1-Amino-3-siloxy-1,3-butadienes: Highly Reactive Dienes for the Diels−Alder Reaction

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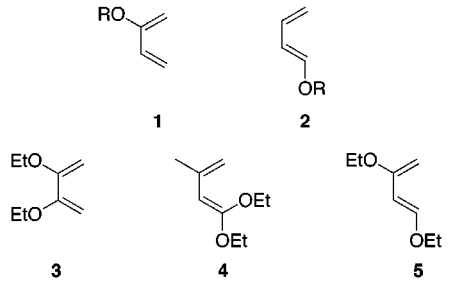
1-Amino-3-siloxy-1,3-butadienes represent a novel class of heteroatom-containing dienes with several useful properties. These dienes can be prepared efficiently by deprotonation of readily available vinylogous amides with potassium hexamethylsilazide, followed by silylation of the corresponding potassium enolates. This protocol has been found to be quite general for the preparation of various dienes containing different silyl and amino groups. Amino siloxy dienes readily undergo [4 + 2] cycloadditions with a wide range of electron-deficient dienophiles. The reactions generally occur under very mild conditions to afford the corresponding [4 + 2] adducts in high yields and with complete regioselectivity. High *endo* selectivity is observed in the case of *N*-phenylmaleimide and methacrolein. Other cycloadducts are usually obtained as mixtures of *endo*/*exo* diastereomers. The cycloadducts are versatile synthetic intermediates. They can be subjected to deprotonation, reduction, and Wittig olefination without any hydrolysis or elimination. In addition, the elimination of the amino group can be cleanly accomplished under acidic conditions leading to the formation of enones. A variety of substituted cyclohexenones can be prepared by this procedure.

Introduction

Over the 70 years since its report by Diels and Alder, the synthetic potential of the Diels−Alder reaction has been greatly expanded through modifications of the diene and dienophile components.[1] The initial empirical observations that introduction of lone-pair containing heteroatoms onto the diene structure leads to an increase in the rate and regioselectivity of the cycloadditions proved to be essential in designing more reactive and specifically functionalized dienes.[2] These experimental results were further supported by theoretical and computational studies.[3] Over the years, various elements of the periodic table have been incorporated into the diene structures.[2a]

The simple monoalkoxy dienes **1** and **2** were among the first examples of heteroatom-substituted dienes used in [4 + 2] cycloadditions.[4] Several dialkoxy dienes, such as **3**, **4**, and **5**, were reported soon after the discovery of the Diels−Alder reaction.[5] However, mainly because of the difficulty of their preparation, which frequently involved pyrolytic eliminations of the corresponding acetals, synthetic applications of these dienes remained limited for many years.



1 **2** **3** **4** **5**

The discovery of efficient synthetic methods for the conversion of carbonyl compounds into silyl enol ethers[6] allowed the preparation of various siloxydienes, such as **6** and **7**, which have become much more popular than their alkoxy counterparts.[7] The most significant advance among siloxy dienes is the development of 1-methoxy-3-trimethylsiloxy-1,3-butadiene (**8**) by Danishefsky,[8] after whom the diene is named. The enormous popularity of this diene stems from its high reactivity toward a range of dienophiles, including heterodienophiles, as well as the ease of conversion of its cycloadducts to enones and to aromatic and heterocyclic compounds.[9] Among the other siloxy dienes prepared over the years, one that merits mention is the trioxygenated diene **9**, in which the

[‡] Recipient of the Pfizer Undergraduate Summer Research Fellowship in Synthetic Organic Chemistry (1997).

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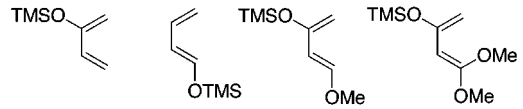
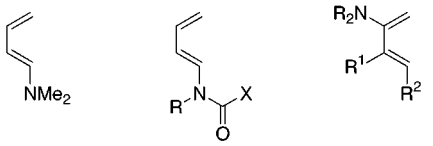
enhanced nucleophilic character overrides the steric problems associated with the (*Z*)-methoxy group.[10]



6 **7** **8** **9**

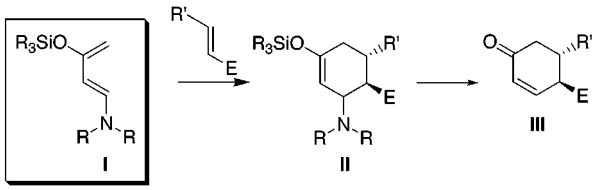
Amino dienes have also played an important role in the development of the Diels−Alder reaction. 1-Amino-substituted diene **10** was first reported in 1936.[11] Although relatively unstable, it was later found to be highly reactive toward several dienophiles.[12] The corresponding 1-*N*-acylamino-1,3-butadienes (**11**) appeared to be much more stable, and several convenient protocols for their preparation were developed.[13] The usefulness of *N*-acylaminodienes was demonstrated through the syntheses of several alkaloids.[14] Curiously, 2-aminodienes (**12**) were predicted, on the basis of theoretical considerations, to be unable to undergo [4 + 2] cycloadditions.[15] Nevertheless, the Diels−Alder reactions of 2-aminodienes have been successfully performed with various dienophiles.[16] Especially noteworthy is the recent application of these dienes in asymmetric synthesis.[17]



10 **11** **12**

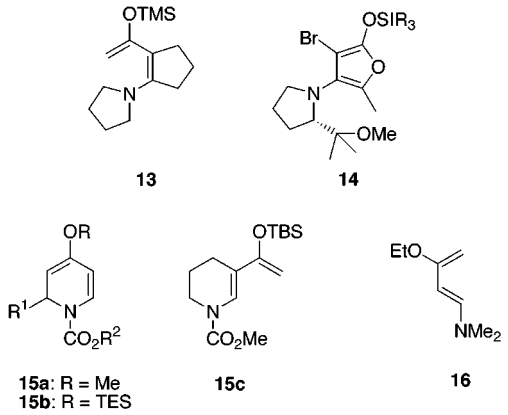
The incorporation of both siloxy (or alkoxy) and amino substituents into the diene structure has received surprisingly little attention. The only examples found include cyclopentene-containing diene **13**,[18] amino siloxy furan **14**,[19] and *N*-acylamino siloxy dienes **15a**[20] and **15b**,[21] and **15c**.[22] It is also very surprising that although

Scheme 1



I **II** **III**

1-(dimethylamino)-3-ethoxy-1,3-butadiene (**16**) was prepared by Meerwein in 1961,[23] there is no report of its use in the Diels−Alder reaction.



13 **14** **15a**: R = Me **15b**: R = TES **15c** **16**

Inspection of the structure of 1-amino-3-siloxy-1,3-butadienes (**I**) reveals the synergetic arrangement of the nitrogen and oxygen substituents, which are set up to confer these dienes with high reactivity in the normal electron demand Diels−Alder reaction (Scheme 1). Further analysis shows that the initial cycloadducts (**II**) can potentially be converted to substituted cyclohexenones (**III**). Although this initially projected sequence of events is similar to the methodology developed by Danishefsky,[9] the presence of the amino group was expected to offer several significant advantages. First, the cycloadditions of amino siloxy dienes will provide access to nitrogen-containing compounds such as **II**, which potentially can be useful intermediates in alkaloid synthesis. Second, as a result of the higher nucleophilicity of the nitrogen atom, amino siloxy dienes were expected to display reactivity higher than that of the corresponding alkoxy siloxy diene **8**. Finally, the amino group in **I** provides an opportunity for the introduction of chirality into the diene structure, which would allow for an extension of this methodology to asymmetric synthesis.

Indeed, in a recent communication we showed that the parent 1-(dimethylamino)-3-siloxy-1,3-butadiene can be efficiently made by the silylation of the corresponding vinylogous amide and that it displays high reactivity in [4 + 2] cycloadditions with several dienophiles.[24a] Another attractive feature of amino siloxy dienes, the possibility for asymmetric induction, was demonstrated by introducing a chiral, C_2-symmetric amino group and using the resulting dienes for the asymmetric synthesis of various

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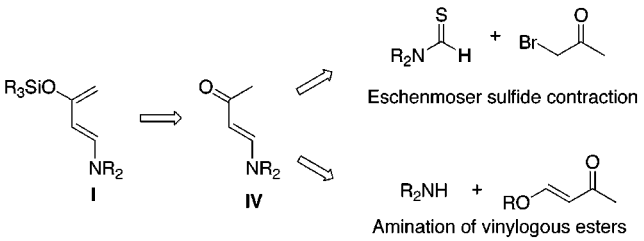
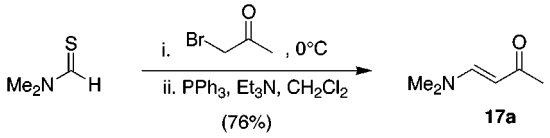
Scheme 2



Scheme 3



substituted cyclohexenones, as well as the terpene (−)-α-elemene.[24b] We have also demonstrated the usefulness of modified amino siloxy dienes in alkaloid synthesis through an efficient, stereocontrolled synthesis of tabersonine.[24c]

The present paper provides a full account of our work on the achiral amino siloxy dienes, including the details of their preparation and their reactivity and stereoselectivity in [4 + 2] cycloadditions with numerous mono- and diactivated dienophiles.

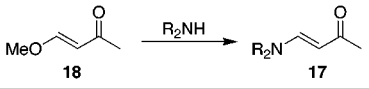
Results and Discussion

Preparation of 1-Amino-3-siloxy-1,3-dienes. The simplest, most direct route to 1-amino-3-siloxy-dienes (**I**) was through silylation of the corresponding vinylogous amides (**IV**), which in turn could be prepared in one of two ways, as shown in a retrosynthetic sense in Scheme 2.

The first method represents the well-documented Eschenmoser sulfide contraction procedure.[25] *N,N*-Dimethylthioformamide was first reacted with bromoacetone, followed by treatment with PPh_3 and Et_3N to promote the sulfide contraction, which afforded the desired vinylogous amide **17a** in 76% yield after distillation (Scheme 3). Although this reaction is preparatively simple and was usually carried out in one pot, the difficulty experienced with removing the large quantities of triphenylphosphine sulfide produced made this procedure inconvenient, especially with preparative scale reactions.

Alternatively, the required vinylogous amides (**17**) can be efficiently prepared by the addition−elimination reaction of secondary amines with vinylogous esters,[26] such as 4-methoxy-3-buten-2-one (**18**),[27] as shown in Table 1. This method was found to be much more convenient and flexible and was utilized for the preparation of several structurally and electronically varied vinylogous amides. These reactions were quite facile—even moderately exothermic with unhindered amines—but required more vigorous conditions with hindered amines (entry 3). In all cases, however, the products were obtained in high yield.

Table 1. Preparation of Vinylogous Amides



entry	R_2NH	time (h)	temp (°C)	product	yield (%)[a]
1	Me_2NH	1	5	**17a**	95
2	Et_2NH	3	5	**17b**	89
3	i-Pr_2NH	8	84	**17c**	92
4		3	5	**17d**	88
5		1	20	**17e**	97

[a] Refers to an isolated yield, after bulb-to-bulb distillation.

Several different procedures were evaluated to find the most effective one for the conversion of the vinylogous amides (**17**) into the corresponding 1-amino-3-siloxy-1,3-butadienes (**19**). The use of a triethylamine−TMSCl protocol[6] resulted only in recovery of the starting material. Deprotonation of the vinylogous amide with LDA followed by addition of the silylating agent was also unsuccessful, as silylation of the lithium enolate was found to be slow at low temperature. Whereas addition of DMPU did accelerate the silylation, removal of this high-boiling polar additive proved impractical. The solution to the problem lay in the use of the more reactive potassium or sodium enolates.

The best set of conditions for enolate formation involved the addition of a solution of the vinylogous amide in THF to 1.05 equiv of potassium hexamethyldisilazide (KHMDS) dissolved in a 1:1 toluene/THF solution. The completion of enolate formation was ensured by allowing the temperature of the cooling bath to rise to −40 °C over a 2 h period. Addition of 1.1 equiv of the silylating agent to a cold solution of the enolate (−70 °C) followed by warming of the reaction mixture to ambient temperature resulted in the clean formation of the desired amino siloxy dienes (**19**).

The procedure described above was found to be convenient and quite general, allowing the preparation of a range of dienes (Table 2). In general, the 1-amino-3-siloxy-1,3-dienes (**19**) are obtained in very high yields and in essentially pure form. Simple filtration of the reaction mixture, to remove the potassium chloride formed, and evaporation of the volatile reagents under reduced pressure afforded the dienes in quantitative yields. If necessary, the crude dienes can be further purified by bulb-to-bulb distillation. The amino siloxy dienes prepared by this method were found to be quite stable to normal

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(26) (a) Lienhard, U.; Fahrni, H.-P.; Neuenschwander, M. *Helv. Chem. Acta* **1978**, *61*, 1609. (b) Markova, N. K.; Zaichenko, Y. A.; Tsil'ko, A. E.; Maretina, I. A. *J. Org. Chem. USSR (Engl. Transl.)* **1984**, *20*, 876.

(27) Although 4-methoxy-3-buten-2-one (**18**) is commercially available, it can be more economically and conveniently obtained by heating acetylacetaldehyde dimethyl acetal in the presence of NaOAc and distilling the product out of the reaction mixture (see ref 26a). The vinylogous amide **(17a)** can also be obtained directly from acetylacetaldehyde dimethyl acetal: Maggiulli, C. A.; Tang, P. W. *Org. Prep. Proc. Int.* **1984**, *16*, 31.

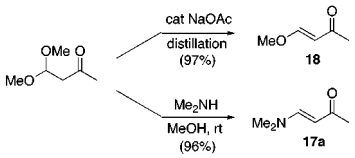
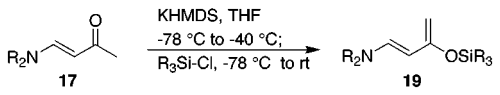


Table 2. Preparation of Amino Siloxy Dienes

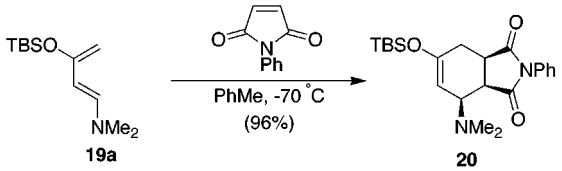


17 19

entry	R_2N-	R_3Si-	product	yield (%)[a]
1	Me_2N	TBS	**19a**	92
2	Me_2N	TIPS	**19b**	90
3	Et_2N	TBS	**19c**	95
4	iPr_2N	TBS	**19d**	85
5		TBS	**19e**	89
6		TBS	**19f**	90

[a] Refers to isolated yields, after bulb-to-bulb distillation.

Scheme 4



handling and could be conveniently stored for several months at low temperature. They do, however, hydrolyze in water and in the presence of common Lewis acids. Generally, TBSCl was used as the silylating reagent, although silylation of the enolate with TIPSCl gave the corresponding TIPS-protected diene **19b** in similarly high yield (entry 2). The parent TBDPS-protected diene was synthesized using the standard procedure, but it could not be further purified by Kugelrohr distillation. Dienes protected with the TMS group were too labile to be isolated in pure form and were always contaminated with the starting vinylogous amide.

The standard protocol was also applied to the preparation of the dienes **19c**−**f** containing sterically and electronically different amino groups (entries 3−6). Having established an efficient access to various 1-amino-3-siloxy-1,3-dienes, the stage was now set for probing their behavior in [4 + 2] cycloadditions.

Cycloadditions with Doubly Activated Dienophiles. The initial Diels−Alder experiments were conducted with 1-(dimethylamino)-3-siloxy-1,3-butadiene, **19a**. Diene **19a** reacted rapidly with *N*-phenylmaleimide, even at −70 °C, and gave exclusively the *endo* adduct **20** in 96% yield after chromatography (Scheme 4). This and the other cycloadducts described below are stable to chromatography, provided the silica gel is pretreated with triethylamine.

The structure of **20** was rigorously established by means of 2D NMR spectroscopy. Figure 1 shows what we believe to be the preferred conformation of this cycloadduct. A COSY experiment allowed the unambiguous assignment of all the signals in the 500 MHz ^{1}H NMR spectrum of **20**. Proton H^2 appeared at 3.39 ppm as a doublet of doublets ($J_{1,2}$ = 5.1 Hz, $J_{2,3}$ = 6.3 Hz). The methylene protons H^5 and H^6 were found at 2.43 and 2.76 ppm, respectively ($J_{5,6}$ = 17.3 Hz). The large coupling constant of 9.6 Hz between H^5 and H^4 indicated that these protons are almost coplanar. On the other hand,

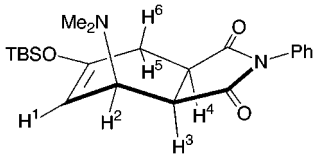
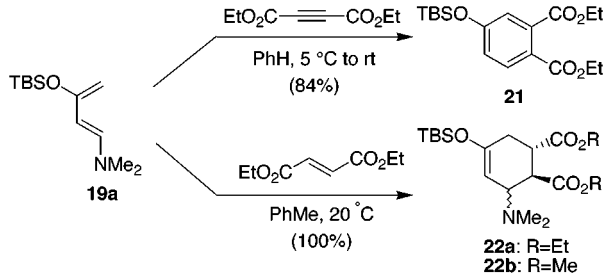
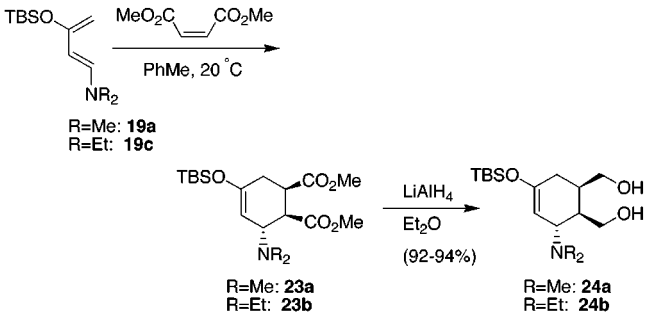


Figure 1. The extended boat conformation of cycloadduct **20**.

Scheme 5



Scheme 6



much smaller coupling was observed between H^6 and H^4 ($J_{4,6}$ = 3.0 Hz). Combined with known literature precedents,[28] this initial analysis suggested that **20** exists in a slightly distorted "extended"[28a] boat conformation, in which the dimethylamino group occupies an axial position. Further support for the assigned structure was obtained from a NOESY[29] experiment. The NOE cross-peaks observed between H^1 and H^2, H^2 and H^3, and H^4 and H,[5] combined with the absence of cross-peaks between H^4 and H^6 or H^2 and H^6 provided additional verification of the assignments shown.

The cycloaddition of **19a** with diethyl acetylenedicarboxylate proceeded efficiently at 5 °C and directly gave the aromatized product **21** (Scheme 5), presumably by elimination of dimethylamine from the initially formed cycloadduct under the reaction conditions. The reaction of dimethylfumarate was complete after 15 h at 20 °C and afforded in quantitative yield a 1.4:1 mixture of the *endo* and *exo* cycloadducts (**22a**), which were readily separable by column chromatography (Scheme 5).

Initially, the reaction of amino siloxy diene **19a** with dimethyl maleate appeared not to be straightforward (Scheme 6). When an excess of the dienophile was used, the desired cycloadduct **23a** was obtained in a modest yield, accompanied by two other products, which were identified as the *endo* and *exo* adducts (**22b**) of **19a** with dimethyl fumarate. The yield of **23a** could be improved

(28) (a) Danishefsky, S.; Yan, C. F.; Singh, R.; Gammill, R.; McCurry, P.; Fritsch, N.; Clardy, J. *J. Am. Chem. Soc.* **1979**, *101*, 7001−7007. (b) Maddaluno, J.; Gaonach, O.; Marcual, A.; Toupet, L.; Giessner-Prettre, C. *J. Org. Chem.* **1996**, *61*, 5290.

(29) States, D. J.; Haberkorn, R. A.; Ruben, D. J. *J. Magn. Reson.* **1982**, *48*, 286.

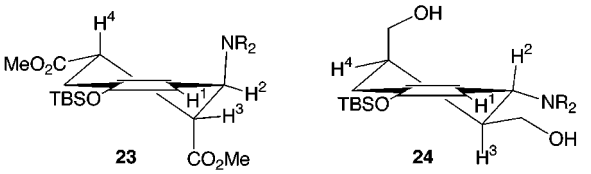


Figure 2. Conformational analysis of **23** and **24**.

significantly by using an excess of diene **19a** (2 equiv), but even in this case the fumarate-derived products were observed. We resisted the temptation to quickly rationalize this result by invoking a stepwise process for the cycloaddition[30] and decided to carry out additional experiments to obtain support for or against a stepwise process. In principle, the byproducts could form if the expected Diels−Alder product (**23a**), which contains a tertiary amine unit, was catalyzing the isomerization of dimethyl maleate to the fumarate, the latter being thermodynamically more stable and significantly more reactive. Support for this hypothesis was obtained through an NMR experiment in which pure cycloadduct **23a** was mixed with dimethyl maleate in toluene-d_8 and the reaction was monitored for 8 days at 20 °C. At the end of this period approximately 30% of the maleate was converted into the fumarate. Additional support for the isomerization hypothesis was obtained from the reaction of dimethyl maleate with diene **19c**, which gave the expected Diels−Alder adduct **23b** in 94% yield, with complete stereospecificity (Scheme 6). The presence of the more hindered amino group—diethyl instead of dimethyl—evidently slows down the conjugate addition−elimination necessary to isomerize maleate to fumarate. Consistent with this, when a mixture of cycloadduct **23b** and dimethyl maleate were observed by NMR, as described above, less than 10% of the maleate was isomerized to the fumarate after 8 days.

The conformational analysis of the maleate cycloadducts (**23**) proved to be nontrivial (Figure 2). On the basis of the coupling constants between protons H^1 and H^2, H^2 and H^3, and H^3 and H^4 ($J_{1,2} = 5.0$ Hz, $J_{2,3} = 2.9$ Hz, $J_{3,4} = 3.6$ Hz), it appeared that two out of the three substituents in this cyclohexene ring were occupying axial positions, a rather unusual situation. To more rigorously establish the relative stereochemistry in the proposed structures, the initial adducts **23** were subjected to reduction with lithium aluminum hydride, which gave the corresponding diols **24**. The reduction was accompanied by a change in preferred conformation of the cyclohexene ring, as evidenced by the NMR coupling constants (Figure 2). The pseudoequatorial orientation of the dimethylamino group in **24** was evident from the small coupling constant of 1.5 Hz between H^1 and H^2. The *cis* relationship of the hydroxymethyl groups was confirmed by the expected 3.5 Hz coupling constant observed between H^3 and H.[4] Finally, the large coupling constant of 10.0 Hz between H^2 and H^3 was diagnostic of the *trans* diequatorial arrangement of the adjacent amino and hydroxymethyl groups.

Cycloadditions with Monoactivated Dienophiles. Next, we turned our attention to simple acyclic dienophiles containing only one electron-withdrawing group. The results of their cycloadditions with 1-(dimethylamino)-3-siloxy-1,3-butadiene are summarized in Table 3. These reactions generally proceeded under relatively mild conditions and afforded the cycloadducts in good yields, with complete regioselectivity. The cycloadducts in most cases are stable to flash chromatography, which allowed the separation and spectroscopic characterization of the *endo* and *exo* adducts.

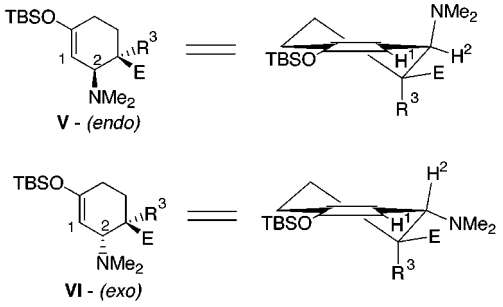
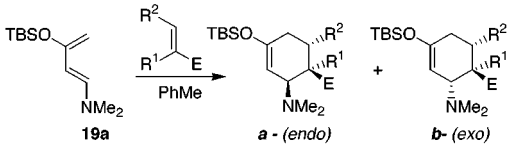


Figure 3. Conformational analysis of *endo* and *exo* cycloadducts.

Table 3. Cycloadditions of Diene 19a with Monoactivated Dienophiles



entry	dienophile	temp (°C)	product	yield (%)[a]	*endo* : *exo*[b]
1		20	**25**	87	> 98 : 2
2		20	**26**	92	1 : 1.5
3		20	**27**	97	1.1 : 1
4		20	**28**	85	1 : 4
5		20	**29**	90	1 : 1.4
6		70	**30**	74	2 : 1
7		90	**31**	87	1 : 3
8		90	**32**	90	1 : 3

[a] Refers to isolated yields, after silica gel chromatography.
[b] Determined by NMR analysis of the crude reaction mixtures.

The structures of these diastereomers were assigned from their characteristic ^{1}H NMR spectra. The *endo* adducts (**V**) generally exist in the conformation in which the amino group is pseudoaxial and the electron-withdrawing group (E) is equatorial (Figure 3). The preferred pseudoaxial orientation of the amino group is presumably for stereoelectronic reasons. This arrangement allows overlap between the occupied π-orbital of the enol ether and σ^* of the C−N bond.[31] This arrangement leads to diagnostic coupling constants between H^1 and

(30) A stepwise mechnism was previously suggested to rationalize a similar outcome of the reaction of 1-(dimethylamino)-1,3-butadiene with dimethyl maleate: Sustmann, R.; Rogge, M.; Nuchter, U.; Bandmann, H. *Chem. Ber.* **1992**, *125*, 1647.

H^2, with $J_{1,2}$ = 5 Hz. For the case when $R^3 = H^3$, an additional coupling is observed between H^2 and H^3, on the order of 5−6 Hz. Conformational analysis of the *exo* adducts (**VI**) follows the same logic as the *endo* adduct. The only difference is that the nitrogen substituent now becomes pseudoequatorial, and very small coupling is observed between H^1 and H^2 ($J_{1,2}$ = 1.5−2.0 Hz). For cases where $R^3 = H^3$, the additional diaxial coupling constant, $J_{2,3}$ = 10 Hz, further confirms the assignment.

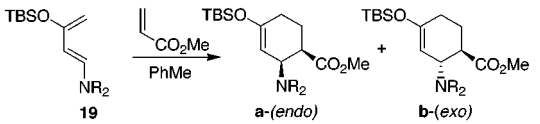
The reaction of diene **19a** with methacrolein was determined to be complete in less than 5 h at 20 °C and was highly stereoselective, affording exclusively the *endo* adduct **25** in 87% isolated yield (entry 1, Table 3). Cycloadditions with methyl acrylate, methyl vinyl ketone, and acrylonitrile also proceeded at room temperature and afforded the corresponding cycloadducts **26**−**28** in good overall yields (entries 2−4). However, in contrast to the high *endo* selectivity observed with methacrolein, the other cycloadditions were less selective and gave significant amounts of *exo* isomers. The cycloaddition with methyl vinyl ketone was conducted in toluene at 20 °C and was found to give a 1.1:1 ratio of *endo*/*exo* isomers. The isomer ratio was not affected significantly either by using a more polar solvent (THF, $CHCl_3$, or CH_3CN) or by starting the reaction at lower temperatures. Simple steric effects also did not give a predictable outcome.

Compared to methyl acrylate, the sterically more demanding *tert*-butyl acrylate was expected to be less reactive and therefore more selective in disfavoring the *endo* approach of the diene. The reaction was indeed slower, requiring 3 days at 20 °C to reach completion, but the stereoselectivity was surprisingly similar (entry 5). Higher temperatures were required for the cycloadditions of dienophiles containing additional substituents at either the α or *β* position. The reaction with methyl methacrylate (entry 6) was carried out at 70 °C and gave a 2:1 mixture of the *endo*/*exo* adducts in 74% yield. Methyl crotonate and methyl cinnamate exhibited very similar behavior (entries 7 and 8). Both cycloadditions required heating the reaction mixture to 90 °C and yielded a 3:1 mixtures of cycloadducts, with the *exo* adducts predominating.

A comparison of the reaction conditions required for the cycloadditions with amino siloxy diene **19** with those reported for Danishefsky's diene (**8**) revealed that the reactions with the former were taking place at much lower temperatures, as anticipated. For example, the Diels−Alder reactions between Danishefsky's diene and several dienophiles, such as maleimide,[32a] dimethyl acetylenedicarboxylate,[32b] methacrolein,[32b] and methyl crotonate,[32c] were reported to occur at a 30−70 °C higher temperature. The higher reactivity of dimethylamino-siloxy diene **16a** compared to that of methoxysiloxy diene **8** was unambiguously established through a study of their kinetics.[33]

Reactivity of Different Dialkylamino Siloxy Dienes. In an effort to better understand the factors influencing the reactivity and *endo*/*exo* selectivity of amino siloxy dienes, we examined the reaction of methyl acrylate with dienes containing a few different amino groups. The results of this study are presented in Table 4.

Table 4. Cyloaddition of Methyl Acrylate with Dialkylamino Siloxy Dienes



entry	diene	R_2N	temp (°C)	product	yield (%)[a]	*endo* : *exo*[b]
1	**19c**	Et_2N	20	**33**	86	1 : 2.5
2	**19d**	iPr_2N	20	**34**	67[c]	1.4 : **1**
3	**19e**		20	**35**	88	1 : 1
4	**19f**		60	**36**	85[c]	1 : 1.5

[a] Refers to isolated yields, after silica gel chromatography.
[b] Determined by NMR analysis of the crude reaction mixtures.
[c] The *endo* and *exo* diastereomers are inseparable by silica gel chromotography.

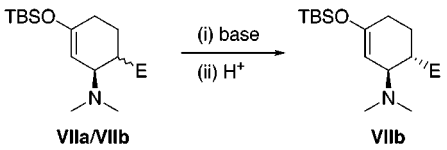
It was found that although dienes possessing the diethylamino and pyrrolidinyl groups (**19c** and **19e**; entries 1 and 3) displayed reactivity similar to that of the parent diene **19a**, the sterically more encumbered diisopropylamino-substituted diene (**19d**) was less reactive (entry 2). The less electron-rich indoline-substituted diene (**19f**) exhibited reactivity markedly lower than that of the dialkyl-substituted dienes and required that the reaction be carried out at 60 °C (entry 4). It may appear intuitive that the steric bulkiness of the dialkylamino group should influence the diastereoselectivity of the [4 + 2] cycloadditions. This assumption turns out to not be supported by facts. Whereas the observed *exo* selectivity was higher in the case of the diethylamino-substituted diene (**19c**) than for the dimethylamino diene (**19a**), suggesting that the bulkier nitrogen substituent disfavors the *endo* approach of the dienophile (entry 1), the opposite effect was found in the case of the diisopropylamino diene (**19d**, entry 2). This and the other results in Table 4 indicate that although the reactivity of the diene follows logical trends, the factors influencing the stereoselectivity of these cycloadditions are not obvious and involve a complex combination of steric and electronic effects of the dienes and dienophiles.

Epimerization and Alkylation of Cycloadducts. In general, the low *endo*/*exo* selectivity of the [4 + 2] cycloaddition step is not of concern, because acid-catalyzed hydrolysis of the *β*-aminoenolsilyl ether eliminates the amino group (vide infra). If control of the relative stereochemistry of the cycloadduct is important, then it can potentially be improved by epimerization at the acidic α-position to the electron-withdrawing group in the cycloadduct mixture (**VIIa**/**VIIb**). This process would allow the preferential formation of the thermodynamically more stable *trans* isomer **VIIb**, in which both of the substituents would occupy equatorial positions in the cyclohexene ring (Scheme 7).

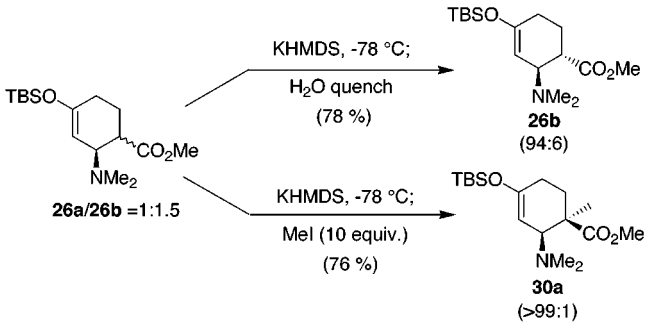
The methyl acrylate adduct **26** was examined to address this question. Although no reaction was observed when the initial 1.5:1 mixture of isomers was treated with *t*-BuOK in *t*-BuOH at room temperature, it was

(31) Lessard, J.; Tan, P. V. M.; Martino, R.; Saunders, J. K. *Can. J. Chem.* **1977**, *55*, 1015.
(32) (a) Baldwin, S. W.; Greenspan, P.; Alaimo, C.; McPhail, A. T. *Tetrahedron Lett.* **1991**, *32*, 5877. (b) Danishefsky, S.; Kitahara, T.; Yan, C. F.; Morris, J. *J. Am. Chem. Soc.* **1979**, *101*, 6996−7000. (c) Vorndam, P. E. *J. Org. Chem.* **1990**, *55*, 3693.
(33) The results of this study have been submitted for publication: Kozmin, S. A.; Green, M. T.; Rawal, V. H., submitted for publication.

Scheme 7



Scheme 8



found that deprotonation with a stronger base followed by aqueous quench led to the desired *trans* isomer (**26b**) as the preponderant product. The best selectivity (94:6) was obtained when the potassium enolate, formed by deprotonation with KHMDS, was quenched at −78 °C with water in THF (Scheme 8). The major product, **26b**, was isolated in 78% yield. Treatment of the same enolate with an excess of methyl iodide was found to produce cleanly the corresponding methylated product, **30a**, as a single diastereomer. Because the NMR spectra of the product obtained were identical with the *endo* adduct of methyl methacrylate (**30a**) the *cis* relationship between the amine and the ester unit was firmly assigned. It is especially noteworthy that no products resulting from the elimination of the amino group were observed in either of these cases.

The opposite stereochemical outcome of protonation and alkylation of **26** may be understood by considering steric and stereoelectronic influences.[34] On the basis of an examination of molecular models, the most reasonable low-energy conformation of the enolate is that shown in Figure 4, in which the potassium may be further bound by coordination with the basic amine. The reaction of the strongly nucleophilic ester enolate **37** is expected to involve an early transition state, in which approach by a bulky electrophile, such as methyl iodide, is expected to be controlled by steric factors.[35] Alkylation would then be favored from the equatorial face, so as to avoid steric interactions with both the adjacent dimethylamino group and the pseudoaxial hydrogen. The preferred axial protonation of enolate **37** can be rationalized by considering initial protonation of the enolate oxygen. Subsequent protonation (tautomerization) of the enol should be much less exothermic and, on the basis of the Hammond postulate, involve a late, product-like transition state, favoring formation of the *trans* product.[36] The possibility cannot be ruled out that the protonated form of the amine

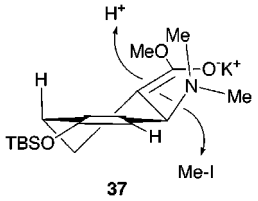
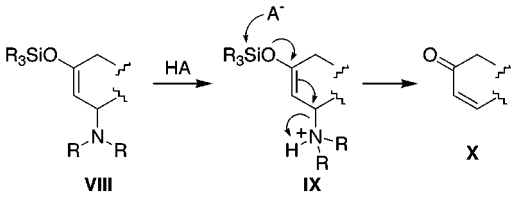
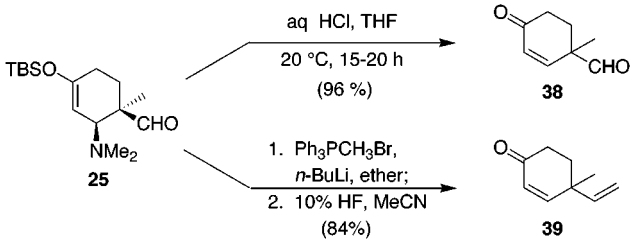


Figure 4. Outcome of protonation and alkylation.

Scheme 9



Scheme 10



is responsible for the selective protonation of the enol intermediate, an example of neighboring group participation.

Further Transformations of the Cycloadducts. The products of the Diels−Alder reactions of amino siloxy dienes are potentially versatile synthetic intermediates. As anticipated, the β-amino enol silyl ether portion of the cycloadduct **VIII** can be converted to the corresponding enone **X** under acidic conditions, which promote the hydrolysis of the silyl enol ether as well as β-elimination of the amino group (Scheme 9).

In the case of the methacrolein adduct (**25**), two different sets of conditions were developed. Subjection of **25** to 1.2 M aqueous HCl in THF cleanly afforded 4-formyl-4-methylcyclohexenone (**38**) in 96% yield (Scheme 10). Close monitoring of this reaction revealed that under these conditions full consumption of the starting material (**25**) requires from 15 to 24 h. The use of a 10% solution of HF in CH_3CN promotes this transformation even more rapidly, and the reaction is usually complete within 1−2 h.

The Diels−Alder adducts are sufficiently stable that certain chemical transformations can be carried out prior to the hydrolysis step. For example, with cycloadduct **25**, the formyl group can be subjected to Wittig olefination and the resulting product can be hydrolyzed to afford the corresponding enone **39**.

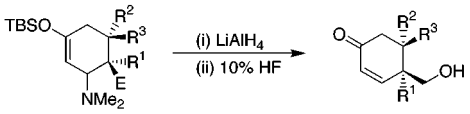
The hydrolysis and reactivity of the methyl acrylate adduct (**26**) was examined next. Acid-mediated hydrolysis of this compound was complicated by the formation of the ester-conjugated enone **41** (Scheme 11). Typically, direct exposure of **26** to either 10% solution of HF or HF−pyridine complex in CH_3CN led to a mixture of isomeric enones **40** and **41** in 1:1−2:1 ratio. The way around this complication was to first reduce the ester group with lithium aluminum hydride, followed by HF-mediated elimination, which gave exclusively 4-hydroxymethyl

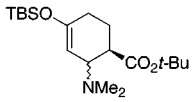
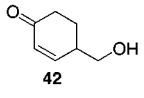
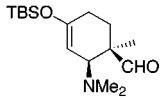
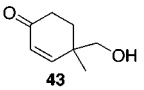
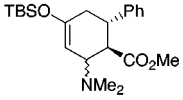
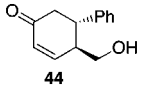
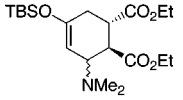
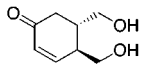
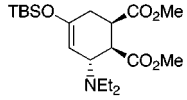
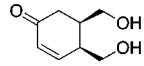
(34) Evans, D. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: Orlando, FL, 1984; Vol. 3, p 1.

(35) (a) House, H. O.; Bare, T. M. *J. Org. Chem.* **1968**, *33*, 943. (b) Krapcho, A. P.; Dundulis, E. A. *J. Org. Chem.* **1980**, *45*, 3236. (c) Hogg, J. A. *J. Am. Chem. Soc.* **1948**, *70*, 161.

(36) Formation of the *trans* product has also been reported during the epimerization of a related, albeit simpler, enolate. Davies, S. G.; Ichihara, O.; Lenoir, I.; Walters, I. A. S. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1411.

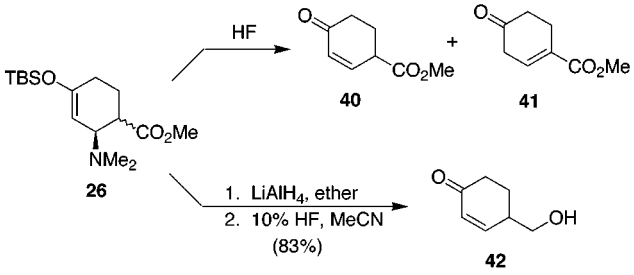
Table 5. Preparation of Substituted Cyclohexenones



Entry	Cycloadduct	Product	Overall yield (%)[a]
1		 **42**	90
2		 **43**	85
3		 **44**	86
4		 **45**	82
5		 **46**	85

[a] Refers to isolated yields, after silica gel chromatography.

Scheme 11

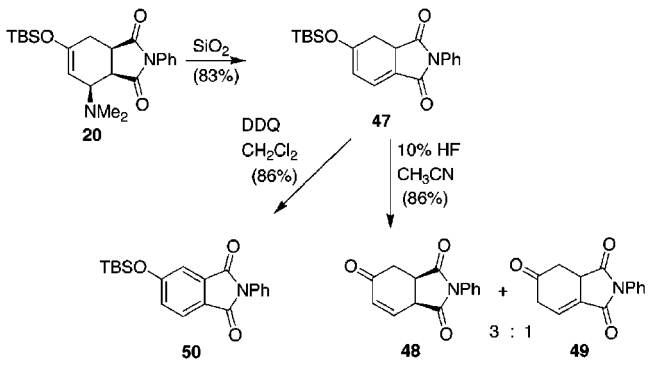


cyclohexenone (**42**) in 83% overall yield. Although this longer sequence contains an additional reduction step, it is very efficient and preparatively simple. In addition, the hydroxyl group in the product can be potentially used as a handle for further functionalization.

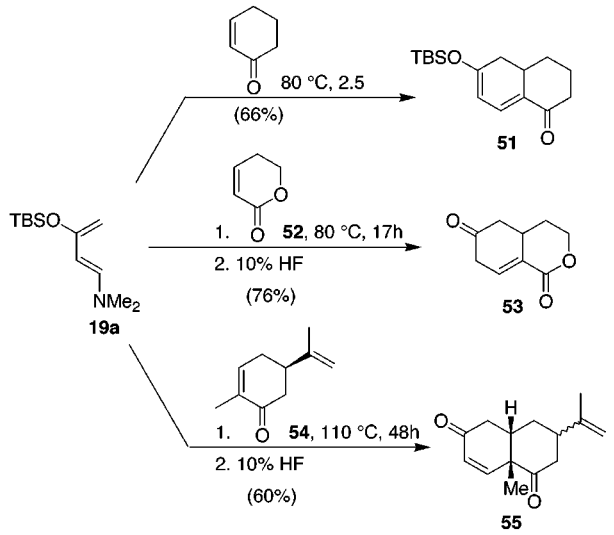
The versatility of this reduction−hydrolysis protocol for the preparation of different cyclohexenones is evident from the different examples shown in Table 5. A wide range of cyclohexenones substituted at the 4- and 5-positions are available by selecting the appropriate substitution pattern in the dienophile component. Further transformations of the cyclohexenone, using well precedented conjugate addition, alkylation, and carbonyl chemistry, could allow the synthesis of cyclohexanes substituted at every position. As mentioned above, the variable *endo*/*exo* selectivity of the Diels−Alder reaction does not diminish the usefulness of this approach to cyclohexenones, because the amino group is eliminated in the last step.

Transformations of *N*-Phenylmaleimide Adduct. The conversion of the *N*-phenylmaleimide adduct **20** to the corresponding enone **48** proved difficult (Scheme 12). The use of either HCl or HF-mediated hydrolysis procedures gave only mixtures of unidentified products, among which **48** could not be detected. Fortunately, it was found

Scheme 12



Scheme 13



that exposure of **20** to silica gel that was not pretreated with triethylamine caused a very clean formation of the dihydrophthalimide, **47**. The acidity of the silica gel was evidently sufficient to promote the elimination of the amino group without hydrolysis of the silyl enol ether moiety. Treatment of **47** with 10% HF solution for a period of 5 h gave a mixture of enones **48** and **49** in a 3:1 ratio. Additionally, DDQ oxidation of **47** provided simple conversion to the corresponding siloxy phthalimide (**50**), obtained in 86% yield.

Cycloadditions with Other Cyclic Dienophiles. Having established the conditions for hydrolysis/elimination of the cycloadducts, we examined the cycloaddition reactions of several monoactivated cyclic dienophiles, which were capable of providing access to different bicyclic systems (Scheme 13). The Diels−Alder reaction of diene **19a** with cyclohexenone was performed in toluene at 80 °C and afforded dienone **51** in 66% yield. The amino group was eliminated under the reaction conditions, presumably as a result of the increased acidity of the hydrogen α to the ketone. Attempts to either isolate the cycloadduct prior to elimination of the amino group or convert **51** to the corresponding enone were unsuccessful. Dihydropyrone **52** underwent the cycloaddition at 80 °C and afforded the corresponding adduct, which was not isolated but was converted to bicyclic lactone **53** as the sole product, isolated in 76% overall yield. Amino siloxy diene **19a** even reacts with trisubstituted dienophiles, which are known to be particularly unreactive in Diels−Alder reactions. The reaction between **19a** and (+)-carvone (**54**) was carried out at 110 °C for 48 h and, after

treatment of the crude reaction mixture with an excess of HF, afforded the bicyclic enone **55** as a 1:1 mixture of diastereomers.[37]

Conclusions

1-Amino-3-siloxy-1,3-butadienes represent a novel class of heteroatom-containing dienes with several properties that make them synthetically useful. They are prepared efficiently by silylation of the corresponding, readily available vinylogous amides. Amino siloxy dienes are highly reactive, considerably more so than the analogous dialkoxy dienes, and undergo [4 + 2] cycloadditions under mild conditions with a broad range of electron-deficient dienophiles. In the case of monoactivated dienophiles, these reactions are completely regioselective. The resulting cycloadducts are versatile synthetic intermediates, as they can be subjected to deprotonation, reduction, and Wittig olefination without any hydrolysis or elimination. In addition, elimination of the amino group can be accomplished cleanly under acidic conditions, leading to the formation of enones. A variety of substituted cyclohexenones can be prepared using the chemistry presented above. We are currently investigating applications of amino siloxy dienes to the synthesis of alkaloid natural products.[24c]

Experimental Section

General Methods. All reactions were carried out under a nitrogen atmosphere. Tetrahydrofuran and diethyl ether were purified by distillation from potassium/benzophenone ketyl. Dichloromethane, benzene, toluene, and triethylamine were distilled from calcium hydride. All other reagents were reagent grade and were purified where necessary. KHMDS was used from newly opened 100 mL bottles and was purchased from Aldrich, Inc. Reactions were monitored by thin-layer chromatography (TLC) using 250 mm Whatman precoated silica gel plates. Flash column chromatography was performed over EM Science Laboratories silica gel (230−400 mesh). Melting points are uncorrected. ^{1}H and ^{13}C NMR chemical shifts are reported as δ values (ppm) relative to TMS, the internal standard. Mass spectra were from The Ohio State University Campus Chemical Instrumentation Center.

Preparation of 4-(Dimethylamino)-3-butene-2-one (17a) by the Eschenmoser Contraction Procedure. To a solution of *N*,*N*-dimethylthioformamide (8.92 g, 0.10 mol) in CH_2Cl_2 (100 mL) was added bromoacetone (15 g, 0.11 mol) at 5 °C, and stirring was continued for 2 h at room temperature. The resulting clear solution was diluted with 250 mL of CH_2Cl_2 and cooled to 5 °C. Triphenylphosphine (29 g, 0.11 mol) was added in one portion followed by a dropwise addition of Et_3N (20 mL, 0.14 mol). The reaction mixture was stirred for 19 h at room temperature, concentrated under reduced pressure to an approximate volume of 150 mL, and diluted with 750 mL of ether under constant stirring. To facilitate precipitation of triphenylphosphine sulfide, the mixture was kept for 20 h at −20 °C and then filtered and concentrated under reduced pressure. The resulting dark oil was purified by a high vacuum distillation (0.5 mmHg, bp 100−120 °C), which afforded 8.6 g (76%) of vinylogous amide **17a** as a light orange oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.10 (s, 3H), 2.88 (br s, 3H), 2.99 (br s, 3H), 5.05 (d, J = 12.8 Hz, 1H), 7.47 (d, J = 12.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.0, 36.9, 44.5, 96.6, 152.6, 195.2. ^{1}H and ^{13}C NMR spectra of this compound were in good agreement with those reported in the literature.[26]

General Procedure A: Preparation of Vinylogous Amides (17) by Amination of Methoxybutenone (18). To a solution of methoxybutenone (**18**) (1.00 g, 10 mmol) in CH_2Cl_2 or THF (7−10 mL) was slowly added secondary amine (15 mmol) at the temperature specified (Table 1). The resulting light yellow solution was stirred for 1−8 h. Concentration in vacuo, followed by bulb-to-bulb distillation afforded the corresponding vinylogous amides **17a**−**e**.

4-(Dimethylamino)-3-butene-2-one (17a). The reaction was performed as described in General Procedure A by addition of the commercially available 2 M solution of dimethylamine in THF (25 mL, 50 mmol) to methoxybutenone (4.08 g, 40.8 mmol) at 5 °C. Bulb-to-bulb distillation (125 °C, 0.25 mmHg) afforded 4.41 g (95%) of the title compound as a colorless oil.

4-(Diethylamino)-3-butene-2-one (17b). The reaction was performed as described in General Procedure A by addition of diethylamine (2.20 mL, 21.2 mmol) to a solution of methoxybutenone (1.41 g, 14.1 mmol) in CH_2Cl_2 (7 mL) at 5 °C. Bulb-to-bulb distillation (140 °C, 0.25 mmHg) afforded 1.74 g (89%) of the title compound as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.19 (t, J = 7 Hz, 6H), 2.10 (s, 3H), 3.34 (m, 4H), 5.12 (d, J = 13 Hz, 1H), 7.49 (d, J = 13 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.0, 14.0, 42.8, 49.6, 95.5, 150.6, 194.9. ^{1}H and ^{13}C NMR spectra of this sample were in good agreement with those reported for this compound.[26]

4-(Diisopropylamino)-3-butene-2-one (17c). The reaction was performed as described in General Procedure A by heating a solution of diisopropylamine (8.3 mL, 59 mmol) and methoxybutenone (0.59 g, 5.9 mmol) to 84 °C for 8 h. Bulb-to-bulb distillation (175 °C, 0.25 mmHg) afforded 0.92 g (92%) of the title compound as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (d, J = 6.6 Hz, 12H), 2.10 (s, 3H), 3.6−3.9 (m, 2H), 5.23 (d, J = 13 Hz, 1H), 7.64 (d, J = 13 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.5, 44.7, 48.4, 96.0, 147.1, 194.9; IR (neat) 2974, 2934, 1646, 1551 cm^{-1}.

4-(Pyrrolidin-1-yl)-3-butene-2-one (17d). The reaction was performed as described in General Procedure A by addition of pyrrolidine (1.80 mL, 21.6 mmol) to a solution of methoxybutenone (1.44 g, 14.4 mmol) in CH_2Cl_2 (7 mL) at 5 °C. Bulb-to-bulb distillation (140 °C, 0.25 mmHg) afforded 1.75 g (88%) of the title compound as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.96 (m, 4H), 2.10 (s, 3H), 3.15−3.49 (m, 4H), 5.01 (d, J = 13 Hz, 1H), 7.68 (d, J = 13 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.8, 44.2, 46.4, 51.8, 9.9, 148.2, 194.7. ^{1}H and ^{13}C NMR spectra of this sample were in good agreement with those reported for this compound.[33]

4-(Indolin-1-yl)-3-butene-2-one (17e). The reaction was performed as described in General Procedure A by addition of indoline (1.88 mL, 16.8 mmol) to a solution of methoxybutenone (2.02 g, 20.2 mmol) in CH_2Cl_2 (2 mL) at 20 °C. Bulb-to-bulb distillation (215 °C, 0.1 mmHg) afforded 3.05 g (97%) of the title compound as a pale yellow solid: mp 103−105 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.22 (s, 3H), 3.23 (t, J = 8.5 Hz, 2H), 3.82 (t, J = 8.5 Hz, 2H), 5.36 (d, J = 13 Hz, 1H), 6.93−7.20 (m, 4H), 8.07 (d, J = 13 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.5, 28.3, 48.0, 101.3, 108.6, 122.8, 125.6, 127.9, 130.9, 139.8, 143.8, 196.0; IR (neat) 3018, 1552, 1259, 1216, 755 cm^{-1}.

General Procedure B: Preparation of 1-Amino-3-siloxy-1,3-butadienes (19). A solution of KHMDS in toluene (0.5 M, 38.4 mL, 19.2 mmol) was diluted with THF (35 mL) and cooled to −78 °C. To the resulting solution was added the vinylogous amide **17** (18.3 mmol) in THF (17 mL) over a period of 20 min. The reaction mixture was warmed to −30 °C over a period of 3 h, cooled to −78 °C, and treated with trialkylchlorosilane (20.1 mmol) dissolved in THF (15 mL). The reaction mixture was allowed to reach room temperature, diluted with ether (350 mL), filtered through dry Celite, and concentrated in vacuo to give essentially pure amino siloxy diene **19** as an oil which can be further purified by bulb-to-bulb distillation.

1-(Dimethylamino)-3-(*tert*-butyldimethylsiloxy)-1,3-butadiene (19a). The reaction was performed according to General Procedure B. The title compound was obtained in 92%

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(39) Gloor, G.; Schaffner, K. *Helv. Chim. Acta* **1974**, *57*, 1815.

yield after bulb-to-bulb distillation (100 °C, 0.25 mmHg): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.19 (s, 6H), 0.98 (s, 9H), 2.70 (s, 6H), 3.84 (s, 1H), 3.92 (s, 1H), 4.78 (d, J = 13.2 Hz, 1H), 6.57 (d, J = 13.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6, 18.3, 25.9, 40.5, 85.8, 95.9, 140.9, 156.4; IR (neat) 2930, 1647, 1333, 1253, 1095, 828 cm^{-1}.

1-(Dimethylamino)-3-(triisopropylsiloxy)-1,3-butadiene (19b). The reaction was performed according to General Procedure B. The title compound was obtained in 90% yield after bulb-to-bulb distillation (100 °C, 0.25 mmHg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.12 (d, 18H, J = 6.8 Hz), 1.25 (m, 3H), 2.70 (s, 6H), 3.85 (s, 1H), 3.89 (s, 1H), 4.78 (d, J = 13.2 Hz, 1H), 6.65 (d, J = 13.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.9, 18.2, 40.6, 85.2, 96.0, 140.9, 156.6; IR (neat) 2944, 1647, 1334, 1094, 1022 cm^{-1}.

1-(Diethylamino)-3-(*tert*-butyldimethylsiloxy)-1,3-butadiene (19c). The reaction was performed according to General Procedure B. The title compound was obtained in 95% yield after bulb-to-bulb distillation (130 °C, 0.25 mmHg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.21 (s, 6H), 1.00 (s, 9H), 1.11 (t, J = 7 Hz, 6H), 3.07 (q, J = 7 Hz, 4H), 3.81 (s, 9H), 3.89 (s, 1H), 4.81 (d, J = 13 Hz, 1H), 6.62 (d, J = 13 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6, 13.1, 18.3, 25.9, 45.3, 84.7, 93.7, 138.3, 156.9; IR (neat) 2959, 2859, 1645, 1251, 1113, 1022, 830, 781 cm^{-1}.

1-(Diisopropylamino)-3-(*tert*-butyldimethylsiloxy)-1,3-butadiene (19d). The reaction was performed according to General Procedure B. The title compound was obtained in 85% yield after bulb-to-bulb distillation (150 °C, 0.25 mmHg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.21 (s, 6H), 1.00 (s, 9H), 1.13 (d, J = 6.6 Hz, 12H), 3.56 (sept, J = 6.7 Hz, 2H), 3.76 (s, 1H), 3.83 (s, 1H), 4.86 (d, J = 13.5 Hz, 1H), 6.78 (d, J = 13.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6, 18.2, 21.7, 25.9, 46.1, 83.8, 92.5, 133.9, 157.3; IR (neat) 2960, 2920, 2850, 1640, 1601, 1305, 1245, 1022, 810, 760 cm^{-1}.

1-(Pyrrolidin-1-yl)-3-(*tert*-butyldimethylsiloxy)-1,3-butadiene (19e). The reaction was performed according to General Procedure B. The title compound was obtained in 89% yield after bulb-to-bulb distillation (130 °C, 0.25 mmHg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.196 (s, 6H), 0.975 (s, 9H), 1.86 (m, 2H), 3.12 (m, 2H), 3.80 (s, 1H), 3.89 (s, 1H), 4.73 (d, J = 13 Hz, 1H), 6.82 (d, J = 13 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.5, 18.3, 25.2, 25.9, 48.8, 85.0, 95.1, 136.6, 156.7; IR (neat) 3026, 2920, 2850, 1601, 1492, 1451, 1372, 1328, 1312, 1028, 842, 758 cm^{-1}.

1-(Indolin-1-yl)-3-(*tert*-butyldimethylsiloxy)-1,3-butadiene (19f). The reaction was performed according to General Procedure B. The title compound was obtained in 90% yield after bulb-to-bulb distillation (200 °C, 0.25 mmHg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.23 (s, 6H), 1.04 (s, 9H), 3.14 (t, J = 8.7 Hz, 1H), 3.72 (t, J = 8.7 Hz, 1H), 4.03 (s, 1H), 4.09 (s, 1H), 5.14 (d, J = 13 Hz, 1H), 6.6−7.2 (m, 4H), 7.27 (d, J = 13 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6, 18.3, 26.0, 27.5, 47.8, 88.8, 100.6, 106.2, 119.4, 125.0, 127.6, 128.1, 129.8, 146.0, 155.6; IR ($CHCl_3$) 2955, 2929, 2857, 1644, 1596, 1491, 1319, 1276, 1023, 839, 780, 741 cm^{-1}.

Reaction of Diene 19a with *N*-Phenylmaleimide. To a solution of diene **19a** (407 mg, 1.80 mmol) in toluene (1 mL) was added *N*-phenylmaleimide (208 mg, 1.20 mmol) in toluene (2 mL) at −70 °C. The reaction mixture was stirred for 2 h at −70 °C, allowed to reach room temperature, and concentrated in vacuo. The NMR analysis of the crude reaction mixture showed the formation of the single *endo* cycloadduct **20**, which was purified by flash chromatography on silica gel (elution with 50% EtOAc in hexanes containing 5% Et_3N) to afford 460 mg (96%) of a yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.15 (s, 3H), 0.18 (s, 3H), 0.92 (s, 9H), 2.31 (s, 6H), 2.43 (dd, J = 17.3, 9.6 Hz, 1H), 2.76 (dd, J = 17.3, 3.0 Hz, 1H), 3.31 (dd, J = 9.5, 6.3 Hz, 1H), 3.36 (ddd, J = 9.6, 9.5, 3.0 Hz, 1H), 3.39 (dd, J = 6.3, 5.1 Hz, 1H), 5.01 (d, J = 5.1 Hz, 1H), 7.27 (d, J = 7.6 Hz, 2H), 7.36 (t, J = 7.6 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.7, −4.4, 17.9, 25.5, 27.3, 39.3, 43.4, 44.3, 61.2, 100.7, 126.3, 128.3, 129.0, 132.2, 152.2, 176.1, 178.5; IR (neat) 2930, 1714, 1659, 1363, 1202, 840, 754 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_{22}H_{32}N_2O_3Si$ 400.2182, found 400.2182.

Reaction of Diene 19a with Diethylacetylenedicarboxylate. To a solution of diene **19a** (350 mg, 1.54 mmol) in benzene (10 mL) was added diethylacetylenedicarboxylate (187 mg, 1.10 mmol) at 5 °C. The reaction mixture was warmed to room temperature, stirred overnight, and concentrated in vacuo. The ^{1}H NMR analysis of the crude reaction mixture showed the formation of the aromatic product **21**, which was purified by flash chromatography on silica gel (elution with 14% EtOAc in hexanes) to afford 320 mg (84%) of a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.22 (s, 6H), 0.98 (s, 9H), 1.35 (t, J = 7.1 Hz, 3H), 1.37 (t, J = 7.1 Hz, 3H), 4.33 (q, J = 7.1 Hz, 2H), 4.35 (q, J = 7.1 Hz, 2H), 6.91 (dd, J = 8.3, 2.8 Hz, 1H), 7.02 (d, J = 2.8 Hz, 1H), 7.74 (d, J = 8.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.5, 14.0, 14.1, 18.1, 25.5, 61.2, 61.6, 119.9, 121.4, 123.4, 131.3, 135.7, 158.5, 166.5, 168.1; IR (neat) 2931, 1725, 1602, 1302, 1120, 844 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_{18}H_{28}O_5Si$ 352.1706, found 352.1711.

Reaction of Diene 19a with Diethyl Fumarate. To a solution of diene **19a** (340 mg, 1.50 mmol) in toluene (3.5 mL) was added diethyl fumarate (180 mg, 1.02 mmol). The reaction mixture was stirred for 15 h at room temperature and concentrated in vacuo. The ^{1}H NMR analysis of the crude product mixture showed the formation of cycloadduct **22** as a mixture of *endo* and *exo* isomers (406 mg, 100%, dr 1.4:1.0), separated by flash chromatography on silica gel (elution with 33% ether in hexanes). Less polar *endo* adduct **22a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.15 (s, 3H), 0.16 (s, 3H), 0.92 (s, 9H), 1.24 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 7.1 Hz, 3H), 2.06 (dddd, J = 17.1, 12.0, 1.8, 1.8 Hz, 1H), 2.23 (s, 6H), 2.33 (dd, J = 17.1, 6.0 Hz, 1H), 2.93 (dd, J = 12.6, 6.9 Hz, 1H), 3.19 (ddd, J = 12.6, 12.0, 6.0 Hz, 1H), 3.67 (ddd, J = 6.0, 5.0, 1.8 Hz, 1H), 4.13 (q, J = 7.1 Hz, 2H), 4.15 (m, 2H), 4.93 (dd, J = 5.1, 1.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.5, 14.0, 17.9, 25.5, 32.5, 38.4, 43.3, 47.0, 58.7, 60.0, 60.6, 99.4, 151.3, 172.7, 174.7; IR (neat) 2934, 2859, 1740, 1669, 1182, 838 cm^{-1}. More polar *exo* adduct **22b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.15 (s, 3H), 0.16 (s, 3H), 0.92 (s, 9H), 1.24 (t, J = 7.3 Hz, 3H), 1.25 (t, J = 7.3 Hz, 3H), 2.25 (s, 6H), 2.30 (m, 2H), 2.70 (dd, J = 11.4, 10.0 Hz, 1H), 2.98 (ddd, J = 11.4, 8.7, 8.1 Hz, 1H), 3.50 (dddd, J = 10.0, 2.0, 2.0, 2.0 Hz, 1H), 4.13 (m, 4H), 4.84 (br d, J = 2.0 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.7, −4.3, 14.0, 17.9, 25.5, 32.3, 40.4, 42.4, 45.5, 60.4, 60.8, 63.0, 102.0, 150.3, 173.0, 174.2; IR (neat) 2932, 1740, 1668, 1464, 1197, 840 cm^{-1}.

Reaction of Diene 19c with Dimethyl Maleate. To a solution of diene **19c** (510 mg, 2 mmol) in toluene (1 mL) was added dimethyl maleate (375 mg, 3 mmol). The reaction mixture was stirred for 3 days at room temperature and concentrated in vacuo. The ^{1}H NMR analysis of the crude reaction mixture showed the formation of a single cycloadduct (*exo*), which was isolated by flash chromatography on silica gel (elution with 50% EtOAc in hexanes containing 1% Et_3N) to give 751 mg of cycloadduct **23b** (94%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.13 (s, 3H), 0.14 (s, 3H), 0.92 (s, 9H), 1.03 (t, 6H, J = 7.0 Hz), 2.31 (dd, J = 17.6, 6.4 Hz, 1H), 2.55 (m, 3H), 2.70 (dq, 2H, J = 14.0, 7.0 Hz), 3.07 (ddd, J = 10.4, 6.4, 4.0 Hz, 1H), 3.24 (dd, J = 4.0, 3.4 Hz, 1H), 3.64 (s, 3H), 3.71 (s, 3H), 3.76 (m, 1H), 4.82 (d, J = 5.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.6, −4.4, 13.1, 17.9, 25.6, 29.0, 37.7, 42.4, 43.6, 51.7, 51.9, 56.5, 103.9, 152.2, 172.9, 174.1; IR (neat) 2931, 2858, 1734, 1668, 1259, 1173, 836 cm^{-1}.

Diol 24b. To a suspension of lithium aluminum hydride (100 mg, 2.6 mmol) in ether (3 mL) was added at 0 °C diester **23b** (265 mg, 0.66 mmol) dissolved in ether (4 mL). The reaction mixture was allowed to reach room temperature, stirred for 2.5 h, diluted with ether (20 mL), and quenched by addition of a minimum amount of water. Anhydrous Na_2SO_4 was then added, and the organic layer was carefully decanted from the solid, which was washed with ether (2 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give 210 mg (93%) of diol **24b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.10 (s, 3H), 0.11 (s, 3H), 0.89 (s, 9H), 1.05 (t, J = 7.2 Hz, 6H), 1.91 (tt, J = 10.0, 3.0 Hz, 1H), 2.06 (m, 1H), 2.13 (br d, J = 17.5 Hz, 1H), 2.22 (m, 1H), 2.31 (dq, 2H, J = 14.4, 7.2 Hz), 2.62 (dq, J = 14.4, 7.2 Hz, 2H), 2.8 (br s, 1H), 3.41 (m, 1H), 3.55 (dd, J = 10.3, 4.8

Hz, 1H), 3.66 (dd, J = 10.0, 3.0 Hz, 1H), 3.84 (dd, J = 10.0, 10.0 Hz, 1H), 4.77 (s, 1H), 6.5 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.6, −4.3, 13.8, 17.9, 25.5, 32.4, 38.8, 39.2, 43.9, 59.8, 61.1, 67.9, 101.1, 151.8; IR (neat) 3300, 2830, 1662, 1463, 1369, 1179, 839, 733 cm^{-1}.

Reaction of Diene 19a with Methacrolein. A solution of diene **19a** (1.14 g, 5.0 mmol) in toluene (3 mL) at 0 °C was treated with methacrolein (294 mg, 0.35 mL, 4.2 mmol). The reaction mixture was allowed to reach room temperature, stirred for 3 h, and concentrated in vacuo. The ^{1}H NMR analysis of the crude reaction mixture showed the formation of the single *endo* cycloadduct **25**, which was purified by flash chromatography on silica gel (elution with 33% ether in hexanes containing 3% Et_3N) to afford 1.08 g (87%) of a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.16 (s, 6H), 0.93 (s, 9H), 1.06 (s, 3H), 1.50 (m, 1H), 2.0−2.2 (m, 3H), 2.20 (s, 6H), 3.28 (d, J = 5.0 Hz, 1H), 4.84 (d, J = 5.0 Hz, 1H), 9.58 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.4, 18.0, 20.4, 24.7, 25.6, 25.9, 43.1, 47.5, 65.4, 97.3, 153.6, 204.0; IR (neat) 2930, 1725, 1661, 1252, 1204, 838, 778 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_{16}H_{31}NO_2Si$ 297.2124, found 297.2110.

Reaction of Diene 19a with Methyl Acrylate. A solution of diene **19a** (377 mg, 1.66 mmol) in toluene (2 mL) at 0 °C was treated with methyl acrylate (0.134 mL, 1.5 mmol). The reaction mixture was stirred for 14 h at room temperature and concentrated in vacuo. The ^{1}H NMR analysis of the crude product mixture showed the formation of cycloadduct **26** as a mixture of *endo* and *exo* isomers (380 mg, 92%, dr 1.0:1.5), which were separated by flash chromatography on silica gel (elution with 12% ether in hexanes containing 2% Et_3N). Less polar *endo* adduct **26a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.16 (s, 6H), 0.93 (s, 9H), 1.83 (m, 1H), 2.0−2.2 (m, 3H), 2.27 (s, 6H), 2.62 (m, 1H), 3.56 (dd, J = 5.0, 5.0 Hz, 1H), 3.70 (s, 3H), 4.95 (d, J = 5.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.4, 18.0, 20.9, 25.6, 28.9, 43.5, 44.8, 51.3, 59.2 100.7, 153.7, 174.6; IR (neat) 2980, 1743, 1662, 1253, 1196, 839, 780 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_{16}H_{31}NO_3Si$ 313.2073, found 313.2074. More polar *exo* adduct **26b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.14 (s, 3H), 0.15 (s, 3H), 0.92 (s, 9H), 1.7−2.0 (m, 2H), 2.0−2.2 (m, 2H), 2.24 (s, 6H), 2.52 (ddd, J = 12.7, 9.2, 3.8 Hz, 1H), 3.66 (m, 1H), 3.70 (s, 3H), 4.84 (dd, J = 2.0, 1.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.5, −4.3, 18.0, 25.5, 25.6, 29.0, 40.6, 42.3, 51.7, 61.9, 102.6, 152.4, 176.0; IR (neat) 2980, 1734, 1662, 1253, 1193, 839, 779 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_{16}H_{31}NO_3Si$ 313.2073, found 313.2068.

Reaction of Diene 19a with Methyl Vinyl Ketone. A solution of diene **19a** (220 mg, 0.97 mmol) in toluene (1 mL) was treated with methyl vinyl ketone (0.15 mL, 2.0 mmol). The reaction mixture was stirred for 3 h at room temperature, and concentrated in vacuo. The ^{1}H NMR analysis of the crude product mixture showed the formation of cycloadduct **27** as a mixture of *endo* and *exo* isomers (280 mg, 97%, dr 1.1:1.0): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.14 (s, 3H, *exo*), 0.15 (s, 3H, *exo*), 0.17 (s, 3H, *endo*), 0.17 (s, 3H, *endo*), 0.92 (s, 9H, *exo*), 0.94 (s, 9H, *endo*), 1.72 (m, 2H), 1.81 (m, 1H), 2.05 (m, 5H), 2.19 (s, 6H, *endo*), 2.21 (s, 3H, *exo*), 2.22 (s, 3H, *endo*), 2.64 (m, 2H, *endo*,*exo*), 3.64 (br d, J = 10.7 Hz, 1H, *exo*), 3.76 (dd, J = 6.5, 5.0 Hz, 1H, *endo*), 4.87 (t, J = 2.0 Hz, 1H, *exo*), 4.96 (d, J = 5.0 Hz, 1H, *endo*); ^{13}C NMR (125 MHz, $CDCl_3$) δ −4.5, −4.4, −4.3, −4.2, 17.9, 18.0, 20.3, 24.9, 25.6, 28.7, 29.0, 29.3, 40.7, 42.8, 49.7, 51.5, 58.8, 62.0, 98.3, 101.8, 152.4, 154.7, 209.3, 212.0.

Reaction of Diene 19a with Acrylonitrile. A solution of diene **19a** (219 mg, 0.96 mmol) in toluene (1 mL) at 0 °C was treated with acrylonitrile (0.13 mL, 2.0 mmol). The reaction mixture was allowed to reach room temperature, stirred for 15 h, and concentrated in vacuo. The ^{1}H NMR analysis of the crude product mixture showed the formation of cycloadduct **28** as a mixture of *endo* and *exo* isomers (231 mg, 85%, dr 1:4), which were separated by flash chromatography on silica gel (elution with 50% ether in hexanes containing 4% Et_3N). Less polar *exo* adduct **28b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.15 (s, 3H), 0.17 (s, 3H), 0.92 (s, 9H), 1.90 (m, 1H), 2.15 (m, 3H), 2.32 (s, 6H), 2.68 (ddd, J = 9.7, 7.6, 3.0 Hz, 1H), 3.47 (m, 1H), 4.80 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.5, −4.4, 17.9, 24.4, 25.5, 27.7, 27.9, 41.1, 62.5, 101.9, 121.8, 152.8; IR (neat) 2929, 2240, 1652, 1456, 1253, 1204, 833 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_{15}H_{28}N_2OSi$ 280.1971, found 280.1958. More polar *endo* adduct **28a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.19 (s, 3H), 0.19 (s, 3H), 0.94 (s, 9H), 1.85 (m, 1H), 2.1 (m, 2H), 2.38 (m, 1H), 2.46 (s, 6H), 3.06 (ddd, J = 5.3, 5.0, 3.3 Hz, 1H), 3.33 (m, 1H), 4.89 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6, −4.3, 17.9, 24.3, 25.6, 26.9, 28.5, 42.1, 61.3, 103.2, 120.8, 152.2; IR (neat) 2930, 2238, 1653, 1456, 1253, 1205, 839 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_{15}H_{28}N_2OSi$ 280.1971, found 280.1969.

Reaction of Diene 19a with *tert*-Butyl Acrylate. To a solution of diene **19a** (312 mg, 1.37 mmol) in toluene (1 mL) was added *tert*-butyl acrylate (0.60 mL, 4.1 mmol) at 20 °C. The reaction mixture was stirred for 64 h at room temperature and concentrated in vacuo. The ^{1}H NMR analysis of the crude product mixture showed the formation of cycloadduct **29** as a mixture of *endo* and *exo* isomers (437 mg, 90%, dr 1.0:1.4), which were separated by flash chromatography on silica gel (elution with 12% ether in hexanes containing 2% Et_3N). Less polar *endo* adduct **29a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.15 (s, 3H), 0.16 (s, 3H), 0.93 (s, 9H), 1.46 (s, 9H), 1.80 (m, 1H),2.0 (m, 3H), 2.26 (s, 6H), 2.51 (ddd, J = 12.7, 6.5, 4.2 Hz, 1H), 3.52 (dd, J = 6.5, 5.0 Hz, 1H), 4.35 (d, J = 5.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.4 (2 carbons), 17.9, 20.9, 25.6, 28.1, 29.0, 43.7, 45.6, 59.1, 79.5, 100.3, 153.6, 173.3; IR (neat) 2930, 2859, 1734, 1662, 1365, 1150, 887, 858 cm^{-1}. More polar *exo* adduct **29b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.14 (s, 3H), 0.15 (s, 3H), 0.92 (s, 9H), 1.45 (s, 9H), 1.9 (m, 2H), 2.1 (m, 2H), 2.26 (s, 6H), 2.41 (ddd, J = 10.4, 8.4, 3.6 Hz, 1H), 3.64 (m, 1H), 4.81 (t, J = 1.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.5, −4.3, 17.9, 25.4, 25.6, 28.0, 28.9, 40.7, 42.4, 61.9, 79.9, 103.8, 152.2, 174.9; IR (neat) 2931, 2859, 1729, 1662, 1366, 1147, 839 cm^{-1}.

Reaction of Diene 19a with Methyl Methacrylate. To a solution of diene **19a** (200 mg, 0.88 mmol) in toluene (1 mL) was added methyl methacrylate (0.14 mL, 1.3 mmol). The reaction mixture was stirred for 15 h at 70 °C and concentrated in vacuo. The ^{1}H NMR analysis of the crude product mixture showed the formation of cycloadduct **30** as a mixture of *endo* and *exo* isomers (215 mg, 74%, dr 2:1), which were separated by flash chromatography on silica gel (elution with 9% ether in hexanes containing 2% Et_3N). Less polar *endo* adduct **30a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.15 (s, 6H), 0.92 (s, 9H), 1.16 (s, 3H), 1.57 (ddd, J = 13.5, 4.4, 1.2 Hz, 1H), 2.04 (m, 2H), 2.20 (m, 1H), 2.23 (s, 6H), 3.09 (dd, J = 5.5, 1.0 Hz, 1H), 3.68 (s, 3H), 4.83 (dt, J = 5.5, 1.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.4, 18.0, 21.9, 25.6, 26.0, 26.4, 43.9, 46.5, 51.2, 65.8 98.6, 152.4, 177.2; IR (neat) 2931, 1734, 1652, 1456, 1252, 1179, 838, 778 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_{17}H_{33}NO_3Si$ 327.2229, found 327.2206. More polar *exo* adduct **30b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.15 (s, 6H), 0.93 (s, 9H), 1.23 (s, 3H), 1.62 (ddd, J = 13.0, 6.2, 6.2 Hz, 1H), 1.95 (m, 1H), 2.05 (m, 2H), 2.32 (s, 6H), 3.68 (s, 3H), 3.78 (m, 1H), 4.90 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.4, −4.3, 18.0, 18.8, 25.6, 26.9, 30.9, 43.8, 46.9, 51.8, 63.2, 102.0, 151.6, 178.0; IR (neat) 2931, 1733, 1663, 1457, 1252, 1179, 838, 778 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_{17}H_{33}NO_3Si$ 327.2229, found 327.2222.

Reaction of Diene 19a with Methylcrotonate. To a solution of diene **19a** (293 mg, 1.29 mmol) in toluene (1 mL) was added methylcrotonate (0.41 mL, 3.9 mmol). The reaction mixture was stirred for 7 h at 90 °C, concentrated in vacuo, and purified by bulb-to-bulb distillation (160−200 °C, 0.25 mmHg). The ^{1}H NMR analysis showed the formation of cycloadduct **31** as a mixture of *endo* and *exo* isomers (368 mg, 87%, dr 1:3), which were separated by flash chromatography on silica gel (elution with 15% ether in hexanes containing 2% Et_3N). Less polar *endo* adduct **31a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.17 (s, 6H), 0.94 (s, 9H), 0.98 (d, J = 5.6 Hz, 3H), 1.71 (ddt, J = 17.0, 10.5, 3.1 Hz, 1H), 2.14 (dd, J = 17.0, 5.0 Hz, 1H), 2.24 (s, 6H), 2.35 (m, 2H), 3.58 (m, 1H), 3.71 (s, 3H), 4.91 (dd, 1H, J = 4.6, 1.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.4, −4.3, 18.0, 20.9, 25.6, 26.9, 37.5, 42.9, 51.1, 52.3, 60.2, 99.0, 152.9, 173.7; IR (neat) 2931, 1745, 1669, 1365, 1197, 838, 779 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_{17}H_{33}NO_3Si$ 327.2230, found 327.2243. More polar *exo* adduct **31b**: ^{1}H NMR (300

MHz, $CDCl_3$) δ 0.15 (s, 3H), 0.17 (s, 3H), 0.92 (m, 3H), 0.93 (s, 9H), 1.81 (m, 3H), 1.9−2.1 (m, 3H), 2.23 (s, 6H), 3.60 (m, 1H), 3.72 (s, 3H), 4.85 (t, J = 2.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6, −4.2 17.9, 19.3, 25.6, 31.6, 38.3, 40.4, 50.7, 51.4, 63.3, 101.9, 151.6, 175.9; IR (neat) 2931, 1739, 1663, 1369, 1194, 839 779 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_{17}H_{33}NO_3Si$ 327.2230, found 327.2229.

Reaction of Diene 19a with Methyl Cinnamate. To a solution of diene **19a** (292 mg, 1.28 mmol) in toluene (1 mL) was added methyl cinnamate (622 mg, 3.8 mmol). The reaction mixture was stirred for 18 h at 90 °C and then concentrated in vacuo. The ^{1}H NMR analysis of the crude product mixture showed the formation of cycloadduct **32** as a mixture of *endo* and *exo* isomers (448 mg, 90%, dr 1:3), which were separated by flash chromatography on silica gel (elution with 20% ether in hexanes containing 1% Et_3N). Less polar *endo* adduct **32a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.18 (s, 6H), 0.92 (s, 9H), 2.18 (m, 1H), 2.30 (m, 1H), 2.32 (s, 6H), 3.08 (dd, J = 12.6, 6.9 Hz, 1H), 3.45 (ddd, J = 12.6, 11.4, 6.3 Hz, 1H), 3.50 (s, 3H), 3.72 (dd, J = 6.9, 4.5 Hz, 1H), 5.01 (dd, J = 4.5, 1.2 Hz, 1H), 7.3 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.4, −4.3, 17.9, 25.6, 38.6, 38.7, 43.1, 50.7, 51.1, 60.1, 99.3, 126.3, 127.2, 128.4, 144.8, 152.6, 172.8; IR (neat) 2930, 2858, 1748, 1668, 1362, 1191, 838 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_{22}H_{35}O_3NSi$ 389.2386, found 389.2385. More polar *exo* adduct **32b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.17 (s, 3H), 0.18 (s, 3H), 0.93 (s, 9H), 2.30 (m, 2H), 2.29 (s, 6H), 2.79 (dd, J = 11.4, 10.2 Hz, 1H), 3.12 (ddd, J = 11.4, 11.4, 5.4 Hz, 1H), 3.86 (m, 1H), 4.94 (t, J = 1.8 Hz, 1H), 7.3 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6, −4.3, 17.9, 25.5, 38.1, 40.5, 43.7, 49.8, 51.2, 63.6, 102.1, 126.8, 127.5, 128.3, 141.8, 151.6, 174.8; IR (neat) 2934, 2858, 1737, 1663, 1361, 1179, 833 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_{22}H_{35}O_3NSi$ 389.2386, found 389.2373.

Reaction of Diene 19c with Methyl Acrylate. To a solution of diene **19c** (511 mg, 2.0 mmol) in toluene (2 mL) was added methyl acrylate (0.27 mL, 3.0 mmol). The reaction mixture was stirred for 20 h at 20 °C and concentrated in vacuo. The ^{1}H NMR analysis of the crude product mixture showed the formation of cycloadduct **33** as a mixture of *endo* and *exo* isomers (584 mg, 86%, dr 1.0:2.5), which were separated by flash chromatography on silica gel (elution with 10% ether in hexanes containing 2−5% Et_3N). Less polar *endo* adduct **33a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.20 (s, 6H), 0.98 (s, 9H), 0.99(t, J = 7.0 Hz, 6H), 1.90 (m, 1H), 2.11 (m, 3H), 2.45−2.66 (m, 5H), 3.77 (s, 3H), 4.9 (d, J = 4.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.4, 13.9, 17.5, 20.6, 25.6, 28.7, 45.5, 45.9, 51.0, 56.2, 102.9, 152.9, 174.3; IR (neat) 2931, 2859, 1743, 1633, 1364, 1259, 1194, 874, 839 cm^{-1}. More polar *exo* adduct **33b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.12 (s, 3H), 0.13 (s, 3H), 0.91(s, 9H), 0.99 (t, J = 7 Hz, 6H), 1.90 (m, 1H), 2.10 (m, 3H), 2.37−2.47 (m, 5H), 3.67 (s, 3H), 3.77 (m, 1H), 4.8 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6 (2 carbons), 14.7, 17.9, 25.3, 25.6, 29.2, 44.3, 44.7, 51.3, 58.6, 104.1, 151.7, 176.1; IR (neat) 2935, 2897, 1740, 1654, 1363, 1179, 875, 837 cm^{-1}.

Reaction of Diene 19d with Methyl Acrylate. To a solution of diene **19d** (273 mg, 1.0 mmol) in toluene (1 mL) was added methyl acrylate (0.14 mL, 1.5 mmol). The reaction mixture was stirred for 37 h at 20 °C and concentrated in vacuo. The ^{1}H NMR analysis of the crude product mixture showed the formation of cycloadduct **34** as a mixture of *endo* and *exo* isomers (240 mg, 67%, dr 1.4:1.0). The crude product was purified by flash chromatography on silica gel (elution with 10% ether in hexanes containing 2−5% Et_3N), which did not separate the two diastereomers: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.13 (s, 6H, *exo*), 0.15 (s, 6H, *endo*), 0.91(s, 9H, *exo*), 0.92(s, 9H, *endo*), 1.93−1.03 (m, 24H, *endo, exo*), 1.86−2.11 (m, 8H, *endo, exo*), 2.50 (m, 1H, *exo*), 2.61 (m, 1H, *endo*), 3.08 (m, 4H, *endo, exo*), 3.63 (s, 3H, *endo*), 3.64 (s, 3H, *exo*), 3.82 (m, 2H), 4.82 (br s, 1H, *exo*), 4.88 (d, 1H, J = 5.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.2, −4.3, −4.4, −4.5, 31.4, 21.5, 21.6, 23.7, 24.1, 25.3, 25.6, 28.5, 29.0, 45.0, 46.5, 46.7, 47.0, 50.3, 50.9, 51.1, 54.0, 106.7, 109.4, 126.9, 128.2, 151.1, 151.8, 174.5, 176.3; IR (neat) 2959, 2859, 1740, 1660, 1366, 1189, 880, 840 cm^{-1}.

Reaction of Diene 19e with Methyl Acrylate. To a solution of diene **19e** (253 mg, 1.0 mmol) in toluene (1 mL) was added methyl acrylate (0.14 mL, 1.5 mmol). The reaction mixture was stirred for 37 h at 20 °C and concentrated in vacuo. The ^{1}H NMR analysis of the crude product mixture showed the formation of cycloadduct **35** as a mixture of *endo* and *exo* isomers (299 mg, 88%, dr 1:1), separated by flash chromatography on silica gel (elution with 10% ether in hexanes containing 2−5% Et_3N). Less polar *endo* adduct **35a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.149 (s, 6H), 0.923 (s, 9H), 1.64 (m, 4H), 1.83−2.09 (m, 4H), 2.61 (m, 5H), 3.67 (s, 3H), 3.7 (m, 1H), 4.93 (d, J = 4.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.4, 18.0, 20.8, 24.1, 25.6, 29.1, 45.1, 50.9, 51.2, 56.7, 101.1, 153.5, 174.7; IR (neat) 2932, 2857, 1743, 1662, 1364, 1253, 1187, 877, 839, 780 cm^{-1}. More polar *exo* adduct **35b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.137 (s, 6H), 0.915 (s, 9H), 1.72 (m, 4H), 1.94−2.08 (m, 4H), 2.55−2.63 (m, 5H), 3.68 (s, 3H), 3.7 (m, 1H), 4.88 (t, J = 1.35 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.5, −4.4, 17.9, 23.8, 24.4, 25.6, 28.7, 43.8, 48.9, 51.6, 58.5, 103.2, 152.4, 175.7; IR (neat) 3097, 2802, 1743, 1661, 1364, 1255, 1194, 1040, 877, 835 cm^{-1}.

Reaction of Diene 19f with Methyl Acrylate. To a solution of diene **19f** (603 mg, 2.0 mmol) in toluene (1 mL) was added methyl acrylate (0.9 mL, 10 mmol). The reaction mixture was stirred for 3 h at 60 °C and concentrated in vacuo. The ^{1}H NMR analysis of the crude product mixture showed the formation of cycloadduct **36** as a mixture of *endo* and *exo* isomers (662 mg, 85%, dr 1.0:1.5). The crude product was purified by flash chromatography on silica gel (elution with 10% ether in hexanes containing 2−5% Et_3N), which did not separate the two diastereomers: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.10 (s, 6H, *exo*), 0.12 (s, 6H, *endo*), 0.91 (s, 9H, *exo*), 0.92 (s, 9H, *endo*), 1.94−2.16 (m, 8H, *endo,exo*), 2.70 (ddd, 1H, J = 11.0, 10.0, 3.5 Hz, *exo*), 2.80 (ddd, 1H, J = 10.0, 6.0, 4.0 Hz, *endo*), 2.8−3.0 (m, 4H, *endo,exo*), 3.30 (q, 1H, J = 9.0 Hz), 3.42−3.51 (m, 3H, *endo,exo*), 3.52 (s, 3H, *endo*), 3.60 (s, 3H, *exo*), 4.6−4.7 (m, 2H, *endo,exo*), 4.68 (br s, 1H, *exo*), 4.73 (d, 1H, J = 5.5 Hz), 6.5−6.6 (m, 4H, *endo,exo*), 7.0−7.1 (m, 4H, *endo,exo*); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.4, −4.5, 17.9, 21.3, 25.1, 25.6, 28.2, 28.5, 29.0, 43.4, 44.5, 47.0, 49.1, 51.4, 51.7, 51.8, 54.3, 101.2, 103.7, 106.5, 107.3, 116.8, 117.2, 124.2, 124.4, 127.0, 127.2, 129.1, 130.0, 150.8, 151.8, 153.2, 154.8, 173.8, 175.2; IR (neat) 2955, 2858, 1738, 1664, 1365, 1199, 868, 780, 742 cm^{-1}.

Epimerization of Adduct 26. A solution of KHMDS in toluene (0.5 M, 1.4 mL, 0.7 mmol) was diluted with THF (1.5 mL) and cooled to −78 °C. A solution of adduct **26** (174 mg, 0.55 mmol, 1:1.5 mixture of diastereomers) in THF (1 mL) was added over a period of 5 min. The reaction mixture was warmed to 0 °C over a period of 3 h, cooled to −78 °C, and treated slowly with a 10:1 solution of THF−H_2O (1.1 mL). The reaction mixture was allowed to reach room temperature and quenched by addition of 10 mL of water. The aqueous layer was extracted with ether (2 × 30 mL), and the combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated. The ^{1}H NMR analysis of the crude product mixture showed the formation of a 94:6 mixture of *trans*/*cis* diastereomers. Flash chromatography on silica gel (elution with 33% hexanes in EtOAc containing 2% of Et_3N) afforded 137 mg (78%) of the *trans* isomer **26b** as a clear oil. ^{1}H and ^{13}C NMR spectra were identical to the same compound described above.

Alkylation of Adduct 26 with Iodomethane. A solution of KHMDS in toluene (0.5 M, 2.2 mL, 1.1 mmol) was diluted with THF (2.5 mL) and cooled to −78 °C. A solution of adduct **26** (315 mg, 1.00 mmol, 1:1.5 mixture of diastereomers) in THF (1.5 mL) was then added over a period of 5 min. The reaction was allowed to warm to 0 °C and kept at this temperature for 15 min. The resulting solution of the enolate was added slowly via cannula to iodomethane (0.62 mL, 10 mmol) dissolved in THF (0.5 mL). Immediately after the addition was complete, the reaction mixture was diluted with ether (50 mL) and washed with water (10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated. ^{1}H NMR analysis of the crude product mixture showed the formation of a

single diastereomeric product **30a**, which was purified by flash chromatography on silica gel (elution with 33% EtOAc in hexanes containing 1% of Et_3N) to afford 248 mg (76%) of a colorless oil. ^1H and ^{13}C NMR spectra were identical to the same compound described above.

4-Formyl-4-methyl-2-cyclohexene-1-one (38). To a solution of **25** (130 mg, 0.44 mmol) in THF (3 mL) was added 1.2 M aqueous solution of HCl (1 mL). The reaction mixture was stirred at room temperature for 24 h, diluted with water, and extracted with ether. The combined organic layers were dried over anhydrous $MgSO_4$, concentrated, and purified by flash chromatography on silica gel (elution with 50% ether in hexane) to afford 58 mg (96%) of **38** as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 1.35 (s, 3H), 1.97 (m, 1H), 2.35 (m, 1H), 2.49 (m, 2H), 6.12 (d, J = 9.6 Hz, 1H), 6.76 (d, J = 9.6 Hz, 1H), 9.58 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0, 29.5, 33.8, 48.4, 130.8, 149.0, 197.8, 199.9; IR (neat) 2930, 1726, 1679, 1457, 1230, 1117, 801 cm^{-1}. The ^1H NMR spectrum of this compound was in agreement with that reported in the literature.[32b]

4-Methyl-4-vinyl-2-cyclohexene-1-one (39). A suspension of methyl triphenylphosphonium bromide (3.00 g, 8.3 mmol) in THF (15 mL) at 0 °C was treated with 2.17 M solution of *n*-butyllithium in hexane (3.6 mL, 7.8 mmol). The resulting yellow solution of the ylide was stirred for 30 min and then cooled to −78 °C. A solution of cycloadduct **25** (1.64 g, 5.5 mmol) in THF (10 mL) was added. The reaction mixture was allowed to warm to room temperature and stirred for 16 h. Water (10 mL) was added, and the aqueous phase was extracted with ether. The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Concentration in vacuo afforded the expected olefinated product, which was carried on to the hydrolysis step.

The crude Wittig product was dissolved in acetonitrile (4 mL) and treated with a 10% solution of HF in acetonitrile (3 mL). After the resulting mixture stirred for 5 h at room temperature, it was diluted with ether (100 mL) and washed with a saturated solution of $NaHCO_3$ (20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated in vacuo, and purified by flash chromatography on silica gel (elution with pentane, followed by 50% ether in pentane) to afford 630 mg (84%) of **39** as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 1.25 (s, 3H), 1.95 (m, 2H), 2.37 (ddd, J = 16.6, 4.8, 4.8 Hz, 1H), 2.46 (ddd, J = 16.6, 8.7, 7.6 Hz, 1H), 5.03 (dd, J = 17.5, 0.8 Hz, 1H), 5.12 (dd, J = 10.4, 0.8 Hz, 1H), 5.80 (dd, J = 17.5, 10.4 Hz, 1H), 6.00 (d, J = 9.6 Hz, 1H), 6.63 (d, J = 9.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.0, 34.2, 34.7, 39.3, 114.2, 128.5, 142.5, 155.9, 199.6; IR (neat) 2962, 2869, 1681, 1455, 1201, 922, 801 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_9H_{12}O$ 136.0888, found 136.0897. The ^1H NMR spectrum of this compound was in agreement with that reported in the literature.[38]

General Procedure C: Preparation of Substituted Cyclohexenones 42−46. To a suspension of lithium aluminum hydride (1−2 mmol) in ether (4 mL) at −78 °C was added a solution of a cycloadduct (1 mmol) in ether (2 mL). The reaction mixture was stirred for 3 h at −78 °C, warmed to room temperature, and stirred until the starting material had completely disappeared (by TLC). The resulting mixture was diluted with ether (10 mL) and quenched by dropwise addition of water (0.3 mL). After vigorous stirring of the suspension for an additional 30 min, anhydrous Na_2SO_4 was added. The organic layer was carefully decanted from the solid, which was washed twice with ether (15 mL each). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give the expected alcohol, which was sufficiently pure for the hydrolysis step.

A solution of the above alcohol in acetonitrile (1−2 mL) was treated with 10% solution of HF in acetonitrile (0.50 mL). The reaction mixture was stirred for 2 h at room temperature and purified directly by flash chromatography on silica gel (elution with ethyl acetate), which afforded the corresponding enones **42−46**.

4-(Hydroxymethyl)-2-cyclohexene-1-one (42). The title compound was prepared in 90% yield according to General Procedure C: ^1H NMR (300 MHz, $CDCl_3$) δ 1.60 (m, 1H), 1.82 (dddd, J = 12.6, 12.6, 9.8, 5.0 Hz, 1H), 2.14 (dddd, J = 12.6, 9.7, 5.0, 1.3 Hz, 1H), 2.42 (ddd, J = 16.8, 12.6, 5.0, Hz, 1H), 2.56 (ddd, J = 16.8, 5.0, 5.0 Hz, 1H), 2.65 (m, 1H), 3.71 (m, 2H), 6.08 (dd, J = 10.0, 2.2 Hz, 1H), 6.96 (ddd, J = 10.0, 2.7, 1.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.3, 36.6, 38.9, 65.1, 130.2, 151.5, 199.9; IR (neat) 3370, 2924, 2871, 1669, 1050, 845 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_7H_{10}O_2$ 126.0681, found 126.0687.

4-(Hydroxymethyl)-4-methyl-2-cyclohexene-1-one (43). The title compound was prepared in 85% yield according to General Procedure C: ^1H NMR (300 MHz, $CDCl_3$) δ 1.17 (s, 3H), 1.56 (dd, J = 6.0, 5.0 Hz, 1H), 1.78 (dddd, J = 13.2, 5.7, 5.7, 1.0 Hz, 1H), 2.10 (ddd, J = 13.2, 8.2, 6.8 Hz, 1H), 2.51 (m, 2H), 3.53 (dd, J = 10.4, 6.0 Hz, 1H), 3.59 (dd, J = 10.4, 5.0 Hz, 1H), 5.99 (d, J = 10.0 Hz, 1H), 6.73 (d, J = 10.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.9, 30.8, 33.9, 38.2, 69.8, 129.1, 155.9, 199.6; IR (neat) 3360, 2924, 1670, 1049, 804 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_8H_{12}O_2$ 140.0837, found 140.0838. The ^1H NMR spectrum of this compound was in agreement with that reported in the literature.[39]

***trans*-4-(Hydroxymethyl)-5-phenyl-2-cyclohexene-1-one (44).** The title compound was prepared in 86% yield according to General Procedure C: ^1H NMR (400 MHz, $CDCl_3$) δ 2.32 (m, 1H), 2.61 (dd, J = 16.4, 4.8 Hz, 1H), 2.70 (dd, J = 16.4, 13.6 Hz, 1H), 2.80 (m, 1H), 3.23 (ddd, J = 13.6, 10.8, 4.8 Hz, 1H), 3.43 (m, 1H), 3.68 (m, 1H), 6.15 (dd, J = 10.0, 2.0 Hz, 1H), 7.12 (dd, J = 10.0, 2.1 Hz, 1H), 7.20−7.30 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.9, 44.8, 45.1, 62.6, 127.2, 127.3, 128.8, 129.8, 141.6, 152.2, 199.2; IR (neat) 3430, 2884, 1676, 1388, 1253, 1073, 701 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_{13}H_{14}O_2$ 202.0993, found 202.1006.

***trans*-4,5-Bis(hydroxymethyl)-2-cyclohexene-1-one (45).** The title compound was prepared in 82% yield according to General Procedure C: ^1H NMR (500 MHz, $CDCl_3$) δ 2.25 (m, 1H), 2.37 (dd, J = 16.5, 12.0 Hz, 1H), 2.50 (dd, J = 16.5, 4.5 Hz, 1H), 2.61 (m, 1H), 3.26 (br s, 1H), 3.65 (dd, J = 11.0, 6.5 Hz, 1H), 3.73 (dd, J = 11.0, 4.5 Hz, 1H), 3.81 (dd, J = 11.0, 6.5 Hz, 1H), 3.86 (dd, J = 11.0, 5.0 Hz, 1H), 6.07 (dd, J = 10.2, 2.4 Hz, 1H), 6.96 (dd, J = 10.2, 2.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 39.8, 40.2, 42.2, 64.3,64.9, 130.1, 151.8, 199.6; IR (neat) 3370, 2884, 1669, 1394, 1075 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_8H_{12}O_3$ 156.0787, found 156.0800.

***cis*-4,5-Bis(hydroxymethyl)-2-cyclohexene-1-one (46).** The title compound was prepared in 85% yield according to General Procedure C: ^1H NMR (500 MHz, $CDCl_3$) δ 2.40 (m, 1H), 2.55 (m, 2H), 2.87 (m, 1H), 3.21 (br s, 1H), 3.56 (br s, 1H), 3.80 (m, 4H), 6.06 (d, J = 10.2 Hz, 1H), 6.89 (dd, J = 10.2, 5.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 38.1, 38.6, 41.03, 60.55, 63.53, 130.3, 149.8, 199.3; IR (neat) 3330, 2886, 1669, 1031 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_8H_{12}O_3$ 156.0787, found 156.0775.

Imide 47. To a solution of diene **19a** (300 mg, 1.32 mmol) in toluene (1 mL) was added *N*-phenylmaleimide (173 mg, 1.00 mmol) in toluene (2 mL) at −20 °C. The reaction mixture was allowed to reach room temperature. Concentration in vacuo, followed by flash chromatography on silica gel that was not pretreated with Et_3N (elution with 20% EtOAc in hexanes), afforded 294 mg (83%) of **47** as a white solid: mp 114−116 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 0.24 (s, 3H), 0.27 (s, 3H), 0.96 (s, 9H), 2.65 (m, 2H), 3.80 (ddd, 1H, J = 13.2, 10.8, 2.7 Hz), 5.45 (dd, 1H, J = 6.0, 1.5 Hz), 7.07 (dd, 1H, J = 6.0, 2.7 Hz), 7.35 (m, 3H), 7.47 (t, 2H, J = 6.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6, −4.4, 18.0, 25.4, 29.8, 39.4, 103.2, 116.9, 126.4, 128.2, 128.9, 131.3, 132.1, 161.8, 166.3, 174.6; IR ($CHCl_3$) 3019, 2932, 1767, 1706, 1549, 1215, 833 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_{20}H_{25}NO_3Si$ 355.1604, found 355.1599.

Enones 48 and 49. A solution of bicyclic imide **47** (294 mg, 0.83 mmol) in acetonitrile (1.5 mL) was treated with 10% solution of HF in acetonitrile (0.50 mL). The reaction mixture was stirred for 5 h at room temperature and purified directly by flash chromatography on silica gel (elution with 30% hexanes in EtOAc), which afforded an inseparable mixture of isomeric enones **48** and **49** in a 3:1 ratio: ^1H NMR (500 MHz, $CDCl_3$) δ 2.47 (dd, 1H, J = 16.0, 12.8 Hz, **49**), 2.75 (dd, 1H, J

= 17.7, 8.8 Hz, **48**), 3.10−3.25 (m, 3H, **49**), 3.15 (dd, 1H, J = 17.7, 3.0 Hz, **48**), 3.64 (ddd, 1H, J = 8.8, 8.8, 3.0 Hz, **48**), 3.92 (ddd, 1H, J = 8.8, 3.6, 2.7 Hz, **48**), 6.26 (dd, 1H, J = 10.2, 2.7 Hz, **48**), 6.93, (dd, 1H, J = 10.2, 3.6 Hz, **48**), 7.09 (m, 1H, **49**), 7.2−7.5 (m, 10H, **48**,**49**); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.1, 37.6, 37.8, 39.6, 41.7, 126.11, 126.2, 128.7, 128.9, 129.1, 129.2, 129.3, 130.7, 131.1, 131.4, 131.6, 141.6, 173.2, 173.6, 176.0, 193.4, 204.4; IR ($CHCl_3$) 3016, 1776, 1714, 1682, 1499, 1382, 1176 cm^{-1}.

Siloxy Phthalimide (50). To a solution of the imide **47** (80 mg, 0.23 mmol) in CH_2Cl_2 (2 mL) was added DDQ (136 mg, 0.6 mmol). The resulting solution was stirred for 16 h at room temperature, concentrated, and purified by flash chromatography on silica gel (elution with 15% EtOAc in hexanes) to afford 69 mg (86%) of the siloxy phthalimide (**50**) as a white solid: mp 106−108 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.28 (s, 6H), 1.01 (s, 9H), 7.16 (dd, 1H, J = 8.0, 2.2 Hz), 7.34 (d, 1H, J = 2.2 Hz), 7.38 (t, 1H, J = 7.4 Hz), 7.42 (d, 2H, J = 7.4 Hz), 7.49 (t, 2H, J = 7.4 Hz), 7.82 (d, 1H, J = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ −4.4, 18.1, 25.4, 114.9, 124.1, 125.5, 125.6, 126.5, 127.9, 128.9, 131.8, 134.2, 161.6, 166.9, 167.0; IR ($CHCl_3$) 3019, 1774, 1723, 1613, 1486, 1377, 1215, 875 cm^{-1}.

Reaction of Diene 19a with Cyclohexenone. To a solution of diene **19a** (310 mg, 1.36 mmol) in toluene (1.5 mL) was added cyclohexenone (0.3 mL, 3.11 mmol). The reaction mixture was stirred for 2.5 h at 80 °C, concentrated in vacuo, and purified by flash chromatography on silica gel (elution with 20% EtOAc in hexanes), which afforded 249 mg (66%) of the bicyclic dienone **51**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.19 (s, 3H), 0.20 (s, 3H), 0.97 (s, 9H), 1.25 (m, 1H), 1.60 (m, 1H), 1.91 (m, 2H), 2.16 (dd, 1H, J = 15.3, 15.3 Hz), 2.20 (m, 1H), 2.47 (dd, 1H, J = 15.3, 4.7 Hz), 2.72 (m, 1H), 5.77 (d, 1H, J = 9.8 Hz), 7.57 (d, 1H, J = 9.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ −3.7, −3.6, 18.3, 21.7, 25.7, 30.0, 31.1, 34.2, 44.7, 115.1, 123.1, 142.2, 155.1, 199.8; IR (neat) 2931, 2858, 1669, 1617, 1404, 1254, 1043, 914, 780 cm^{-1}.

Reaction of Diene 19a with Unsaturated Lactone 52. To a solution of diene **19a** (390 mg, 1.71 mmol) in toluene (1 mL) was added lactone **52** (0.10 mL, 1.16 mmol). The reaction mixture was stirred for 9 h at 80 °C, concentrated in vacuo, and diluted with 6 mL of acetonitrile. The resulting mixture was treated with 10% solution of HF in acetonitrile (0.46 mL, 1.7 mmol). The reaction mixture was immediately passed through a plug of silica gel using EtOAc as an eluent. The crude product obtained upon evaporation of the solvent was further purified by flash chromatography on silica gel (elution with EtOAc) to afford 145 mg (76%) of the bicyclic lactone **53** as a pale-yellow solid: mp 122 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.86 (m, 1H), 2.09 (dq, J = 13.9, 2.3 Hz, 1H), 2.31 (dd, J = 15.0, 12.4 Hz, 1H), 2.69 (dd, J = 15.0, 4.6 Hz, 1H), 2.99 (m, 1H), 3.05 (dt, J = 23.5, 3.0 Hz, 1H), 3.24 (ddd, J = 23.5, 4.8, 2.8 Hz, 1H), 4.39 (ddd, J = 23.3, 11.6, 2.3 Hz, 1H), 4.51 (ddd, J = 23.3, 4.6, 2.8 Hz, 1H), 7.35 (ddd, J = 4.8, 3.0, 2.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.7, 33.7, 40.5, 44.5, 68.1, 129.3, 139.3, 163.5, 206.0; IR ($CHCl_3$) 3019, 1717, 1642, 1400, 1255, 1216, 668 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_9H_{10}O_3$ 166.0630, found 166.0633.

Reaction of Diene 19a with (+)-Carvone (54). To a solution of diene **19a** (305 mg, 1.34 mmol) in toluene (1 mL) was added (+)-carvone (0.10 mL, 0.7 mmol). The reaction mixture was stirred for 48 h at 110 °C, concentrated in vacuo, and diluted with 2 mL of acetonitrile. The resulting mixture was treated with 10% solution of HF in acetonitrile (0.5 mL, 1.9 mmol). The reaction mixture was stirred for 12 h, diluted with ether, and washed with a saturated solution of $NaHCO_3$. The combined organic layers were dried over anhydrous Na_2SO_4, concentrated, and purified by flash chromatography on silica gel (elution with 20% EtOAc in hexanes, followed by 40% EtOAc in hexanes) to afford 91 mg (60%) of bicyclic enone **55** as a 1:1 mixture of diastereomers that were separated by MPLC. Less polar diastereomer **55a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (s, 3H), 1.71 (s, 3H), 1.95 (m, 1H), 1.80 (m, 1H), 2.35 (m, 4H), 2.50 (m, 1H), 2.85 dd, J = 17.0, 5.0 Hz, 1H), 4.70 (s, 1H), 4.77 (s, 1H), 6.06 (d, J = 10.0, Hz, 1H) 6.44 (dd, J = 10.0, 2.0 Hz, ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.3, 20.9, 33.6, 40.7, 42.8, 43.8, 44.8, 50.6, 110.3, 128.8, 149.6, 197.1, 210.7; IR (neat) 2919, 1713, 1681, 1645, 1242, 894, 774 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_{14}H_{18}O_2$ 218.1307, found 218.1295. More polar diastereomer **55b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.48 (s, 3H), 1.76 (m, 1H), 1.77 (s, 3H), 2.38 (m, 1H), 2.4 (m, 3H), 2.53 (m, 1H), 2.64 (m, 1H), 2.67 (m, 1H), 4.77 (s, 1H), 4.86 (s, 1H) 6.06 (d, J = 10.5, Hz, 1H), 6.75 (d, J = 10.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.8, 24.2, 31.2, 40.7, 41.5, 42.7, 50.9, 110.9, 128.4, 146.3, 153.4, 198.5, 212.6; IR (neat) 2900, 1704, 1680, 1644, 1375, 894, 774 cm^{-1}; HRMS m/z [M$^+$] calcd for $C_{14}H_{18}O_2$ 218.1307, found 218.1303.

The ^{1}H and ^{13}C NMR spectra of both diastereomers **59a** and **59b** were in good agreement with those reported in the literature.[37]

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Supporting Information Available: ^{1}H and ^{13}C NMR of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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