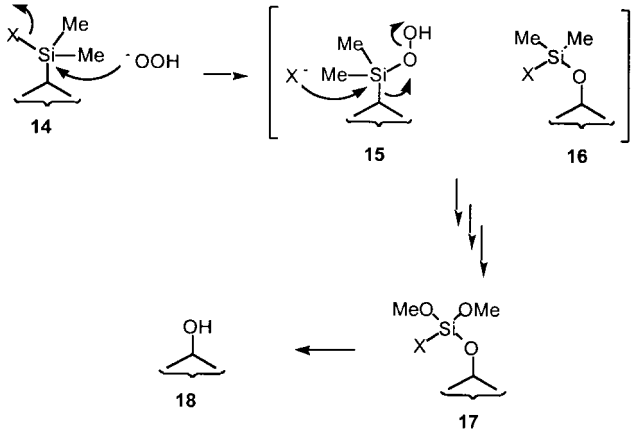
Danheiser throughout the 1980s, it was not until Knölker's work[8] in 1990 that the optimization of the annulation of allylsilanes onto enones was described (Scheme 1).

Another useful feature of the allylsilane annulation is the predictable stereochemistry of the annulated products (Scheme 2). The cyclopentane products form with a high propensity for the carbonyl group to be *trans* to the trisubstituted silyl moiety (**10**). It has been suggested by various groups[9] that this stereochemical outcome arises from a preference for a synclinal approach (**7**) which proceeds to the transition state (**8**), in accord with the general topological rule for Michael additions proposed by Seebach and Golinski.[10]

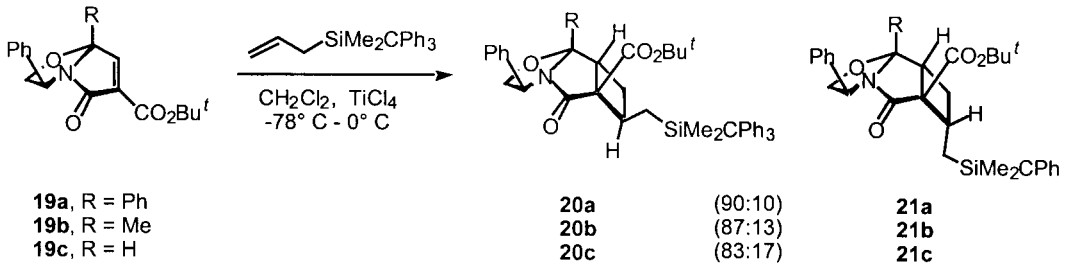
During this same period, Tamao[11] and Fleming[12] independently discovered a synthetically useful property of the silicon moiety; the oxidative conversion of the silicon–carbon bond (e.g. **11** via **12**) into a oxygen–carbon bond (e.g. **13**, Scheme 3). Since that time silicon's ability to act as a hydroxyl surrogate has increased its versatility and utility in synthetic organic chemistry.

Both of these methods were inspired by the work of Buncel and Davies[13] who reported that basic perbenzoic acid oxidized chlorodimethylphenylsilane to dimethyl(phenoxy)-silyl benzoate. Rearrangements of silyl peroxides, especially phenyl migration, was studied by Yablokov.[14] The sequence that produces an alcohol from the alkylsilane **14** is depicted in Scheme 4. Usually, the alkylsilane contains a nucleofugal group (Cl, OH, OR, etc.), which is initially displaced by the peroxide ion (**15**) and then return of the nucleofugal group to effect a silicon to oxygen rearrangement (**16**). Repetition of this sequence produces the silyl ethers (**17**), which are solvolyzed to the carbinols (**18**).

The ability of the silane to be transformed into an alcohol, allows one to exploit the nucleophilicity of the allylsilanes along with the annulation to access a variety of hydroxy-functionalized cyclobutanes and cyclopentanes, usually



Scheme 4.

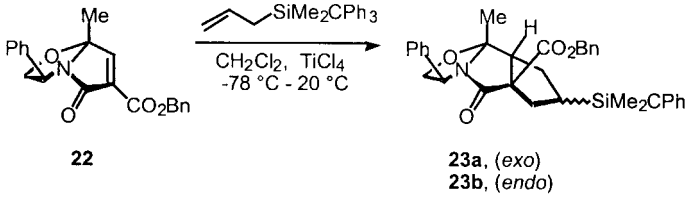


Scheme 5.

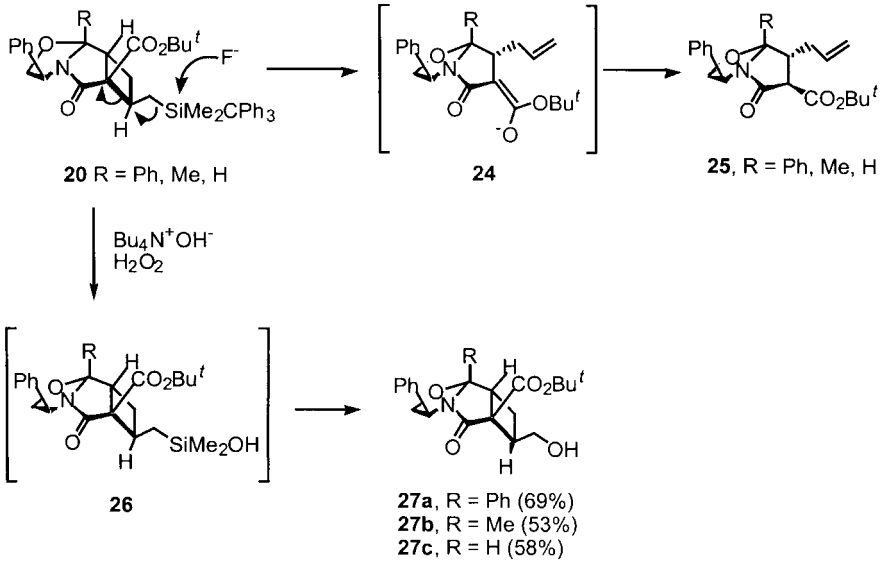
difficult to reach.[15] Although functionalized carbocycles,[16] as well as heterocycles, such as oxetanes,[17] tetrahydrofurans,[18] azetidines and pyrrolidines[19] have been accessed, little has been done using both the annulation and silane oxidation.[20] We have previously described[21] how both processes may be maximized using allyldimethyltritylsilane (ADTS). We were able to construct stereochemically defined cyclopentanols, oxetanes, and tetrahydrofurans using this method.

In order to assess the versatility and scope of the annulations, we examined the reactions with the chiral bicyclic lactams (**19**) reported earlier[21] to give either 4 or 5-membered ring annulation.[22] The annulations previously performed using triisopropylallyl silanes (allylTIPS) were incapable of being oxidized to the alcohols. The bicyclic lactams (**19**) were treated with titanium(IV) tetrachloride in dichloromethane at −78°C, and after addition of the allylsilane (ADTS) the reaction mixture was allowed to warm to 0°C. A 50–75% yield of cyclobutane adducts (**20**, **21**) was exclusively obtained as a mixture of *exo*–*endo* silyl substituent with the major product in each instance being the *exo*-products (**20**). It is noteworthy to mention that no cyclopentane products (i.e. **23**) were observed as was previously described[21] when warming the allylTIPS adducts to 0°C in the presence of $TiCl_4$ (Scheme 5).

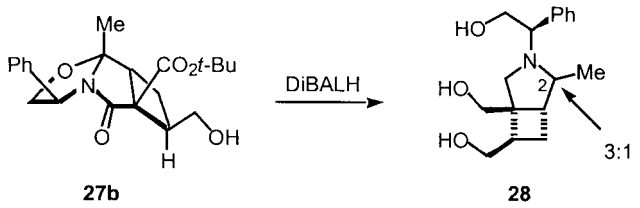
Furthermore, the rates of reaction were qualitatively slower with ADTS when compared to those exhibited by allylTIPS additions, presumably due to slightly less inductive stabilization by the methyl and trityl groups. Titanium(IV) tetrachloride mediated rearrangement of the initially formed cyclobutane from **20** to cyclopentane products **23** 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 albeit in poor yield and with loss of



Scheme 6.



Scheme 7.



Scheme 8.

stereochemical integrity (Scheme 6). Thus, **23** was obtained in 21% yield, but with only a diastereomeric ratio of 78:22, indicating the rearrangement took place with poor stereochemical integrity.

Attempts to oxidize the silane **21** to the corresponding carbinol using standard Tamao conditions resulted in formation of the Sakurai product (**25**) (Scheme 7). This was considered to be a result of nucleophilic attack on the silicon by the fluoride ion and subsequent elimination to the alkene (**24**). 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 (**20**) with only tetrabutylammonium hydroxide in the presence of hydrogen peroxide produced the solvolyzed intermediate **26** which was readily oxidized to the primary alcohols (**27a**–**c**) in moderate yields.

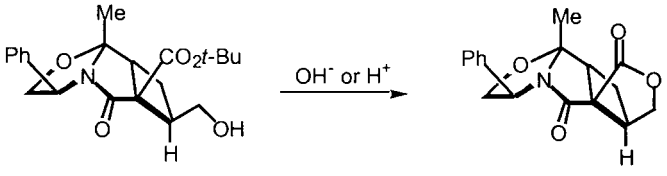
Initial attempts to remove the chiral auxiliary began with diisobutylaluminum hydride reduction to afford a 3:1 inseparable mixture of diastereomers **28** at the C-2 methyl position (Scheme 8).[23] Other reducing agents (Red-Al, BH_3, AlH_3, 9-BBN, L-Selectride) were investigated with equally poor diastereoselectivity being observed.

Concurrent studies on these cyclobutane adducts revealed that the free hydroxymethyl group had a high propensity to lactonize onto the vicinal ester to form **29** under both acidic and basic conditions (Scheme 9). It was felt that the first step in the reduction process was formation of the lactone **29**, which adversely affected the stereochemical outcome of the subsequent reductions.

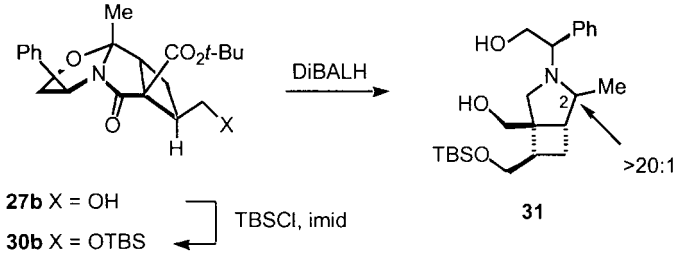
In an effort to test this hypothesis, the hydroxymethyl group was protected as its *tert*-butyldimethylsilyl ether (**30**) and subjected to the orginal reduction conditions (Scheme 10). The reduction proceeded with excellent selectivity at the C-2 methyl position, producing only one detectable diastereomer (**31**).

Assignment of the newly formed stereogenic center was initially attempted with ^{1}H NMR using previously reported[24] reductions of tricyclic lactam systems (**32**–**34**) as models (Scheme 11). Their assignments were resolved comparing the coupling constants of the vicinal hydrogens and later confirmed by X-ray crystallography.

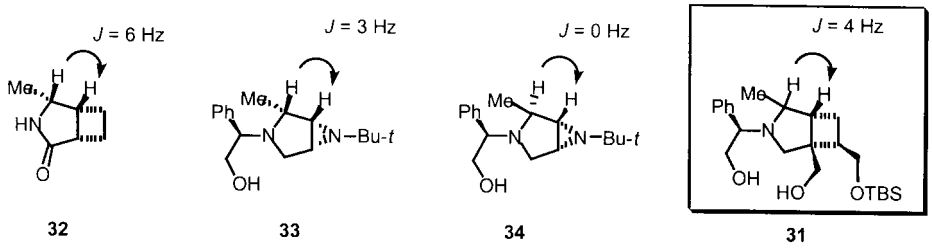
Based on these data, it would appear that the stereochemical assignment should be that of reduction with inversion at the angular methyl in **30b**. However, after analysis of the



Scheme 9.



Scheme 10.



Scheme 11.

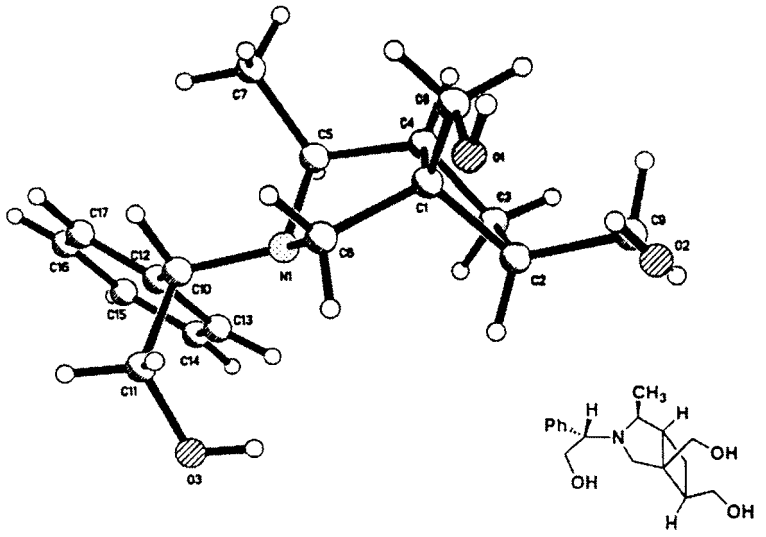
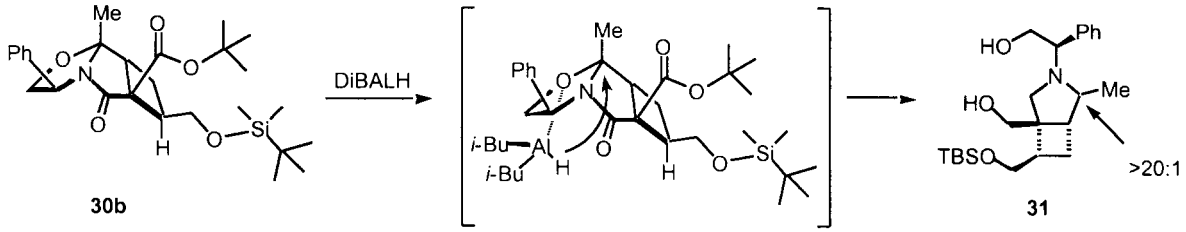
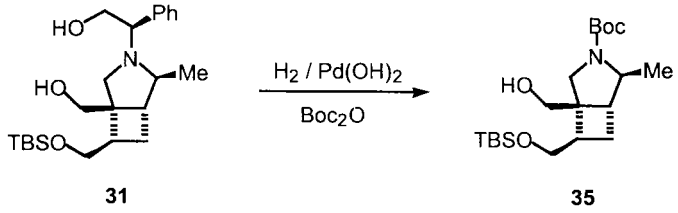


Figure 1.



Scheme 12.



Scheme 13.

dihedral angles in models of the two possible products, the coupling constants were predicted to be ~7 Hz for the cis isomer and ~3 Hz for the *trans* isomer. It was neccesary to confirm the structure by X-ray crystallography to eliminate any doubt. Removal of the *tert*-butyldimethylsilyl ether using tetrabutylammonium fluoride, afforded the triol as a colorless solid with X-ray quality crystals. X-Ray analysis revealed that the reduction occurred with *retention* of stereochemistry at the angular position (Fig. 1).

This seemingly anomolous result could be rationalized by the abundance of steric bulk on the convex (*exo*) face of the tricyclic system **30b**, forcing the delivery of the hydride to occur from the concave (*endo*) face of the tricyclic lactam thus furnishing **31** (Scheme 12).

With the stereochemistry of the cyclobutano[*c*]pyrrolidine, **31**, unequivocally established, all that remained was the hydrogenolysis of the benzylic carbon–nitrogen bond. This was accomplished by treatment of pyrrolidine **31** with palladium(II) hydroxide under an atmosphere of hydrogen with in the presence of $(Boc)_2O$ to give *tert*-butyl carbamate (**35**) (Scheme 13).

In summary, the application of allylsilane additions to the bicyclic lactam have been shown to undergo annulations employing allyldimethyltritylsilane. This has resulted in a novel route to enantiomerically pure cyclobutano[*c*]pyrrolidines.

1. Experimental

1.1. General method for cyclopentannulation onto bicyclic lactam 19 (a–c)

To a solution of the bicyclic lactam **19** (**a**–**c**) (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[20b] (600 mg, 1.75 mmol) was added as a solution in CH_2Cl_2 dropwise. The temperature was allowed to rise to 0°C

over 4 h. The reaction was monitored via TLC (4:1 Hex/EtOAc) then treated with sat. aq. 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 **20** and **21**. The crude products were purified by flash chromatography on SiO_2 eluting with EtOAc/Hex (1:1). **21** (**a**–**c**) were not characterized due to the rather small quantities that were formed.

1.1.1. Bicyclic lactam 20a. Colorless solid (0.59 g, 68% yield), mp 180°C (EtOAc/Hex). ^{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 Hz, 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}. $[\alpha]_D^{23}$=−11.5 (c=0.80, CH_2Cl_2).

1.1.2. Bicyclic lactam 20b. Colorless solid (0.15 g, 75% yield), mp 140–143°C (EtOAc/Hex). ^{1}H NMR ($CDCl_3$, 300 MHz) δ=0.13 (s, 6H), 0.81 (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, 1H), 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}; Anal. Calcd for $C_{39}H_{53}NO_4Si$: C 76.67, H 7.20, found C 76.70, H 7.24; $[\alpha]_D^{23}$=+32.3 (c=0.86, CH_2Cl_2).

1.1.3. Bicyclic lactam 20c. Colorless solid (100 mg, 50% yield), mp 82–85°C (EtOAc/Hex). ^{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}; Anal. Calcd for $C_{41}H_{45}NO_4Si$: C 76.48, H 7.04, found: C 76.30, H 7.09; $[\alpha]_D^{23}$=+90.6 (c=0.64, CH_2Cl_2).

1.1.4. Bicyclic lactam 23a,23b. Colorless oil (50 mg, 21% 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}.

1.2. General procedure for the oxidative removal of silicon from 20

To a solution of the silylcyclobutane **20** (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 hydroxymethylcyclobutanes **27**.

1.2.1. Bicyclic lactam 27a. Viscous oil/foam (50 mg, 63% yield). ^{1}H NMR ($CDCl_3$, D_2O wash, 300 MHz) δ=1.40 (s, 9H), 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; $[\alpha]_D^{23}$=+19.1 (c=0.68, CH_2Cl_2).

1.2.2. Bicyclic lactam 27b. 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; $[\alpha]_D^{23}$=+103.1 (c=1.3, CH_2Cl_2).

1.2.3. Lactone 29. To a flame-dried round bottom flask was added bicyclic lactam **27b** (400 mg, 1.07 mmol) followed by 5 mL of dichloromethane. PTSA (5 mg) was added at room temperature and the reaction was stirred under an argon atmosphere for 2 h. The reaction mixture was concentrated under reduced pressure to afford a pale yellow residue. The crude mixture was purified via chromatography (SiO_2, 4:1 Hex/EtOAc) to give a colorless solid (291 mg, 91%), mp=112–114°C (EtOAc/Hex), $[\alpha]_{D23}$=24° (c=1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ=1.42 (s, 3H), 2.07 (ddd, J=3, 8, 11 Hz, 1H), 2.83 (ddd, J=6, 8, 12 Hz, 1H), 3.17−3.28 (m, 2H), 4.24 (dd, J=7, 9 Hz, 1H), 4.36 (J=5, 10 Hz, 1H), 4.70 (app. t, J=8 Hz, 1H), 4.83 (app. t, J=8Hz, 1H), 5.26 (app. t, J=8 Hz, 1H), 7.23–7.38 (m, 5H); ^{13}C NMR ($CDCl_3$, 75MHz) δ=23.2, 25.4, 36.5, 44.5, 56.7, 57.6, 74.1, 74.3, 97.9, 125.2, 127.5, 128.7, 139.0, 172.4, 172.9; IR (film) 1769, 1708 cm^{-1}.

1.2.4. Lactam 30b. To a dichloromethane solution of **27b**

(128 mg, 0.34 mmol) was added imidazole (22 mg, 1.1 equiv) followed by *tert*-butyldimethylsilyl chloride (56 mg, 1.1 equiv). A voluminous colorless precipitate formed and after 1 h the reaction mixture was partitioned between dichloromethane and water. The aqueous layer was washed with dichloromethane, the combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated to a colorless oil. The residue was chromatographed (SiO_2, 4:1 Hex/EtOAc) to afford a colorless oil (165 mg, 89%). $[\alpha]_D^{23}=73$ ($c=1.1$, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) $\delta=0.13$ (s, 3H), 0.14 (s, 3H), 0.98 (s, 9H), 1.56 (s, 9H), 1.62 (s, 3H), 1.95 (ddd, $J=12$, 9, 3 Hz, 1H), 2.33 (ddd, $J=12$, 9, 8 Hz, 1H), 2.70 (ddd, $J=9$, 6, 2 Hz, 1H), 3.30 (dd, $J=9$, 8 Hz, 1H), 3.77 (dd, $J=10$, 3 Hz, 1H), 4.16 (dd, $J=10$, 4 Hz, 1H), 4.28 (dd, $J=9$, 7 Hz, 1H), 4.87 (app. t, $J=8$ Hz, 1H), 5.23 (app. t, $J=8$ Hz, 1H), 7.23–7.41 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) $\delta=-5.5$, -5.3, 18.3, 19.1, 24.6, 25.9, 28.2, 41.2, 46.3, 57.1, 62.1, 62.4, 75.2, 81.7, 98.7, 125.5, 127.5, 128.7, 139.6, 166.7, 174.95; IR (film) 1742, 1711 cm^{-1}; Anal. calcd for $C_{31}H_{41}NO_5Si$: C 66.49, H 8.47, found: C 66.57, H 8.48.

1.2.5. Pyrrolidine 31. A THF solution of **30b** (130 mg, 0.24 mmol) was cooled to $-78°C$ and DIBALH(0.9 mL (neat), 10 equiv.) was added dropwise via syringe. The mixture was allowed to warm to room temperature over 8 h at which time the solution was cooled to $-78°C$ and MeOH was slowly added until the evolution of hydrogen ceased. The solution was warmed to room temperature, an equal volume of 10% KOH was added, and vigorously stirred for 1 h. The mixture was partitioned between dichloromethane and water. The layers were separated, the aqueous layer was washed with dichloromethane, the combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated to a colorless oil. Crude ^1H NMR analysis revealed a single methyl doublet at 0.85 ppm, therefore the d.r. was determined to be >20:1. The residue was chromatographed (SiO_2, Et_2O) to afford a colorless oil (85 mg, 84%) $[\alpha]_D^{23}=-6$ ($c=0.8$, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) $\delta=0.13$ (s, 3H), 0.14 (s, 3H), 0.85 (d, $J=9$ Hz, 3H), 0.92 (s, 9H), 1.52 (ddd, $J=12$, 9, 7 Hz, 1H), 1.76 (ddd, $J=11$, 9, 8 Hz, 1H), 1.87 (dd, $J=11$, 8 Hz, 1H), 2.36 (ddd, $J=10$, 8, 7 Hz, 1H), 2.81 (ddd, $J=11$, 7, 6 Hz, 1H), 2.90–3.03 (m, 2H), 3.39 (d, $J=11$ Hz, 1H), 3.67 (dd, $J=10$, 7 Hz, 1H), 3.80–3.92 (m, 4H), 4.09 (d, $J=11$ Hz, 1H), 7.29–7.42 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) $\delta=-5.6$, -5.4, 14.2, 18.2, 23.5, 25.8, 41.4, 43.1, 50.5, 58.3, 63.8, 64.7, 65.4, 127.7, 128.4, 128.8; IR (film) 3360, 2957 cm^{-1}. Anal. calcd for $C_{24}H_{41}NO_3Si$: C 68.71, H 9.84, found: C 68.76, H 9.73.

1.2.6. Pyrrolidine 35. To an ethanol solution of *N*-benzyl pyrrolidine **31** (50 mg, 0.12 mmol) was added $Pd(OH)_2$ and di-*tert*-butylpyrocarbonate (50 mg, 1.5 equiv.) and stirred under an atmosphere of hydrogen. After 10 h, the reaction solution was purged with argon, filtered through a plug of Celite and concentrated to a colorless oil. Column chromatography (SiO_2, 10% MeOH/$CHCl_3$) yielded the pyrrolidine as a colorless oil (43 mg, 91%): $[\alpha]_D^{23}=-13$ ($c=0.6$, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) $\delta=0.09$ (s, H), 0.88 (s, 9H), 1.05 (d, $J=11$ Hz, 3H), 1.48 (s, 9H), 1.51–1.62 (m, 3H), 1.63–1.79 (br. m, 1H), 1.92–2.1 (br. m, 1H), 2.27–2.41 (br. m, 1H), 3.29–3.41 (m, 2H), 3.63 (dd, $J=11$, 9 Hz, 1H), 3.67–3.82 (m, 3H), 3.9–4.11 (br. m, 2H); −5.6, −5.4, 18.2, 19.3, 23.5, 25.8, 28.6, 40.8, 43.3, 56.8, 59.6, 64.6, 65.3, 79.2, 100.1, 154.6; IR (film) 3456, 1692 cm^{-1}. Anal. calcd for $C_{21}H_{41}NO_4Si$: C 63.14, H 10.32, found: C 63.04, H 10.39.

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References

1. For reviews discussing the use of allylsilanes see: (a) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063. (b) Majetich, G. In *Allylsilanes in Organic Synthesis in Organic Synthesis: Theory and Applications*, Hudlicky, T., Ed.; JAI: Greenwich, CT, 1989; Vol. 1.
2. For a review discussing the use of chiral allylsilanes see: Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293.
3. For a review on [3+2] annulation reactions of allyltriisopropylsilane, see: Knölker, H.-J. *J. Prakt. Chem.* **1997**, *339*, 304.
4. Danheiser, R. L.; Carini, D. J.; Basak, A. *J. Am. Chem.Soc.* **1981**, *103*, 1604.
5 Danheiser, R. L.; Dixon, B. R.; Gleason, R. W. *J. Org. Chem.* **1992**, *57*, 6094.
6. (a) Majetich, G.; Casares, A. M.; Chapman, D.; Behnke, M. *Tetrahedron Lett.* **1983**, *24*, 1909. (b) Majetich, G.; Desmond Jr, R. W.; Soria, J. J. *J. Org. Chem.* **1986**, *51*, 1753. (c) Majetich, G.; Defauw, J.; Ringold, C. *J. Org. Chem.* **1988**, *53*, 50. (d) Majetich, G.; Hull, K.; Casares, A. M.; Khetani, V. *J. Org. Chem.* **1991**, *56*, 3958. (e) Majetich, G.; Song, J.-S.; Leigh, A. J.; Condon, S. M. *J. Org. Chem.* **1993**, *58*, 1030.
7. (a) Danheiser, R. L.; Carini, D. J. *J. Org. Chem.* **1980**, *45*, 3925. (b) Danheiser; Carini, D. J.; Basak, A. *J. Am. Chem. Soc.* **1981**, *103*, 1604. (c) Danheiser; Carini, D. J.; Fink, D. M.; Basak, A. *Tetrahedron* **1983**, *39*, 935. (d) Danheiser, R. L.; Fink, D. M. *Tetrahedron Lett.* **1985**, *26*, 2513. (e) Danheiser, R. L.; Kwasigroch, C. A.; Tsai, Y.-M. *J. Am. Chem. Soc.* **1985**, *107*, 7233. (f) Danheiser, R. L.; Decker, D. A. *Heterocycles* **1987**, *25*, 277. (g) Danheiser, R. L.; Tsai, Y.-M.; Fink, D. M. *Org. Synth.* **1988**, *66*, 1. (h) Danheiser, R. L.; Tsai, Y.-M.; Fink, D. M. *Org. Synth.* **1988**, *66*, 8. (i) Becker, D. A.; Danheiser, R. L. *J. Am. Chem. Soc.* **1989**, *111*, 389. (j) Danheiser, R. L.; Stoner, E. J.; Koyama, H.; Yamashita, D. S.; Klade, C. A. *J. Am. Chem. Soc.* **1989**, *111*, 4407.
8. (a) Knölker, H.-J.; Jones, P. G.; Pannek, J.-B. *Synlett* **1990**, 429. (b) Knölker, H.-J.; Jones, P. G.; Wanzyl, G. *Synlett.* **1998**, 613.
9. (a) Knölker, H.-J.; Foitzik, N.; Graf, R.; Pannek, J.-B. *Tetrahedron* **1993**, *49*, 9955. (b) Panek, J. S.; Jain, N. F. *J. Org. Chem.* **1993**, *58*, 2345. (c) Danheiser, R. L.; Dixon, B. R.; Gleason, R. W. *J. Org. Chem.* **1992**, *57*, 6094. (d) Danheiser, R. L.; Takahashi, T.; Bertók, B.; Dixon, B. R. *Tetrahedron Lett.* **1993**, *34*, 3845.
10. Seebach, D.; Golinski, J. *Helv. Chim. Acta* **1981**, *64*, 1413.

11. (a) Tamao, K.; Ishida, N.; Tanaka, T.; Kumada, M. *Organometallics* **1983**, *2*, 1694. (b) Tamao, K.; Ishida, N. *J. Organomet. Chem.* **1984**, *269*, C37.
12. Fleming, I.; Henning, R.; Plaut, H. *J. Chem. Soc., Chem. Commun.* **1984**, 29.
13. Buncel, E.; Davies, A. G. *J. Chem. Soc.* **1958**, 1550.
14. Yablokov, V. A.; Tarabarina, A. P.; Yablokova, N. Y.; Stal'nova, M. I. *Zh. Obsch. Khim.* **1971**, *41*, 887.
15. (a) Ghosh, S.; Patra, D. *Pure Appl. Chem.* **1996**, *68*, 597. (b) Paquette, L. A. *Top. Curr. Chem.* **1984**, *119*, 1.
16. (a) Knölker, H.-J.; Baum, G.; Graf, R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1612. (b) Akiyama, T.; Yamanaka, M. *Tetrahedron Lett.* **1998**, *39*, 7885. (c) Murphy, W. S.; Neville, D. *Tetrahedron Lett.* **1997**, *38*, 7933. (d) Angle, S. R.; Boyce, J. P. *Tetrahedron Lett.* **1994**, *35*, 6461.
17. Akiyama, T.; Yamanaka, M. *Synlett* **1996**, 1095.
18. (a) Akiyama, T.; Yasusa, T.; Ishikawa, K.; Ozaki, S. *Tetrahedron Lett.* **1994**, *35*, 8401. (b) Panek, J. S.; Yang, M. *J. Am. Chem. Soc.* **1991**, *113*, 9868.
19. (a) Peng, Z.-H.; Woerpel, K. A. *Org. Lett.* **2000**, *2*, 1379. (b) Roberson, C. W.; Woerpel, K. A. *Org. Lett.* **2000**, *2*, 621. (c) Panek, J. S.; Jain, N. J. *J. Org. Chem.* **1994**, *59*, 2674.
20. Knölker, H.-J.; Baum, G.; Schmitt, O.; Wanzyl, G. *Chem. Comm.* **1999**, 1737.
21. (a) Brengel, G. P.; Meyers, A. I. *J. Org. Chem.* **1996**, *61*, 3230. (b) Groaning, M. D.; Brengel, G. P.; Meyers, A. I. *J. Org. Chem.* **1998**, *63*, 5517.
22. (a) Burgess, L. E.; Meyers, A. I. *J. Org. Chem.* **1992**, *52*, 1656. (b) Munchof, M. J.; Meyers, A. I. *J. Org. Chem.* **1995**, *60*, 7084.
23. (a) Burgess, L. E.; Meyers, A. I. *J. Org. Chem.* **1992**, *52*, 1656. (b) Munchof, M. J.; Meyers, A. I. *J. Org. Chem.* **1995**, *60*, 7084.
24. Andres, C. J.; Meyers, A. I. *Tetrahedron Lett.* **1995**, *36*, 3491. (b) Meyers, A. I.; Tschantz, M. A.; Brengel, G. P. *J. Org. Chem.* **1995**, *6*, 4359.