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Full Paper

Reactivities of *trans*-Cycloalkenes

[4+2] Cycloadditions of Seven-Membered-Ring *trans*-Alkenes: Decreasing Reactivity with Increasing Substitution of the Seven-Membered Ring

John Santucci III,[a] Jillian R. Sanzone,[a] and K. A. Woerpel*[a]

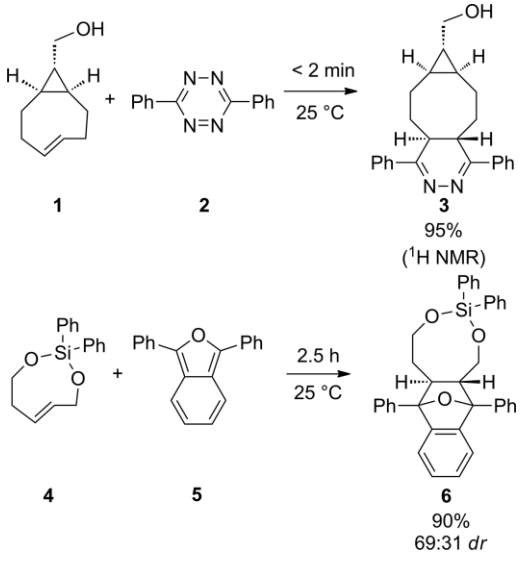
Abstract: The reactivity of *trans*-oxasilacycloheptenes in [4+2] cycloadditions depends on the substitution pattern on the seven-membered ring. Unhindered *trans*-alkenes undergo [4+2] cycloadditions with 1,3-diphenylisobenzofuran faster than the most reactive *trans*-cyclooctene. Increasing the substitution of the seven-membered ring or increasing the electron density of the *trans*-alkene decreases reactivity with 1,3-dienes in concerted cycloaddition reactions. Although highly substituted *trans*-alkenes are unreactive in concerted cycloaddition reactions, these alkenes react rapidly in stepwise reactions with diethyl azodicarboxylate (DEAD), an electrophilic diene.

Introduction

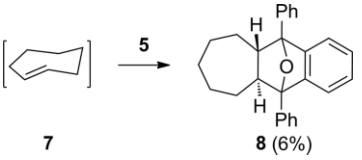
The enhanced reactivity of strained alkenes and alkynes compared to their unstrained counterparts has prompted numerous investigations into their reactivity.[1] Strain-accelerated reactions have been utilized in a variety of applications in synthesis,[2–4] including the synthesis of natural products.[5] These reactions have also been applied in bioorthogonal reactions,[6,7] such as site-specific protein labeling and in vivo imaging.[8,9]

trans-Cyclooctenes have been shown to be highly reactive in Diels–Alder cycloaddition reactions. *trans*-Cyclooctene **1**, a highly distorted *trans*-alkene, underwent a rapid inverse-electron-demand Diels–Alder cycloaddition with 3,6-diphenyl-*s*-tetrazine (**2**) to form cycloadduct **3** (Scheme 1).[10] The cyclopropane ring forces the eight-membered ring to adopt a half-chair conformation, which is more strained than the crown conformation of *trans*-cyclooctene, leading to enhanced reactivity of alkene **1**.[10] *trans*-Cyclooctene **4** also participated in a [4+2] cycloaddition, reacting with 1,3-diphenylisobenzofuran (**5**) to provide cycloadduct **6** as a mixture of diastereomers.[11] A competition experiment between *trans*-alkene **4** and *trans*-cyclooctene showed that alkene **4** is four times more reactive with furan **5** than *trans*-cyclooctene.

In contrast to *trans*-cyclooctenes, few examples of seven-membered-ring *trans*-alkenes undergoing [4+2] cycloaddition reactions have been reported. The smaller *trans*-cycloheptenes should be more reactive than *trans*-cyclooctenes because they are more strained.[12] *trans*-Cycloheptene (**7**), generated in situ from *trans*-1,2-cycloheptene thionocarbonate and trimethyl phosphite, underwent a Diels–Alder cycloaddition with diene **5** to afford bicyclic ether **8** in 6 % yield from the thionocarbonate [Equation (1)].[13,14] Seven-membered-ring *trans*-alkenes were also reported to undergo [4+2] cycloadditions with 1,3-dipoles such as diazomethane[15] and phenyl azide.[16]



Scheme 1. [4+2] Cycloadditions of *trans*-cyclooctenes.



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In this article, we demonstrate that the reactivity of seven-membered-ring *trans*-alkenes in concerted [4+2] cycloadditions is greatly influenced by the substituents on the seven-mem-

[a] *Department of Chemistry, New York University, 100 Washington Square East, New York, NY 10003 USA*
E-mail: kwoerpel@nyu.edu
https://wp.nyu.edu/woerpelgroup/

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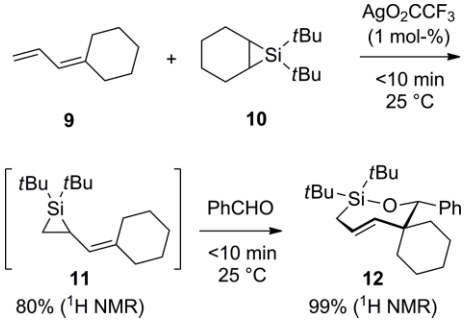
bered ring. Preliminary studies showed that unhindered *trans*-oxasilacycloheptenes are more reactive than a *trans*-cyclooctene.[17] Additional studies show that strain energy is not the only factor that influences the reactivity of these strained compounds.[18] Steric effects play a significant role in cycloaddition reactivity. Highly substituted *trans*-alkenes react slowly or are unreactive in cycloadditions with dienes **2** and **5**. Although hindered *trans*-alkenes are sluggish in concerted Diels–Alder cycloadditions, they display high reactivity in stepwise reactions with diethyl azodicarboxylate (DEAD). These results indicate that steric effects can be more significant than ring strain in the reactivity of strained *trans*-cycloalkenes.

Results and Discussion

Synthesis of *trans*-Oxasilacycloheptenes

Seven-membered-ring *trans*-alkenes were synthesized from dienes, aldehydes, and silylenes generated in situ. The synthesis of *trans*-alkene **12** illustrates the protocol (Scheme 2). Silver-catalyzed silylene transfer to 1,3-diene **9** afforded vinylsilacyclopropane **11** in 80 % yield. Addition of benzaldehyde to vinylsilacyclopropane **11** yielded *trans*-oxasilacycloheptene **12** in 99 % yield.[17,19] *trans*-Alkene **12** was unstable to atmospheric conditions and it underwent thermal rearrangement.[19] It could, however, be characterized and stored at –20 °C for greater than ten days, and it could be used in further transformations.



Scheme 2. Synthesis of *trans*-oxasilacycloheptene **12**.

A variety of *trans*-oxasilacycloheptenes were prepared with different substituent patterns to determine the reactivity of the *trans* double bond in both concerted and stepwise reactions (Figure 1). Because previous studies indicated that increased substitution at the allylic position decreased reactivity in Diels–Alder cycloadditions,[17] additional substituents were placed at the allylic position to quantify this effect (alkenes **12** and **14**). It was hypothesized that fusing a second ring to the seven-membered ring would lead to heightened reactivity. The fused ring system would limit the ability of the double bond to alleviate strain by altering bond and torsion angles.[20,21] Bicyclic trisubstituted alkenes **15**–**17** were synthesized to examine the effect of the fused ring and to determine how the size of the fused ring impacts reactivity.

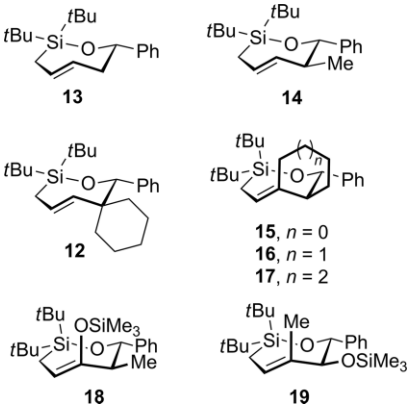
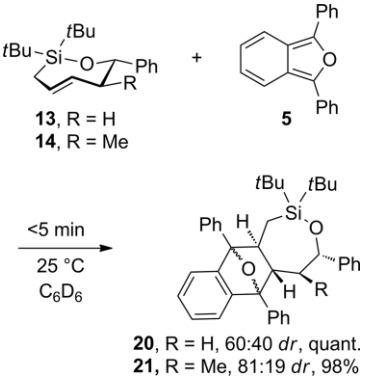


Figure 1. Seven-membered-ring *trans*-alkenes synthesized for this study.

Silyl enol ether **18** and trisubstituted alkene **19** were synthesized to determine how the electron density of the *trans* double bond influenced reactivity. Silyl enol ether **18** should be particularly reactive because silyl enol ethers are more nucleophilic than most alkenes.[22] *trans*-Alkene **19**, which is isomeric to silyl enol ether **18** and should have similar strain energy, was synthesized to control for electronic effects. The electron-withdrawing group at the allylic position of the *trans*-alkene should decrease the electron density of the double bond, making the *trans* double bond in **19** electron-poor relative to *trans*-alkenes **12**–**18**.

[4+2] Cycloadditions with 1,3-Diphenylisobenzofuran

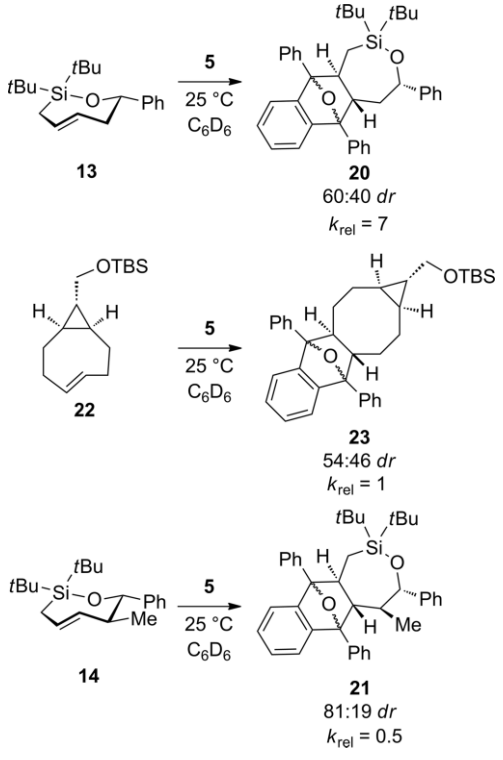
As predicted, *trans*-alkenes **13** and **14** were highly reactive in Diels–Alder cycloaddition reactions with furan **5** (Scheme 3).[17] In less than five minutes, *trans*-alkenes **13** and **14** were consumed, forming cycloadducts **20** and **21** in high yields as mixtures of diastereomers. Spectroscopic studies enabled the assignment of the relative stereochemistry about the seven-membered ring, but they did not reveal the relative stereochemistry at the bridgehead carbon atoms of the oxabicyclic framework. Although the cycloaddition occurred with retention of the geometry of the *trans*-alkene,[23] facial selectivity on the diene was low.



Scheme 3. Cycloadditions of *trans*-alkenes **13** and **14** with diene **5**.

The high reactivity of alkenes **13** and **14** prompted comparison to *trans*-cyclooctene **1**, which is reported to have unparal-

leled second-order kinetics in Diels–Alder cycloadditions (Scheme 1).[10] Because these reactions were too rapid to determine the second-order rate constants by ^{1}H NMR spectroscopy, competition experiments were performed (Scheme 4). Silyl-protected *trans*-cyclooctene **22** was used because *trans*-cyclooctene **1** was insoluble under the reaction conditions. Diene **5** was added to an excess of the two *trans*-alkenes. Spectroscopic analysis was conducted immediately after mixing to determine relative rates of the reactions. *trans*-Oxasilacycloheptene **13** reacted seven times faster with diene **5** than *trans*-cyclooctene **22** did. This enhanced rate is likely due to the high distortion of the *trans* double bond in alkene **13**,[24] and therefore more orbital distortion,[18] compared to *trans*-cyclooctene **22**, leading to enhanced reactivity in the Diels–Alder cycloaddition.



Scheme 4. Relative rates of reactions with 1,3-diphenylisobenzofuran (**5**).

Because *trans*-alkene **14** was predicted to have similar ring strain to alkene **13**, it was expected to be comparably reactive. *trans*-Cycloalkene **14** differs from alkene **13** only by the presence of a methyl group at the allylic position. Competition experiments, however, revealed that the presence of the allylic methyl group decreased the rate of cycloaddition by over one order of magnitude (Scheme 4).[17] The decrease in rate is likely due to the *syn*-pentane interaction[25] that develops between the allylic methyl group on alkene **14** and the phenyl group on diene **5** in the transition state (Figure 2). This unfavourable steric interaction raises the energy of the transition state leading to cycloadduct **21** compared to cycloadduct **20**. The steric hindrance is significant enough that the less strained *trans*-cyclooctene **22** reacts faster than the more distorted *trans*-cycloheptene **14**.

Increased substitution of the seven-membered ring further decreased reactivity with diene **5** (Scheme 5). When *trans*-

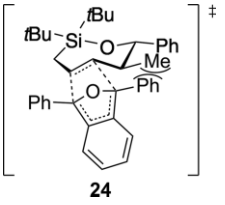
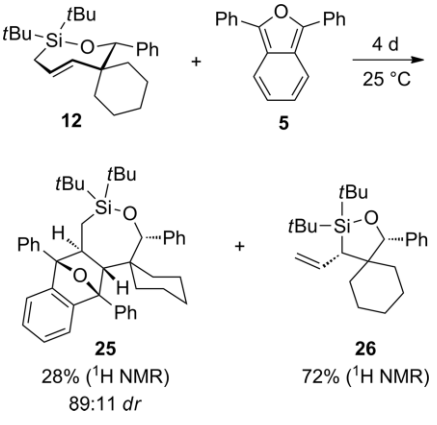


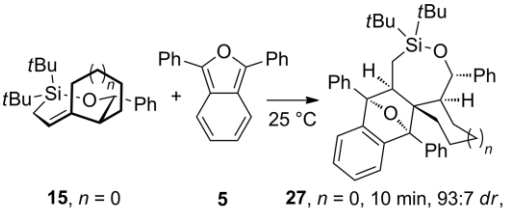
Figure 2. Transition state for the reaction of alkene **14** and diene **5**.

alkene **12** was subjected to similar conditions with diene **5**, the reaction was over 1000 times slower than the reactions with *trans*-alkenes **13** and **14** (greater than four days compared to less than five minutes, Schemes 3 and 5). The reaction with diene **5** was slow compared to thermal rearrangement:[19] only 28 % of cycloadduct **25** was formed as a mixture of diastereomers by ^{1}H NMR spectroscopy. The major product resulted from thermal rearrangement.[26] When compared to the results in Scheme 4, these results indicate that substitution at the allylic position severely hinders reactivity with diene **5**.



Scheme 5. [4+2] Cycloaddition of *trans*-alkene **12** with diene **5**.

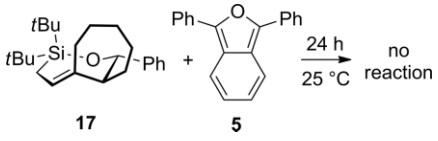
Highly substituted seven-membered ring *trans*-alkenes can be extremely reactive. Bicyclic *trans*-alkenes **15** and **16** underwent Diels–Alder cycloadditions in ten and twenty minutes, respectively [Equation (2)]. Cycloadducts **27** and **28** were formed in high yields with high diastereoselectivity. Bicyclic alkene **15** reacted faster than alkene **16**, indicating that a smaller fused ring increases reactivity. These observations suggest that the additional ring increased strain sufficiently to permit reactivity with diene **5** even though the *trans* double bond is sterically congested.



(2)

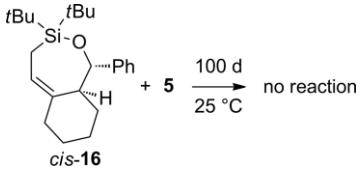
If the fused ring were too large, however, the *trans*-alkene was no longer reactive. Bicyclic alkene **17** did not react with

diene **5** after 24 hours [Equation (3)]. The decreased reactivity of alkene **17** compared to alkenes **15** and **16** likely results because the larger fused ring allows the *trans*-alkene to alleviate strain by altering torsion and bond angles, thereby decreasing the distortion of the double bond.[20,21] Steric effects are also likely to be more significant with the additional seven-membered ring, leading to decreased reactivity.



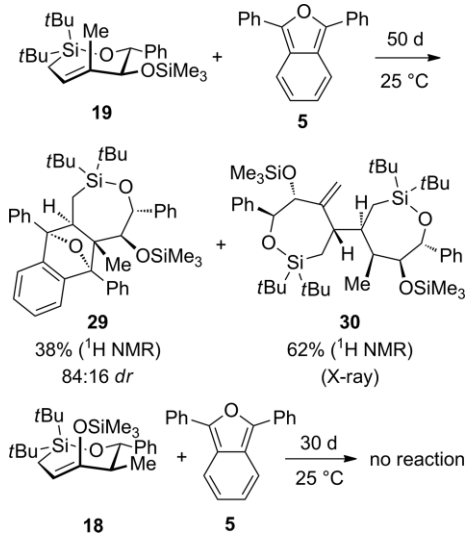
17 **5** (3)

Strain is necessary for the reaction of bicyclic alkene **16** with diene **5** to occur. To control for strain, the *cis* isomer of alkene *trans*-**16** (i.e., *cis*-**16**), was synthesized by the photoisomerization of *trans*-**16**. *cis*-Alkene **16** did not undergo a reaction with 1,3-diphenylisobenzofuran (**5**) even after 100 days [Equation (4)].



cis-**16** (4)

Although making the carbon–carbon double bond more electron-deficient should have accelerated the reaction with electron-rich diene **5**, steric effects played a larger role than electronic effects. In contrast to the expected results, alkene **19** was relatively unreactive: only 38 % of cycloadduct **29** had formed after 50 days, as determined by ^{1}H NMR spectroscopy (Scheme 6). The formation of dimer **30**, which could be formed from small amounts of an acid, outcompeted the formation of cycloadduct **29**, consuming *trans*-alkene **19**. The low reactivity of *trans*-alkene **19** with diene **5** is likely due to the large silyloxy group at the allylic position, which blocks the approach of isobenzofuran **5**. In addition, the methyl substituent on the trisubstituted *trans* double bond may also sterically destabilize the transition state leading to cycloadduct **19**.



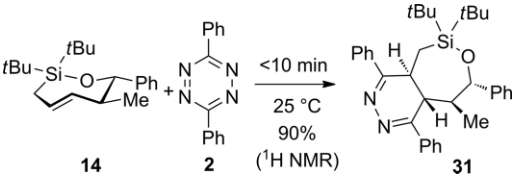
Scheme 6. Reactions of *trans*-alkenes **18** and **19** with diene **5**.

Electron-rich *trans*-alkene **18** was also unreactive with diene **5**. After 30 d, no cycloaddition reaction was observed between diene **5** and strained silyl enol ether **18** (Scheme 6). This lack of reactivity is likely because both reaction partners are electron-rich. The high HOMO of silyl enol ether **18**[27] is unlikely to interact effectively with the high LUMO of diene **5**.[28]

[4+2] Cycloadditions with 3,6-Diphenyl-*s*-tetrazine

To compare the reactivity of *trans*-oxasilacycloheptenes with that of *trans*-cyclooctenes (Scheme 1), seven-membered-ring *trans*-alkenes were subjected to inverse-electron-demand Diels–Alder reactions with 3,6-diphenyl-*s*-tetrazine (**2**). The high HOMO's of the electron-rich *trans*-alkenes should interact well with the low-lying LUMO+1 of the electron-deficient tetrazine **2**, leading to rapid reactions.[29]

Similar to the cycloaddition with isobenzofuran **5**, sterically unhindered *trans*-alkene **14** reacted rapidly in the inverse-demand Diels–Alder cycloaddition with tetrazine **2** [Equation (5)]. In less than ten minutes, *trans*-oxasilacycloheptene **14** was consumed, forming cycloadduct **31**, through a Diels–Alder cycloaddition followed by a reverse [4+2] cycloaddition.[30]

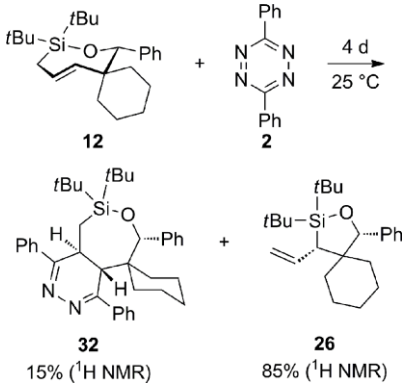


14 **2** **31** (5)

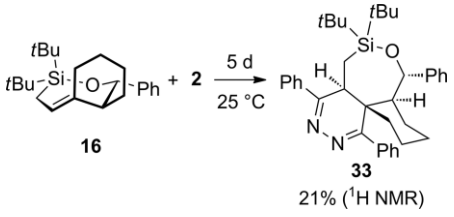
Increasing substitution of the seven-membered ring resulted in a significant decrease in reactivity. When *trans*-alkene **12** was treated with tetrazine **2**, only 15 % of cycloadduct **32** was formed after four days, as determined by ^{1}H NMR spectroscopy (Scheme 7). The thermal rearrangement of *trans*-alkene **12** to oxasilacyclopentane **26** outcompeted the reaction with tetrazine **2**.[19] It is likely that increasing the substitution at the allylic position of *trans*-alkene **12** relative to alkene **14** hinders the approach of sterically hindered tetrazine **2**, resulting in decreased reactivity.

Compared to the reaction of bicyclic alkene **16** with diene **5** [Equation (2)], the reaction of alkene **16** with tetrazine **2** was slow and unselective [Equation (6)]. After five days, *trans*-alkene **16** was consumed, giving a mixture of products. Cycloadduct **33**, the only identifiable product, was formed in only 21 % yield, as determined by ^{1}H NMR spectroscopy.

The [4+2] cycloaddition of silyl enol ether **18** and tetrazine **2** was also sluggish. After 84 d, only 80 % of the *trans*-alkene was consumed. Bicyclic compound **34** was formed in 53 % yield, as determined by ^{1}H NMR spectroscopy [Equation (7)]. Bicyclic compound **34** decomposed into benzonitrile and a complex mixture of products, likely through a reverse [4+2] cycloaddition.[31]



Scheme 7. [4+2] Cycloaddition of tetrazine **2** and *trans*-alkene **12**.



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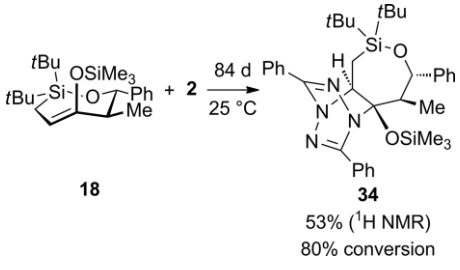
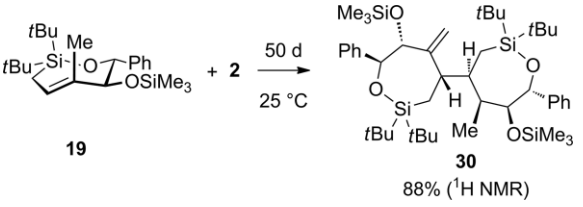


(7)

The slow formation and regiochemistry of compound **34** were unexpected. Silyl enol ether **18** should react easily with tetrazine **2** because the alkene should be particularly electron-rich.[29,30] The steric strain between the phenyl groups on tetrazine **2** and the substituents on the ring of *trans*-alkene **18** leads to increased reaction time. The nucleophilic character of the *trans* double bond in **18** likely accounts for the observed regiochemistry of this reaction.[32] Stepwise reaction mechanisms have been proposed for the reactions of tetrazine **2** with strong nucleophiles. Strained silyl enol ether **18** likely attacks the carbon atom of **2** forming a zwitterionic intermediate,[33] and subsequent ring closure leads to products with different regiochemistry.

Trisubstituted alkene **19**, which is isomeric to silyl enol ether **18**, did not react with tetrazine **2**. After 50 days, *trans*-alkene **19** was consumed to yield dimer **30** in 88 % yield [Equation (8)]. No other compounds were observed, and the concentration of tetrazine **2** did not decrease during the reaction time, as determined by ^{1}H NMR spectroscopy.

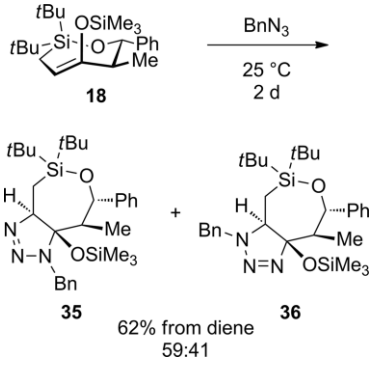


(8)

[4+2] Cycloadditions with Benzyl Azide

Previous studies of the high reactivity of strained cycloalkenes and cycloalkynes[34] with azides prompted investigations of the reactivity of *trans*-oxasilacycloheptenes with benzyl azide. Seven-membered-ring *trans*-alkenes were expected to undergo reactions with azides because alkyl azides react well with electrophilic and nucleophilic compounds.[35] Additionally, *trans*-cycloalkenes are more reactive than *cis*-cycloalkenes in 1,3-dipolar cycloadditions with picryl azide, with rate accelerations of greater than 10^4.[36]

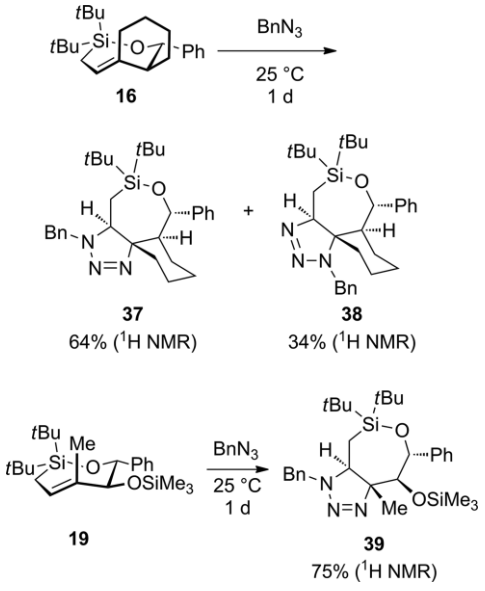
Silyl enol ether **18** reacted with benzyl azide in a [4+2] cycloaddition (Scheme 8) despite its sluggish reactivity with dienes **2** and **5**. Triazoles **35** and **36** were formed in two days and isolated in 62 % isolated yield over three steps from the 1,3-diene. The regioselectivity of this cycloaddition reaction was poor, which is typical for these reactions.[11,34]



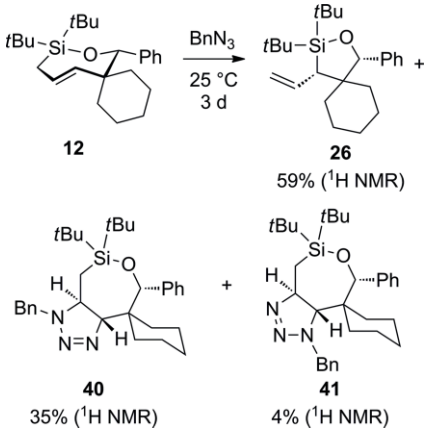
Scheme 8. [4+2] Cycloaddition of benzyl azide and silyl enol ether **18**.

trans-Alkenes **16** and **19** also underwent 1,3-dipolar cycloadditions with benzyl azide (Scheme 9). Triazoles **37**, **38**, and **39** were formed in one day in 64 %, 34 %, and 75 % yields, respectively, as determined by ^{1}H NMR spectroscopy. The high regioselectivity of the reaction of alkene **19** with benzyl azide to form triazole **39** is unusual because 1,3-dipolar cycloadditions are typically unselective.[11,34] The cycloadducts were not stable to chromatography, so they were characterized from the unpurified reaction mixtures. Upon exposure to mild acid (SiO_2), the triazoles decomposed to form new products through the loss of nitrogen gas and subsequent rearrangements (see Supporting Information for details).[37]

The thermal rearrangement of sterically hindered *trans*-alkene **12** outcompeted the [4+2] cycloaddition with benzyl azide (Scheme 10). The major product of the reaction of benzyl azide with *trans*-alkene **12** was oxasilacyclopentane **26**, the product of thermal rearrangement. Isomeric triazoles **40** and **41** were formed in only 35 % and 4 % yields, respectively.[38]



Scheme 9. Reactions of *trans*-alkenes **16** and **19** with benzyl azide.



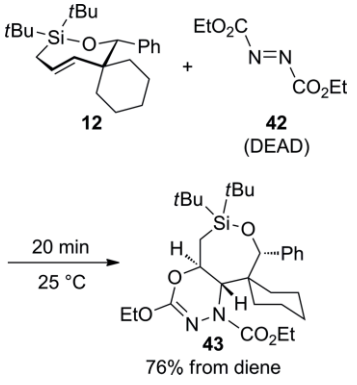
Scheme 10. 1,3-Dipolar cycloaddition of alkene **12** and benzyl azide.

The higher reactivity of *trans*-alkenes with benzyl azide when compared to the reactivity with tetrazine **2** is likely influenced by steric and electronic effects. Benzyl azide is less sterically hindered than tetrazine **2**, which facilitates reactivity with substituted *trans*-alkenes. Additionally, incorporating an electron-withdrawing group or other substituents near the dipolarophile has been shown to decrease activation energies for cycloadditions with azides.[34]

Stepwise Reactions with DEAD

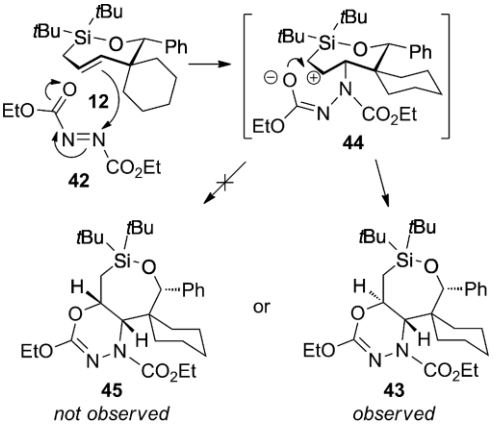
Considering the reactivity of substituted *trans*-cycloalkenes with azides, [4+2] cycloadditions involving less sterically demanding electrophilic dienes were explored. *trans*-Alkenes were predicted to be particularly reactive with electrophilic dienes. Previous studies indicated that the *trans* double bond of oxasilacycloheptene **12** is nucleophilic.[17,24]

The reaction of sterically hindered *trans*-alkene **12** with DEAD proceeded rapidly at room temperature (Scheme 11). Heterocycle **43** was formed in 76 % yield over three steps from the starting diene. The high reactivity of *trans*-alkene **12** with DEAD contrasts markedly with its low reactivity with other dienes (Scheme 5 and Scheme 7).



Scheme 11. Formal [4+2] cycloaddition of DEAD with *trans*-alkene **12**.

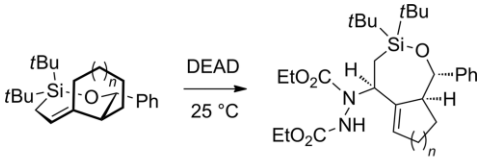
The difference in reactions with DEAD compared to other dienes may arise because the mechanisms are different.[17] Unlike concerted Diels–Alder reactions, the reaction between *trans*-alkene **12** and DEAD is expected to proceed by a stepwise mechanism through a zwitterionic intermediate.[39] The nucleophilic *trans* double bond attacks the electrophilic nitrogen atom on DEAD, forming zwitterion **44** (Scheme 12). Ring closure of the anionic oxygen atom onto the β-silyl carbocation forms heterocycle **43**.



Scheme 12. Proposed mechanism for formation of **43**.

The stereochemical outcome of the addition of DEAD to *trans*-alkene **12** is consistent with a stepwise reaction. Ring closure of intermediate **44** could lead to two different diastereomers of product (Scheme 12). Trapping of intermediate **44** without a change in conformation would preserve the stereochemistry of the *trans* double bond in the product. If bond rotation occurred in intermediate **44**, however, subsequent ring closure would give diastereomer **45**. Only diastereomer **43** was observed, suggesting that bond rotation had not occurred. The retention of configuration observed likely results because the β-silyl carbocation is configurationally stable due to the hyperconjugation between the σ_{Si-C} bond and the carbocation.[24,40]

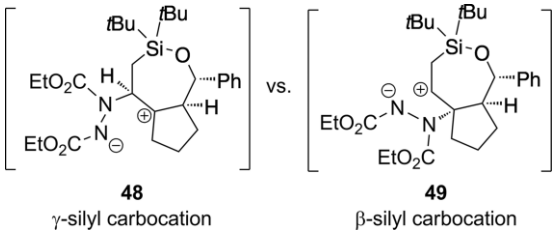
Bicyclic alkenes **15** and **17** reacted rapidly with DEAD to give the ene-type products **40** and **41** [Equation (9)]. Even *trans*-alkene **17**, which was unreactive in a Diels–Alder cycloaddition with isobenzofuran **5**, underwent a rapid reaction with DEAD. Alkenes **46** and **47** were formed with complete control of relative stereochemistry.



15, $n = 0$
17, $n = 2$

46, $n = 1$, 10 min, 42% from diene
47, $n = 2$, 20 min, 54% from diene (9)

The regiochemistry of alkenes **46** and **47** was opposite of what was expected. Because these reactions likely proceed through stepwise mechanisms,[39] bicyclic alkenes **15** and **17** should react similar to allylic silanes, forming a β-silyl carbocation in the first step (Figure 3).[41] Instead, reactions proceeded via an intermediate involving a tertiary γ-silyl carbocation (Figure 3),[42] possibly because it is stabilized by the additional cycloalkyl group.



48
γ-silyl carbocation

49
β-silyl carbocation

Figure 3. Possible intermediates in the reaction of alkene **15** with DEAD.

Conclusions

trans-Oxasilacycloheptenes underwent a variety of [4+2] cycloaddition reactions. Unhindered *trans*-alkenes and strained bicyclic *trans*-alkenes reacted rapidly with dienes. The relative reactivity of these strained alkenes was influenced by the substitution pattern of the seven-membered ring. Increasing substitution of the *trans* double bond or at the allylic position of the double bond decreased the reactivity of these *trans*-alkenes in concerted [4+2] cycloadditions. Reactivity was increased, however, by additional distortion of the *trans* double bond (increased strain), despite increasing substitution. Although some highly substituted alkenes were unreactive in concerted cycloadditions, stepwise reactions with DEAD proceeded rapidly despite low reactivity with dienes **2** and **5**. These results indicate that steric strain can drastically influence the reactivity of a compound, overriding the impact ring strain has on reactivity. Even though sterically hindered compounds react slowly in concerted reactions, reactivity can be restored by stepwise reactions that avoid destabilizing steric interactions in the rate-determining step.

Experimental Section

General Methods: See supporting information for full details. The synthesis and characterization of compounds **2**,[43] **9**,[44] **10**,[45] **14**,[19] **13**, **16**, **18**, and **20**–**23** were reported previously.[17]

Vinylsilacyclopropane 11: The synthesis of *trans*-oxasilacycloheptene **11** was adapted from a reported procedure.[19] To a solution of diene **9** (0.012 g, 0.10 mmol), thering-fused cyclohexane-silacyclopropane **10** (0.034 g, 0.15 mmol), and mesitylene (0.0020 mL, 0.014 mmol, internal standard) in C_6D_6 (0.64 mL) in a J. Young NMR tube was added $AgOCOCF_3$ (0.030 mL, 0.030 M in C_6D_6). Vinylsilacyclopropane **11** was formed in 10 min in 80 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of the alkene CH peak (δ = 5.32 ppm). Vinylsilacyclopropane **11** could not be purified and was used without further purification: ^{1}H NMR (600 MHz, C_6D_6, diagnostic peaks): δ = 5.32 (dt, J = 7.4, 1.1 Hz, 1 H), 2.32–2.30 (m, 2 H), 1.83–1.77 (m, 1 H), 1.60–1.54 (m, 3 H), 1.12 (s, 9 H), 1.03 (s, 9 H), 0.57 (dd, J = 11.1, 8.6 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, C_6D_6, diagnostic peaks): δ = 126.8 (CH), 30.6 (CH_3), 30.2 (CH_2), 30.1 (CH_3), 29.5 (CH_2), 27.9 (CH_2), 5.6 (CH_2) ppm. ^{29}Si NMR (99.3 MHz, C_6D_6): δ = –49.4 ppm.

***trans*-Oxasilacycloheptene 12:** To a solution of vinylsilacyclopropane **11** (0.021 g, 0.080 mmol) in C_6D_6 (0.67 mL) was added benzaldehyde (0.010 mL, 0.10 mmol). *trans*-Oxasilacycloheptene **12** was formed in 10 min in 99 % yield from vinylsilacyclopropane **11** (79 % over two steps) based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of the alkene CH peak (δ = 6.01 ppm). *trans*-Oxasilacycloheptene **12** could not be purified and was used without further purification: ^{1}H NMR (500 MHz, C_6D_6, diagnostic peaks): δ = 7.28–7.27 (m, 2 H), 7.20–7.17 (m, 2 H), 7.11–7.07 (m, 1 H), 6.01 (ddd, J = 17.6, 12.9, 4.6 Hz, 1 H), 4.99 (d, J = 17.6 Hz, 1 H), 4.32 (s, 1 H), 2.45–2.39 (m, 1 H), 2.14–2.10 (m, 1 H), 1.95 (dd, J = 12.2, 4.6 Hz, 1 H), 1.65–1.58 (m, 1 H), 1.45–1.37 (m, 3 H), 1.30–1.26 (m, 1 H), 1.10 (s, 9 H), 0.95 (s, 9 H), 0.82–0.74 (m, 1 H) ppm. ^{13}C NMR (125 MHz, C_6D_6, diagnostic peaks): δ = 133.6 (CH), 133.5 (CH), 128.3 (CH), 128.0 (CH), 127.8 (CH), 84.3 (CH), 35.7 (CH_2), 29.3 (CH_3), 28.5 (CH_3), 25.9 (CH_2), 25.2 (CH_2), 19.5 (CH_2) ppm. ^{29}Si NMR (99.3 MHz, C_6D_6): δ = 1.7 ppm.

Bicyclic Ether 25: To a solution of *trans*-oxasilacycloheptene **12** (0.066 mmol) in C_6D_6 (0.500 mL) was added 1,3-diphenylisobenzofuran **5** (0.021 g, 0.077 mmol). The NMR tube was flame-sealed under vacuum and the reaction mixture was monitored by ^{1}H NMR spectroscopy until *trans*-oxasilacycloheptene **12** was consumed (4 d). Alkene **26** was formed in 72 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of one of the alkene CH_2 peaks (δ = 4.82 ppm). The spectroscopic data are consistent with the data reported in the Supporting Information for alkene **26**. The major diastereomer of bicyclic ether **25** was also formed in 4 d in 25 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of the benzylic ether peak (δ = 5.04 ppm). The minor diastereomer of bicyclic ether **25** was formed in 3 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of the benzylic ether peak (δ = 4.47 ppm). The NMR tube was opened and the reaction mixture was concentrated in vacuo. Purification by flash chromatography (2:98 EtOAc/hexanes) afforded bicyclic ether **25** as a yellow crystalline solid (0.008 g, 19 % over three steps): m.p. 158–160 °C. ^{1}H NMR (500 MHz, C_6D_6): δ = 8.12–8.11 (m, 2 H), 7.83–7.77 (m, 1 H), 7.73–7.72 (m, 2 H), 7.41–7.37 (m, 3 H), 7.29–7.21 (m, 4 H), 7.13–7.10 (m, 2 H), 7.06–6.99 (m, 5 H), 5.04 (s, 1 H), 3.30 (d, J = 5.0 Hz, 1 H), 2.99–2.95 (m, 1 H), 2.13–2.10 (m, 1 H), 1.83–1.76 (m, 1 H), 1.60–1.57 (m, 1 H), 1.17 (s, 9 H, and m, 2 H), 1.08–1.02

(m, 1 H), 0.96 (s, 9 H, and m, 3 H), 0.76–0.70 (m, 1 H), 0.42–0.34 (m, 1 H), –0.34 to –0.40 (m, 1 H). ^{13}C NMR (125 MHz, C_6D_6): δ = 151.4 (C), 145.1 (C), 144.1 (C), 140.0 (C), 139.7 (C), 129.5 (CH), 129.13 (CH), 129.06 (CH), 129.0 (CH), 128.7 (CH), 128.3 (CH), 128.0 (CH), 127.7 (CH), 127.6 (CH), 126.7 (CH), 126.3 (CH), 124.7 (CH), 120.2 (CH), 92.8 (C), 91.9 (C), 89.6 (CH), 66.3 (CH), 45.7 (CH), 44.4 (C), 34.3 (CH_2), 29.5 (CH_3), 28.8 (CH_3), 24.5 (CH_2), 24.2 (CH_2), 23.5 (CH_2), 23.3 (CH_2), 22.11 (C), 22.07 (C), 15.8 (CH_2) ppm. IR (ATR): $\tilde{\nu}$ = 1310, 1069, 823 cm^{-1}. HRMS (ESI) *m/z* calcd. for $C_{44}H_{52}NaO_2Si$ $[M + Na]^+$ 663.3629, found 663.3654.

Bicyclic Ether 27: To a solution of 1-vinylcyclopentene (0.0087 mL, 8.64 M in Et_2O, 0.075 mmol) and the ring-fused cyclohexane-silacyclopropane **10** (0.020 g, 0.090 mmol) in C_6D_6 (0.480 mL) was added $AgOCOCF_3$ (0.015 mL, 0.050 M in C_6D_6). After 10 min, benzaldehyde (0.008 mL, 0.08 mmol) was added followed by isobenzofuran **5** (0.020 g, 0.075 mmol). Ether **27** was formed in 10 min as a mixture of diastereomers (93:7 *dr*) in 74 % yield from 1-vinylcyclopentene based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of the benzylic CH peak (δ = 4.47 ppm). The reaction mixture was concentrated in vacuo. Purification by flash chromatography (3:97 EtOAc/hexanes) afforded ether **27** as a white solid (0.029 g, 62 % over three steps). ^{1}H NMR spectroscopic analysis showed that ether **27** was isolated as a mixture of diastereomers in a 90:10 ratio: m.p. 137–141 °C. ^{1}H NMR (400 MHz, C_6D_6): δ = 8.15 (dd, *J* = 8.4, 1.2 Hz, 2 H), 8.06 (dd, *J* = 8.4, 1.2 Hz, 2 H), 7.74–7.70 (m, 1 H), 7.65–7.61 (m, 1 H), 7.39–7.35 (m, 2 H), 7.28–7.23 (m, 3 H), 7.20–7.17 (m, 2 H), 7.10–7.04 (m, 5 H), 6.99–6.94 (m, 1 H), 4.47 (d, *J* = 10.4 Hz, 1 H), 3.68 (d, *J* = 12.8 Hz, 1 H), 2.58 (dd, *J* = 10.0, 6.4 Hz, 1 H), 1.86–1.70 (m, 2 H), 1.65–1.58 (m, 1 H), 1.49 (d, *J* = 15.2 Hz, 1 H), 1.25–1.19 (m, 1 H), 0.97 (s, 9 H), 0.96–0.94 (m, 1 H), 0.75 (s, 9 H), 0.68–0.59 (m, 1 H), 0.38 (dd, *J* = 15.2, 13.2 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 149.4 (C), 146.1 (C), 144.9 (C), 140.5 (C), 140.4 (C), 128.9 (CH), 128.7 (CH), 128.3 (CH), 128.1 (CH), 128.00 (CH), 127.98 (CH), 127.7 (CH), 127.4 (CH), 126.74 (CH), 126.70 (CH), 126.6 (CH), 122.1 (CH), 121.9 (CH), 94.1 (C), 89.5 (C), 81.0 (CH), 65.6 (C), 54.5 (CH), 51.7 (CH), 29.9 (CH_3), 29.7 (CH_2), 28.4 (CH_3), 25.1 (CH_2), 22.0 (C), 21.7 (C), 21.2 (CH_2), 6.3 (CH_2) ppm. IR (ATR): $\tilde{\nu}$ = 1063, 822 cm^{-1}. HRMS (APCI) *m/z* calcd. for $C_{42}H_{49}O_2Si$ $[M + H]^+$ 613.3496, found 613.3497.

Bicyclic Ether 29: To a solution of *trans*-oxasilacycloheptene **19** (0.051 mmol) in C_6D_6 (0.50 mL) was added 1,3-diphenylisobenzofuran (0.021 g, 0.078 mmol). After 50 d, the major diastereomer of bicyclic ether **29** was formed in 32 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of the benzylic ether peak (δ = 5.04 ppm). The minor diastereomer of bicyclic ether **29** was formed in 6 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of the benzylic ether peak (δ = 4.88 ppm). Alkene **30** was also formed in 31 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of one of the alkene CH_2 peaks (δ = 5.33 ppm). The spectroscopic data are consistent with the data reported in the Supporting Information for alkene **30**. The NMR tube was opened and the reaction mixture was concentrated in vacuo. Purification by flash chromatography (2:98 EtOAc/hexanes) afforded bicyclic ether **29** as a yellow solid (0.010 g, 29 % over three steps): m.p. 118–121 °C. ^{1}H NMR (500 MHz, C_6D_6): δ = 8.32–8.31 (m, 0.3 H), 8.11–8.09 (m, 2 H), 8.01–8.00 (m, 2 H), 7.97–7.95 (m, 0.3 H), 7.54–7.52 (m, 1 H), 7.45–7.20 (m, 11 H), 7.11–7.05 (m, 1.4 H), 7.05–6.97 (m, 4 H), 5.11 (d, *J* = 7.7 Hz, 1 H), 5.04 (d, *J* = 7.7 Hz, 1 H), 4.88 (d, *J* = 8.9 Hz, 0.2 H), 3.74 (d, *J* = 8.9 Hz, 0.2 H), 2.95 (d, *J* = 13.1 Hz, 0.2 H, and d, *J* = 13.0 Hz, 1 H), 1.79 (s, 0.5 H), 1.37 (s, 3 H), 1.25 (s, 1.4 H), 1.02–1.01 (m, 0.2 H), 0.97 (s, 9 H), 0.86 (s, 1.4 H), 0.58 (s, 9 H), 0.31 (dd, *J* = 15.1, 13.3 Hz, 1 H, and m, 2.2 H), –0.27 (s, 1.4 H), –0.49 (s, 9 H) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 151.0 (C), 150.2 (C), 147.3 (C), 144.4 (C), 144.0 (C), 143.8 (C), 140.5 (C), 140.4 (C), 139.8 (C), 139.5 (C), 132.4 (CH), 130.0 (CH), 129.8 (CH), 129.1 (CH), 129.01 (CH), 128.97 (CH), 128.83 (CH), 128.78 (CH), 128.5 (CH), 128.3 (CH), 127.9 (CH), 127.8 (CH), 127.73 (CH), 127.70 (CH), 127.6 (CH), 127.4 (CH), 127.2 (CH), 127.1 (CH), 126.8 (CH), 126.7 (CH), 126.4 (CH), 123.9 (CH), 123.1 (CH), 123.0 (CH), 121.3 (CH), 117.4 (CH), 96.3 (C), 93.4 (C), 90.5 (C), 90.2 (C), 83.0 (CH), 82.7 (CH), 80.5 (CH), 80.1 (CH), 56.0 (C), 55.7 (C), 54.2 (CH), 53.9 (CH), 29.7 (CH_3), 28.8 (CH_3), 28.2 (CH_3), 27.9 (CH_3), 22.6 (C), 22.2 (C), 21.1 (C), 22.0 (C), 18.4 (CH_3), 17.9 (CH_3), 8.8 (CH_2), 6.0 (CH_2), 3.0 (CH_3), 1.6 (CH_3) ppm. IR (ATR): $\tilde{\nu}$ = 1250, 1084, 837 cm^{-1}. HRMS (ESI) *m/z* calcd. for $C_{43}H_{54}NaO_3Si_2$ $[M + Na]^+$ 697.3507, found 697.3505.

Pyrazine 31: To a solution of *trans*-oxasilacycloheptene **14** (0.077 mmol) in C_6D_6 (0.87 mL) was added 3,6-diphenyl-*s*-tetrazine (0.022 g, 0.093 mmol). After 10 min, pyridazine **31** was formed in 90 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of the benzylic CH peak (δ = 4.77 ppm). All attempts to purify pyridazine **31** resulted in decomposition. Spectroscopic data for **31** were collected on the unpurified reaction mixture: ^{1}H NMR (600 MHz, C_6D_6, diagnostic peaks): δ = 7.23–7.20 (m, 2 H), 4.77 (d, *J* = 9.6 Hz, 1 H), 3.39–3.36 (m, 1 H), 3.17 (t, *J* = 5.9 Hz, 1 H), 1.00 (s, 9 H), 0.96 (s, 9 H), 0.79–0.74 (m, 1 H), 0.27 (d, *J* = 7.2 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, C_6D_6, diagnostic peaks): δ = 162.1 (C), 158.3 (C), 130.2 (CH), 87.5 (CH), 42.9 (CH), 40.2 (CH), 29.4 (CH_3), 28.6 (CH_3), 17.8 (CH_3), 17.5 (CH_2) ppm. HRMS (APCI) *m/z* calcd. for $C_{34}H_{43}N_2OSi$ $[M + H]^+$ 523.3139, found 523.3155.

Pyrazine 32: To a solution of *trans*-oxasilacycloheptene **12** (0.068 mmol) in C_6D_6 (0.47 mL) was added 3,6-diphenyl-*s*-tetrazine (0.017 g, 0.073 mmol). After 4 d, pyridazine **32** was formed in 15 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of the benzylic ether peak (δ = 5.11 ppm). Alkene **26** was also formed in 85 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of one of the alkene CH_2 peaks (δ = 4.82 ppm). The spectroscopic data are consistent with the data reported in the Supporting Information for alkene **26**. All attempts to purify pyridazine **32** resulted in decomposition. Spectroscopic data for **32** was collected on the unpurified reaction mixture: ^{1}H NMR (600 MHz, C_6D_6, diagnostic peaks): δ = 8.26 (dd, *J* = 8.4, 1.2 Hz, 1 H), 8.00–7.98 (m, 2 H), 5.11 (s, 1 H), 3.88–3.85 (m, 1 H), 3.29 (d, *J* = 4.3 Hz, 1 H), 1.04 (s, 9 H), 0.96 (s, 9 H), 0.50–0.44 (m, 1 H) ppm. ^{13}C NMR (100 MHz, C_6D_6, diagnostic peaks): δ = 163.7 (C), 159.4 (C), 129.4 (CH), 128.9 (CH), 91.4 (CH), 46.0 (CH), 30.7 (CH), 29.5 (CH_3), 28.8 (CH_3), 26.2 (CH_2) ppm. HRMS (ESI) *m/z* calcd. for $C_{38}H_{49}N_2OSi$ $[M + H]^+$ 577.3609, found 577.3606.

Pyrazine 33: To a solution of *trans*-oxasilacycloheptene **16** (0.064 mmol) in C_6D_6 (0.50 mL) was added 3,6-diphenyl-*s*-tetrazine (0.018 g, 0.076 mmol). After 5 d, pyridazine **33** was formed in 21 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of the benzyl ether peak (δ = 4.98 ppm). The NMR tube was opened and the reaction mixture was purified by flash chromatography (1:99 MeOH/CH_2Cl_2) to afford pyridazine **33** as a yellow solid. All purification attempts resulted in minor decomposition of pyridazine **33**. Spectroscopic data were collected on the product that was not analytically pure: ^{1}H NMR (500 MHz, C_6D_6): δ = 7.63–7.62 (d, *J* = 7.3, 2 H), 7.47–7.46 (m, 2 H), 7.23–7.22 (m, 2 H), 7.15–7.12 (m, 5 H), 7.09–7.03 (m, 3 H), 7.00–6.97 (m, 1 H), 4.99–4.97 (d, *J* = 8.3 Hz, 1 H), 3.76 (dd, *J* = 9.8, 5.5 Hz, 1 H), 2.90–2.88 (m, 1 H), 2.60–2.58 (m, 1 H), 1.56–1.40 (m, 4

H), 1.15–1.13 (m, 3 H), 1.09 (s, 9 H), 0.95–0.91 (m, 2 H), 0.77 (s, 9 H) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 172.0 (C), 168.0 (C), 144.6 (C), 142.8 (C), 140.1 (C), 128.8 (CH), 128.6 (2 CH), 128.5 (2 CH), 128.3 (2 CH), 127.8 (CH), 127.4 (CH), 76.6 (CH), 48.4 (CH), 42.4 (CH), 41.2 (C), 29.7 (CH_3), 28.7 (CH_3), 27.3 (CH_2), 25.2 (CH_2), 23.4 (CH_2), 21.8 (C), 21.7 (CH_2), 21.2 (C), 9.3 (CH_2) ppm. IR (ATR): $\tilde{\nu}$ = 1689, 1050, 823 cm^{-1}. HRMS (ESI) *m/z* calcd. for $C_{37}H_{47}N_2OSi$ [M + H]$^+$ 563.3452, found 563.3451.

Bicyclic Compound 34: To a solution of *trans*-oxasilacycloheptene **18** (0.058 mmol) in C_6D_6 (0.50 mL) was added 3,6-diphenyl-1,2,4,5-tetrazine (0.018 g, 0.076 mmol). After 84 d, 80 % of *trans*-oxasilacycloheptene **18** had converted to product. Bicyclic compound **34** was formed in 84 d in 53 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of the CH peak next to nitrogen (δ = 3.52 ppm). ^{1}H NMR spectroscopic analysis showed bicyclic compound **34** was a mixture of diastereomers in a 95:5 ratio. This ratio was persevered from the starting diene. It was characterized in situ: ^{1}H NMR (600 MHz, C_6D_6, diagnostic peaks): δ = 7.66–7.65 (m, 2 H), 7.63–7.61 (m, 2 H), 7.51–7.50 (m, 1 H), 5.08 (d, *J* = 7.6 Hz, 1 H), 3.52 (dd, *J* = 13.5, 1.5 Hz, 1 H), 2.94–2.90 (m, 1 H), 1.09 (s, 9 H), 0.83 (s, 9 H), 0.32 (s, 9 H) ppm. ^{13}C NMR (150 MHz, C_6D_6, diagnostic peaks): δ = 167.3 (C), 166.8 (C), 76.0 (CH), 49.0 (CH), 45.5 (CH), 29.4 (CH_3), 28.7 (CH_3), 3.3 (CH_3) ppm.

Triazoles 35 and 36: To a solution of (*Z*)-trimethyl(penta-1,3-dien-3-yloxy)silane[17] (0.017 g, 0.11 mmol) and the ring-fused cyclohexane-silacyclopropane **10** (0.027 g, 0.12 mmol) in C_6D_6 (0.70 mL) was added $AgOCOCF_3$ (0.035 mL, 0.030 M in C_6D_6). After 10 min, benzaldehyde (0.011 mL, 0.11 mmol) was added, followed by benzyl azide (0.014 mL, 0.11 mmol). After 2 d, the NMR tube was opened and the reaction mixture was concentrated in vacuo. ^{1}H NMR spectroscopic analysis of the unpurified reaction mixture showed a mixture of regioisomers in a 59:41 (**35**/**36**) ratio. The regioisomers were assigned by an HMBC experiment. ^{1}H NMR spectroscopic analysis of the unpurified reaction mixture showed triazoles **35** and **36** were mixtures of diastereomers in a 95:5 ratio. This ratio was persevered from the starting diene. Purification by flash chromatography (3:97 EtOAc/hexanes) afforded triazoles **35** and **36** as a colorless oil (0.035 g, 62 % over three steps): ^{1}H NMR (500 MHz, C_6D_6): δ = 7.24–7.17 (m, 4.2 H), 7.14–6.99 (m, 12.5 H), 5.32 (d, *J* = 16.8 Hz, 1 H), 5.03 (d, *J* = 9.5 Hz, 0.7 H, and d, *J* = 15.4 Hz, 0.7 H), 4.94 (d, *J* = 8.9 Hz, 1 H), 4.53 (d, *J* = 16.8 Hz, 1 H, and dd, *J* = 13.5, 1.1 Hz, 1 H), 4.21 (d, *J* = 15.4 Hz, 0.7 H), 3.20 (dd, *J* = 13.5, 2.9 Hz, 0.7 H), 2.09–2.00 (m, 2.7 H), 1.61 (dd, *J* = 15.5, 13.5 Hz, 1 H), 1.15 (d, *J* = 6.9 Hz, 2.1 H), 1.09 (s, 9 H), 1.03 (s, 6.3 H), 0.98 (s, 9 H, and m, 0.7 H), 0.92–0.90 (m, 0.7 H), 0.80 (s, 6.3 H), 0.57 (d, *J* = 6.9 Hz, 3 H), 0.35 (s, 6.3 H), 0.26 (s, 9 H) ppm. ^{13}C NMR (125 MHz, C_6D_6, major regioisomer **35**): δ = 144.51 (C), 140.4 (C), 129.3 (CH), 128.81 (CH), 127.8 (CH), 127.7 (CH), 127.4 (CH), 127.1 (CH), 96.9 (C), 83.8 (CH), 78.6 (CH), 52.4 (CH_2), 50.6 (CH), 29.0 (CH_3), 28.5 (CH_3), 22.0 (C), 21.6 (C), 14.4 (CH_3), 7.3 (CH_2), 2.7 (CH_3) ppm. ^{13}C NMR (125 MHz, C_6D_6, minor regioisomer **36**): δ = 144.54 (C), 136.8 (C), 129.4 (CH), 128.9 (CH), 128.78 (CH), 128.5 (CH), 127.9 (CH), 127.5 (CH), 106.1 (C), 78.6 (CH, overlapping with major regioisomer), 63.8 (CH), 52.1 (CH_2), 51.1 (CH), 29.2 (CH_3), 28.1 (CH_3), 21.8 (C), 21.2 (C), 14.0 (CH_3), 4.3 (CH_2), 3.0 (CH_3) ppm. IR (ATR): $\tilde{\nu}$ = 1470, 1061, 822 cm^{-1}. HRMS (APCI) *m/z* calcd. for $C_{30}H_{48}N_3O_2Si_2$ [M + H]$^+$ 538.3280, found 538.3295. $C_{30}H_{47}N_3O_2Si_2$ (537.89): calcd. C 66.99, H 8.81; found C 67.39, H 8.70.

Triazoles 37 and 38: To a solution of *trans*-oxasilacycloheptene **16** (0.043 mmol) in C_6D_6 (0.50 mL) was added benzyl azide (0.010 mL, 0.080 mmol). After 1 d, triazole **37** was formed in 64 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of the benzyl ether peak (δ = 5.23 ppm). Triazole **38** was formed in 33 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of the benzyl ether peak (δ = 5.05 ppm). All purification attempts resulted in decomposition of triazoles **37** and **38**. Spectroscopic data were collected on the unpurified reaction mixture: ^{1}H NMR (500 MHz, C_6D_6, diagnostic peaks): δ = 7.31–7.28 (m, 3 H), 7.21–7.19 (m, 2 H), 7.14–7.11 (m, 5 H), 7.09–7.00 (m, 5 H), 5.27 (d, *J* = 15.8 Hz, 0.5 H), 5.23 (d, *J* = 10.4 Hz, 1 H), 5.05 (d, *J* = 10.2 Hz, 0.5 H), 4.86 (d, *J* = 15.4 Hz, 1.5 H), 4.44 (d, *J* = 15.4 Hz, 1 H), 4.37 (dd, *J* = 14.3, 1.4 Hz, 0.5 H), 3.28 (dd, *J* = 13.8, 2.6 Hz, 1 H), 2.82 (tt, *J* = 13.5, 4.8 Hz, 1 H), 2.15 (m, *J* = 16.2, 1.7 Hz, 1 H, and dd, 1 H), 2.08–2.01 (m, 1 H), 1.89–1.81 (m, 1.5 H), 1.68 (dd, *J* = 13.5, 4.4 Hz, 1 H, and m, 1 H), 1.57–1.40 (m, 5.5 H), 1.02 (s, 4.5 H), 0.96 (s, 4.5 H), 0.93 (s, 9 H), 0.77 (s, 9 H) ppm. ^{13}C NMR (125 MHz, C_6D_6, diagnostic peaks): δ = 144.6 (C), 144.4 (C), 141.2 (C), 137.9 (C), 129.1 (CH), 129.0 (CH), 128.8 (CH), 128.7 (CH), 127.9 (CH), 127.7 (CH), 127.0 (CH), 126.9 (CH), 82.4 (C), 81.7 (C), 76.5 (CH), 71.9 (CH), 66.1 (CH), 56.0 (CH_2), 53.0 (CH_2), 50.0 (CH), 47.8 (CH), 29.3 (CH_3), 28.6 (CH_3), 28.4 (CH_3), 26.1 (CH_2), 24.7 (CH_2), 24.6 (CH_2), 22.8 (CH_2) ppm. HRMS (ESI) *m/z* calcd. for $C_{30}H_{44}N_3OSi$ [M + H]$^+$ 490.3248, found 490.3263.

Triazole 39: To a solution of *trans*-oxasilacycloheptene **19** (0.0087 mmol) in C_6D_6 (0.450 mL) was added benzyl azide (0.004 mL, 0.03 mmol). Triazole **39** was formed in 1 d in 75 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.74 ppm) and the area of the benzyl ether peak (δ = 4.86 ppm). All purification attempts resulted in decomposition of triazole **39**. Spectroscopic data were collected on the unpurified reaction mixture: ^{1}H NMR (500 MHz, C_6D_6, diagnostic peaks): δ = 7.36–7.35 (m, 2 H), 7.24–7.23 (m, 2 H), 7.15–7.01 (m, 6 H), 4.86 (d, *J* = 9.0 Hz, 1 H), 4.81 (d, *J* = 15.4 Hz, 1 H), 4.34 (d, *J* = 15.4 Hz, 1 H), 3.88 (d, *J* = 9.0 Hz, 1 H), 3.25 (dd, *J* = 13.4, 3.0 Hz, 1 H), 1.29 (s, 3 H), 0.88 (s, 9 H), 0.79 (s, 9 H), 0.03 (s, 9 H) ppm. ^{13}C NMR (125 MHz, C_6D_6, diagnostic peaks): δ = 143.9 (C), 137.6 (C), 129.3 (CH), 129.0 (CH), 128.2 (CH), 128.1 (CH), 85.1 (CH), 81.5 (CH), 77.7 (CH), 62.8 (CH), 52.9 (CH_2), 29.0 (CH_3), 28.3 (CH_3), 22.0 (C), 21.3 (C), 10.5 (CH_3), 5.2 (CH_2), 0.8 (CH_3) ppm. HRMS (APCI) *m/z* calcd. for $C_{30}H_{47}NO_2Si_2$ [M – N_2]$^+$ 510.3218, found 510.3221.

Triazoles 40 and 41: To a solution of *trans*-oxasilacycloheptene **12** (0.070 mmol) in C_6D_6 (0.50 mL) was added benzyl azide (0.009 mL, 0.08 mmol). After 3 d, triazole **40** was formed in 35 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of the one of the benzyl CH_2 peaks (δ = 4.31 ppm). Triazole **41** was formed in 4 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of the one of the benzyl CH_2 peaks (δ = 4.09 ppm). Alkene **26** was formed in 59 % yield based on ^{1}H NMR spectroscopic analysis of the area of a peak of the standard (δ = 6.71 ppm) and the area of one of the alkene CH_2 peaks (δ = 4.82 ppm). The spectroscopic data are consistent with the data reported in the Supporting Information for alkene **26**. All purification attempts resulted in decomposition of triazoles **40** and **41**. Spectroscopic data were collected on the unpurified product: ^{1}H NMR (600 MHz, C_6D_6, diagnostic peaks): δ = 5.44 (d, *J* = 14.9 Hz, 0.1 H), 4.95–4.91 (m, 0.1 H), 4.31 (d, *J* = 15.1 Hz, 1 H), 4.09 (d, *J* = 14.9 Hz, 0.1 H), 3.61 (d, *J* = 15.1 Hz, 1 H), 3.39 (ddd, *J* = 15.1, 12.2, 2.9 Hz, 1 H), 0.91 (s, 9 H), 0.80 (s, 9 H) ppm. ^{13}C NMR (100 MHz, C_6D_6, diagnostic peaks): δ = 96.6 (CH), 80.8 (CH), 71.9 (CH), 57.8 (CH), 57.1 (CH_2), 53.3 (CH_2), 29.0 (CH_3), 28.5 (CH_3) ppm. HRMS (ESI) *m/z* calcd. for $C_{31}H_{49}N_4OSi$ [M + NH_4]$^+$ 521.3670, found 521.3649.

Heterocycle 43: To a solution of diene **9** (0.017 g, 0.14 mmol) and the ring-fused cyclohexane-silacyclopropane **10** (0.039 g,

0.18 mmol) in C_6H_6 (0.88 mL) was added $AgOCOCF_3$ (0.027 mL, 0.050 M in C_6H_6). After 10 min, benzaldehyde (0.014 mL, 0.14 mmol) was added followed by diethyl azodicarboxylate (0.021 mL, 0.14 mmol). After 20 min, the reaction mixture was concentrated in vacuo. Purification by flash chromatography (10:90 EtOAc/hexanes) afforded heterocycle **43** as a white solid (0.060 g, 81 % over three steps): m.p. 157–159 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32–7.23 (m, 5 H), 4.84 (s, 1 H, and m, 1 H), 4.75–4.71 (m, 1 H), 4.38–4.27 (m, 2 H), 4.24–4.19 (m, 2 H), 1.85–1.83 (m, 1 H), 1.72–1.66 (m, 1 H), 1.59–1.56 (m, 2 H), 1.38 (t, J = 7.1 Hz, 3 H, and m, 2 H), 1.32 (t, J = 7.1 Hz, 3 H, and m, 1 H), 1.28–1.23 (m, 2 H), 1.08 (s, 9 H, and m, 1 H), 1.00 (s, 9 H, and m, 1 H), 0.88–0.79 (m, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.0 (C), 155.3 (C), 141.8 (C), 128.9 (CH), 127.4 (2 CH), 85.9 (CH), 82.2 (CH), 68.5 (CH), 65.0 (CH_2), 62.3 (CH_2), 47.8 (C), 30.1 (CH_2), 28.6 (CH_3), 27.8 (CH_3), 25.6 (CH_2), 24.7 (CH_2), 21.6 (C), 21.5 (CH_2), 21.4 (CH_2), 21.2 (C), 19.7 (CH_2), 14.8 (CH_3), 14.3 (CH_3) ppm. IR (ATR): $\tilde{\nu}$ = 1690, 1645, 1095, 825 cm^{-1}. HRMS (ESI) *m/z* calcd. for $C_{30}H_{49}N_2O_5Si$ $[M + H]^+$ 545.3405, found 545.3456. $C_{30}H_{48}N_2O_5Si$ (544.81): calcd. C 66.17, H 8.88; found C 66.17, H 8.85.

Alkene 46: To a solution of 1-vinylcyclopentene (0.017 mL, 8.64 M in Et_2O, 0.15 mmol) and the ring-fused cyclohexane-silacyclopropane **10** (0.040 g, 0.18 mmol) in C_6H_6 (0.952 mL) was added $AgOCOCF_3$ (0.030 mL, 0.050 M in C_6H_6). After 10 min, benzaldehyde (0.016 mL, 0.15 mmol) was added followed by diethyl azodicarboxylate (0.023 mL, 0.15 mmol). After 10 min, the reaction mixture was concentrated in vacuo. Purification by flash chromatography (25:75 EtOAc/hexanes) afforded alkene **46** as a white solid (0.032 g, 42 % over three steps): m.p. 162–166 °C. ^{1}H NMR (500 MHz, C_6D_6): δ = 7.30 (d, J = 7.0 Hz, 2 H), 7.19–7.17 (m, 2 H), 7.10–7.07 (m, 1 H), 6.98–6.34 (b, 1 H), 5.72–5.33 (b, 2 H), 4.64 (d, J = 10.0 Hz, 1 H), 4.06–3.96 (m, 4 H), 3.04–2.97 (b, 1 H), 2.19–2.16 (b, 1 H), 1.99–1.96 (b, 1 H), 1.85–1.71 (b, 1 H), 1.59–1.49 (m, 2 H), 1.38–1.33 (m, 1 H), 1.20 (s, 9 H), 1.01–0.97 (m, 6 H), 0.95 (s, 9 H) ppm. ^{13}C NMR (150 MHz, C_6D_6): δ = 157.9 (C), 156.2 (C), 151.4 (C), 145.2 (C), 128.9 (CH), 128.0 (CH), 127.5 (CH), 126.6 (CH), 81.4 (CH), 62.7 (CH_2), 62.3 (CH_2), 57.9 (CH), 57.5 (CH), 30.9 (CH_2), 29.1 (CH_2), 28.9 (CH_3), 28.7 (CH_3), 22.1 (C), 21.6 (C), 14.91 (CH_3), 14.86 (CH_3), 14.6 (CH_2) ppm. IR (ATR): $\tilde{\nu}$ = 3283, 1711, 1230, 1011 cm^{-1}. HRMS (APCI) *m/z* calcd. for $C_{28}H_{45}N_2O_5Si$ $[M + H]^+$ 516.3092, found 517.3091.

Alkene 47: To a solution of 1-vinylcycloheptene (0.018 g, 0.15 mmol) and the ring-fused cyclohexane-silacyclopropane **10** (0.037 g, 0.17 mmol) in C_6H_6 (0.970 mL) was added $AgOCOCF_3$ (0.030 mL, 0.050 M in C_6H_6). After 10 min, benzaldehyde (0.016 mL, 0.15 mmol) was added followed by diethyl azodicarboxylate (0.024 mL, 0.15 mmol). After 20 min, the reaction mixture was concentrated in vacuo. Purification by flash chromatography (15:85 EtOAc/hexanes) afforded alkene **47** as a white solid (0.044 g, 54 % over three steps). Purification gave a mixture of alkene **47** and a minor isomer (98:2 alkene **47**:minor isomer). The minor isomer could not be characterized because of an insufficient yield. Alkene **47** was a mixture of rotamers. The characterization data reported below were recorded at 22 °C. A variable temperature ^{1}H NMR experiment was performed at 70 °C and the rotamer peaks sharpened: m.p. 137–141 °C. ^{1}H NMR (500 MHz, C_6D_6, 22 °C): δ = 7.32 (d, J = 7.2 Hz, 2 H), 7.19–7.17 (m, 2 H), 7.11–7.08 (m, 1 H), 6.98–6.40 (b, 1 H), 5.88–5.74 (b, 1 H), 5.05 (d, J = 9.6 Hz, 1 H), 4.98–4.83 (m, 1 H), 4.07–3.95 (m, 4 H), 3.03–2.95 (b, 1 H), 2.21–2.10 (b, 2 H), 1.66–1.44 (m, 5 H), 1.36–1.28 (m, 3 H), 1.18 (s, 9 H), 1.00 (s, 9 H), 0.98–0.95 (m, 6 H) ppm. ^{1}H NMR (500 MHz, C_6D_6, 70 °C): δ = 7.36–7.34 (m, 2 H), 7.20–7.17 (m, 2 H), 7.11–7.07 (m,1 H), 6.42–6.37 (b, 1 H), 6.07–5.84 (b, 1 H), 5.06–5.04 (d, J = 10.0 Hz, 1 H), 4.89–4.87 (m, 1 H), 4.10–3.97 (m, 4 H), 2.99–2.95 (m, 1 H), 2.23–2.09 (m, 2 H), 1.66–1.57 (m, 2 H), 1.52–1.44 (m, 3 H), 1.41–1.26 (m, 3 H), 1.10 (s, 9 H), 1.06–1.03 (m, 6 H), 1.02 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.8 (C), 156.6 (C), 152.1 (C), 144.3 (C), 128.9 (CH), 128.1 (CH), 127.5 (CH), 125.7 (CH), 80.6 (CH), 65.6 (CH), 62.5 (CH_2), 62.2 (CH_2), 55.6 (CH), 29.2 (CH_2), 28.8 (CH_3), 28.3 (CH_2), 28.2 (CH_3), 27.9 (CH_2), 25.9 (CH_2), 22.3 (C), 21.9 (C), 16.3 (CH_2), 15.0 (CH_3), 14.9 (CH_3) ppm. IR (ATR): $\tilde{\nu}$ = 3283, 1708, 1229, 1011 cm^{-1}. HRMS (ESI) *m/z* calcd. for $C_{30}H_{49}N_2O_5Si$ $[M + H]^+$ 545.3405, found 545.3409. $C_{30}H_{48}N_2O_5Si$ (544.81): calcd. C 66.14, H 8.88; found C 65.86, H 8.91.

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[1] S. Vázquez, P. Camps, *Tetrahedron* **2005**, *61*, 5147–5208.
[2] A. Duda, A. Kowalski, S. Penczek, H. Uyama, S. Kobayashi, *Macromolecules* **2002**, *35*, 4266–4270.
[3] F. R. Fischer, C. Nuckolls, *Angew. Chem. Int. Ed.* **2010**, *49*, 7257–7260; *Angew. Chem.* **2010**, *122*, 7415–7418.
[4] O. Nuyken, S. D. Pask, *Polymers* **2013**, *5*, 361–403.
[5] M. R. Wilson, R. E. Taylor, *Angew. Chem. Int. Ed.* **2013**, *52*, 4078–4087; *Angew. Chem.* **2013**, *125*, 4170–4180.
[6] M. F. Debets, S. S. van Berkel, J. Dommerholt, A. J. Dirks, F. P. J. T. Rutjes, F. L. van Delft, *Acc. Chem. Res.* **2011**, *44*, 805–815.
[7] R. Selvaraj, J. M. Fox, *Curr. Opin. Chem. Biol.* **2013**, *17*, 753–760.
[8] K. Lang, L. Davis, S. Wallace, M. Mahesh, D. J. Cox, M. L. Blackman, J. M. Fox, J. W. Chin, *J. Am. Chem. Soc.* **2012**, *134*, 10317–10320.
[9] R. Rossin, P. R. Verkerk, S. M. van der Bosch, R. C. M. Vulders, I. Verel, J. Lub, M. S. Robillard, *Angew. Chem. Int. Ed.* **2010**, *49*, 3375–3378; *Angew. Chem.* **2010**, *122*, 3447–3450.
[10] M. T. Taylor, M. L. Blackman, O. Dmitrenko, J. M. Fox, *J. Am. Chem. Soc.* **2011**, *133*, 9646–9649.
[11] K. Tomooka, S. Miyasaka, S. Motomura, K. Igawa, *Chem. Eur. J.* **2014**, *20*, 7598–7602.
[12] K. B. Wiberg, *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 312–322; *Angew. Chem.* **1986**, *98*, 312–322.
[13] E. J. Corey, F. A. Carey, R. A. E. Winter, *J. Am. Chem. Soc.* **1965**, *87*, 934–935.
[14] R. Hoffmann, Y. Inoue, *J. Am. Chem. Soc.* **1999**, *121*, 10702–10710.
[15] Y. Inoue, T. Ueoka, T. Kuroda, T. Hakushi, *J. Chem. Soc. Perkin Trans. 2* **1983**, 983–988.
[16] A. Krebs, K.-I. Pforr, W. Raffay, B. Thölke, W. A. König, I. Hardt, R. Boese, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 159–160; *Angew. Chem.* **1997**, *109*, 159–161.
[17] J. R. Sanzone, K. A. Woerpel, *Angew. Chem. Int. Ed.* **2016**, *55*, 790–793; *Angew. Chem.* **2016**, *128*, 800–803.
[18] A. Sella, H. Basch, S. Hoz, *J. Am. Chem. Soc.* **1996**, *118*, 416–420.
[19] M. A. Greene, M. Prévost, J. Tolopilo, K. A. Woerpel, *J. Am. Chem. Soc.* **2012**, *134*, 12482–12484.
[20] J. A. Marshall, *Acc. Chem. Res.* **1980**, *13*, 213–218.
[21] G. W. Wijsman, G. A. Iglesias, M. C. Beekman, W. H. de Wolf, F. Bickelhaupt, H. Kooijman, A. L. Spek, *J. Org. Chem.* **2001**, *66*, 1216–1227.
[22] H. Mayr, B. Kempf, A. R. Ofial, *Acc. Chem. Res.* **2003**, *36*, 66–77.
[23] X-ray crystallography and nuclear Overhauser enhancement measurements confirmed the relative configuration for all products. Details are provided as Supporting Information.
[24] B. Hurlocker, C. Hu, K. A. Woerpel, *Angew. Chem. Int. Ed.* **2015**, *54*, 4295–4298; *Angew. Chem.* **2015**, *127*, 4369–4372.

[25] D. Crich, K. Ranganathan, *J. Am. Chem. Soc.* **2005**, *127*, 9924–9929.
[26] The rearrangement of *trans*-alkene **12** to oxasilacyclopentane **26** is relatively slow, requiring 21 h to consume 50 % of *trans*-alkene **12**.
[27] S. Deuri, P. Phukan, *J. Mol. Struct. THEOCHEM* **2010**, *945*, 64–70.
[28] H. Zhang, A. Wakamiya, S. Yamaguchi, *Org. Lett.* **2008**, *10*, 3591–3594.
[29] F. Liu, Y. Liang, K. N. Houk, *J. Am. Chem. Soc.* **2014**, *136*, 11483–11493.
[30] M. L. Blackman, M. Royzen, J. M. Fox, *J. Am. Chem. Soc.* **2008**, *130*, 13518–13519.
[31] The high strain energy of bicyclic compound **34** likely contributed to the facile decomposition.
[32] Diels–Alder cycloadditions with tetrazine **2** are likely concerted, but a stepwise mechanism cannot be ruled out for the reaction of silyl enol ether **18** and diene **2**.
[33] M. J. Haddadin, E. H. Ghazvini Zadeh, *Tetrahedron Lett.* **2010**, *51*, 1654–1656.
[34] F. Schoenebeck, D. H. Ess, G. O. Jones, K. N. Houk, *J. Am. Chem. Soc.* **2009**, *131*, 8121–8133.
[35] S. Bräse, C. Gil, K. Knepper, V. Zimmerman, *Angew. Chem. Int. Ed.* **2005**, *44*, 5188–5240; *Angew. Chem.* **2005**, *117*, 5320–5374.
[36] K. J. Shea, J.-S. Kim, *J. Am. Chem. Soc.* **1992**, *114*, 4846–4855.
[37] D. S. Reddy, W. R. Judd, J. Aubé, *Org. Lett.* **2003**, *5*, 3899–3902.
[38] Triazoles **40** and **41** were also unstable to purification by column chromatography, but the decomposition products could not be identified.
[39] T. Kanzian, H. Mayr, *Chem. Eur. J.* **2010**, *16*, 11670–11677.
[40] T. Müller, M. Juhasz, C. A. Reed, *Angew. Chem. Int. Ed.* **2004**, *43*, 1543–1546; *Angew. Chem.* **2004**, *116*, 1569–1572.
[41] J. B. Lambert, *Tetrahedron* **1990**, *46*, 2677–2689.
[42] J. Coope, V. J. Shiner Jr., M. W. Ensinger, *J. Am. Chem. Soc.* **1990**, *112*, 2835–2837.
[43] R. Selvaraj, J. M. Fox, *Tetrahedron Lett.* **2014**, *55*, 4795–4797.
[44] L. T. Kliman, S. N. Mlynarski, G. E. Ferris, J. P. Morken, *Angew. Chem. Int. Ed.* **2012**, *51*, 521–524; *Angew. Chem.* **2012**, *124*, 536–539.
[45] T. G. Driver, K. A. Woerpel, *J. Am. Chem. Soc.* **2003**, *125*, 10659–10663.

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