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Developing a Diastereoselective Intramolecular [4 + 3] Cycloaddition of Nitrogen-Stabilized Oxyallyl Cations Derived from *N*-Sulfonyl-Substituted Allenamides

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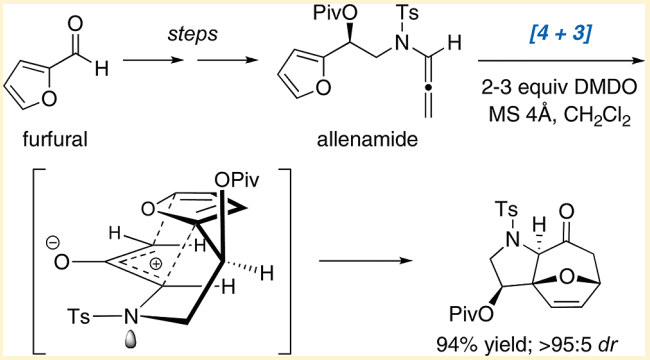
Supporting Information

ABSTRACT: Efforts toward achieving a practical and diastereoselective intramolecular [4 + 3] cycloaddition of nitrogen-stabilized oxyallyl cations with tethered dienes are described. Epoxidation of *N*-sulfonyl substituted allenamides with dimethyldioxirane (DMDO) generates nitrogen-stabilized oxyallyl cations that readily undergo stereoselective [4 + 3] cycloaddition with dienes. Selectivity is found to depend on the tethering length as well as the stability of the oxyallyl cation intermediate, whether generated from *N*-carbamoyl- or *N*-sulfonyl-substituted allenamides. The use of chiral *N*-sulfonyl-substituted allenamides provided minimal diastereoselectivity in the cycloaddition, while high diastereoselectivity can be achieved with a stereocenter present on the tether. These studies provide further support for the synthetic utility of allenamides.



INTRODUCTION

Over the past 30 years, the utility of heteroatom-stabilized oxyallyl cations has risen to the forefront of [4 + 3] cycloadditions.[1,2] Heteroatom substituents such as oxygen[3] and sulfur,[4] as well as halogens,[5] provide electronically biased oxyallyl cations that have become attractive intermediates for developing not only highly regioselective but also stereoselective [4 + 3] cycloadditions.[1,2] However, only recently has the utility of nitrogen-substituted oxyallyl cations in these cycloadditions received significant attention.[6] Almost 10 years ago, we first developed stereoselective [4 + 3] cycloadditions of chiral nitrogen-stabilized[7] oxyallyl cations **2b** derived from allenamides **1** via epoxidation [Scheme 1].[8] These efforts rendered allenamides highly visible as a new organic functional group,[9] while allowing us to contribute to the area of [4 + 3] cycloadditions through advancing its regio-[10] and stereoselective manifolds,[11,12] as well as establishing the first asymmetric [4 + 3] cycloaddition using Cu(II)-bisoxazoline catalysts.[13,14]

The trivalency of the nitrogen atom offers the flexibility to simultaneously tune its electron-donating ability toward the oxyallyl cation through various substitutions while tethering a chiral auxiliary [**R***] and a coordinating unit [**W**] to achieve both highly regio- and stereoselective [4 + 3] oxyallyl cycloadditions, which remain a challenge in this field.[1,11,12] While we recently reported the first systematic study on the regioselectivity of intermolecular [4 + 3] cycloadditions with unsymmetrical furans,[10a] we have also been engaging in developing intramolecular variants[11d,e] of our [4 + 3] cycloaddition via two approaches: I, *N*-tethered **4** → **6**; and II, C-tethered through either the α-position **7** → **8** or γ-position **9** → **10** [Scheme 2]. We elected to focus on approach I because it underscores a distinct advantage as well as significance of using nitrogen-stabilized oxyallyl cations in constructing complex nitrogen heterocycles for natural or non-natural product synthesis,[15] thereby also further accentuating the synthetic utility of allenamides.

Our first report on the intramolecular [4 + 3] cycloaddition utilized *N*-carbamoyl-substituted *N*-tethered allenamides that could be prepared in three steps from furanyl iodide **11** [Scheme 3].[11e] Initial attempts using a direct addition of 2−5 equiv of DMDO led to low yields of the desired cycloadducts **13a** and **13b** with mostly oxidative ring opening of the furan. However, it was quickly found that slow addition of DMDO via a syringe pump allowed for selective epoxidation of the allenic double bond in **14** or **15** and slowed the competing oxidation of furan. The ensuing intramolecular [4 + 3] cycloaddition of the corresponding oxyallyl cations with furan led to the desired cycloadducts **16** and **17** in 80% and 75% yields, respectively, as single diastereomers. In addition, a small amount of the epoxidized cycloadduct **18** as also isolated from the reaction of **14**. Although using the improved syringe pump addition protocol we were able to show that a few other *N*-carbamoyl-substituted allenamides could also

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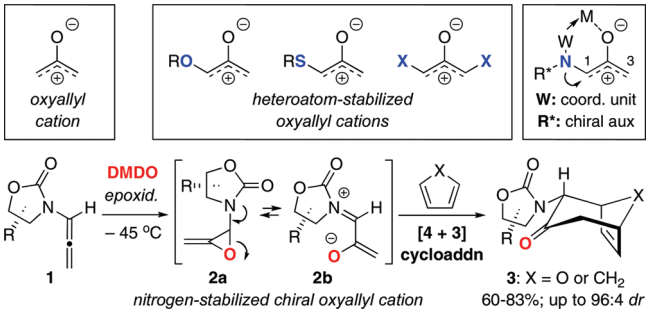
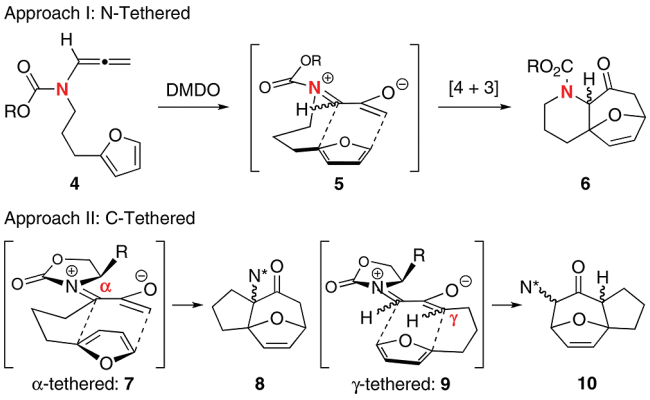
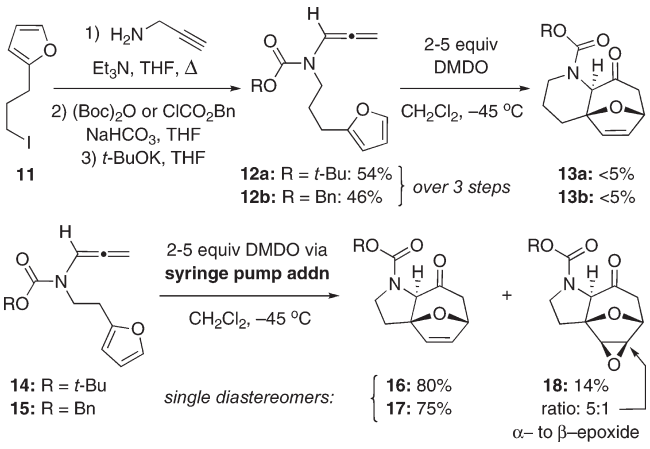
Scheme 1. Intermolecular [4 + 3] Cycloaddition



Scheme 2. Approaches to Intramolecular [4 + 3]



Scheme 3. Previous Work on [4 + 3] Cycloadditions

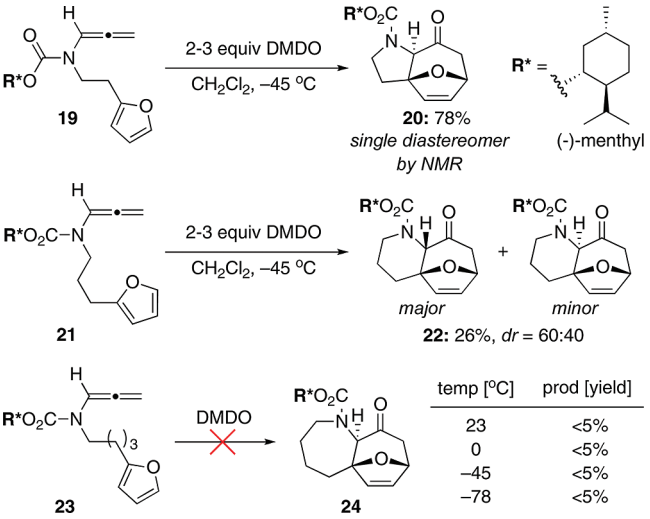


undergo successful intramolecular [4 + 3] cycloaddition,[11e] most of these examples in our communication were overengineered, and the generality as well as practicality remained elusive. We report here details of our efforts in evolving this intramolecular reaction into a useful and stereoselective cycloaddition manifold for constructing nitrogen heterocycles.

RESULTS AND DISCUSSION

***N*-Carbamoyl-Substituted Allenamides.** To commence our studies, we reinvestigated intramolecular [4 + 3] cycloadditions

Scheme 4. [4 + 3] Cycloaddition of Chiral Allenamides



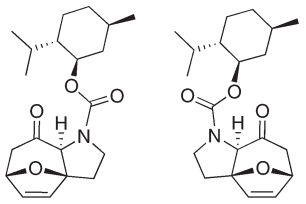


Figure 1. One-to-one mixture of diastereomeric **20**.

of *N*-carbamoyl-substituted allenamides but chose to use those containing a chiral carbamoyl group, which could serve as an auxiliary to provide asymmetric induction in the intramolecular cycloaddition and gain access to optically enriched cycloadducts. Consequently, our first attempt using chiral allenamide **19** with the menthyl auxiliary gave cycloadduct **20** in 78% yield and what appeared to be a single diastereomer based on NMR [Scheme 4]. Using a 3-carbon tether, the yield dropped dramatically in giving cycloadduct **22**. The stereoselectivity also dropped significantly with respect to the ring fusion with only a 60:40 diastereomeric ratio, which was also observed with achiral allenamides in our previous work.[11e] Furthermore, an increase to the 4-carbon tether failed to give the desired cycloadduct **24** regardless of reaction temperature, most likely due to the increase in conformational entropy associated with the longer carbon tether.

While we were quite pleased with the apparent asymmetric induction achieved in cycloadduct **20** when using the chiral menthyl auxiliary for the 2-carbon tether, the excitement did not last long. Upon examination of the X-ray crystal structure obtained for cycloadduct **20**, we were very surprised to find that the X-ray structure contains a 1:1 mixture of diastereomers with respect to the chiral auxiliary [Figure 1]. While it is quite unusual to co-crystallize two diastereomers, this data suggests that the chiral influence of the carbamate auxiliary is too far removed from the rest of the molecule to provide any facial bias during the cycloaddition and that it exerted very little influence in differentiating the two diastereomers spectroscopically based on proton NMR [Figure 2].[16]

***N*-Sulfonyl-Substituted Allenamides.** We then decided to shift our efforts from *N*-carbamoyl-substituted to *N*-sulfonyl-substituted

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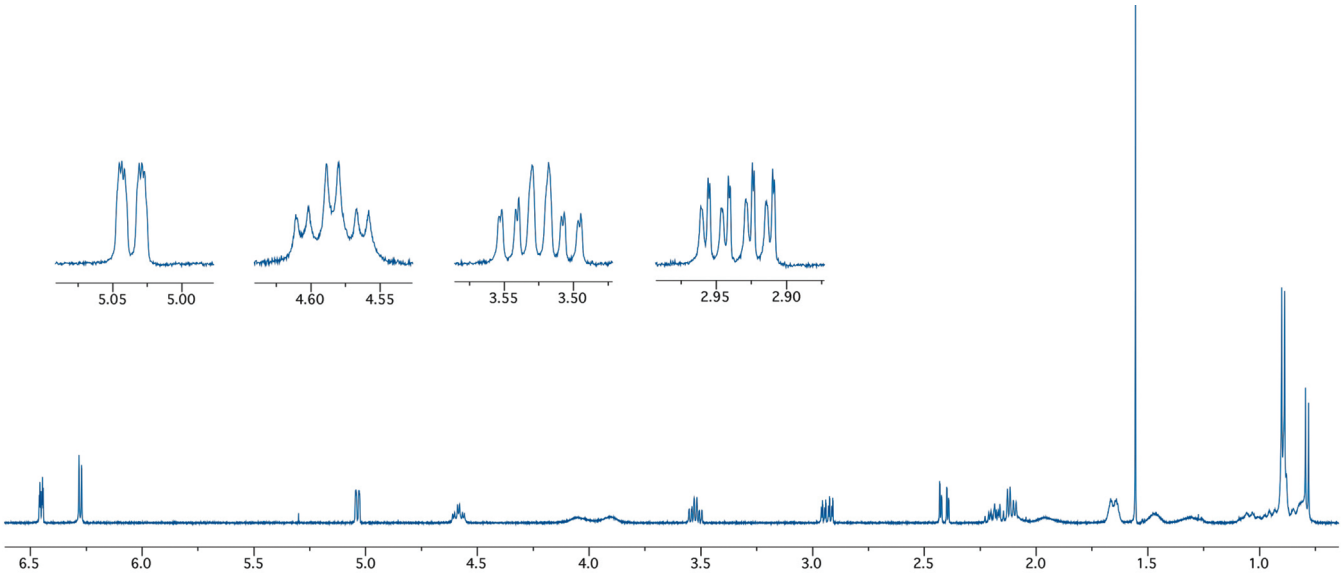
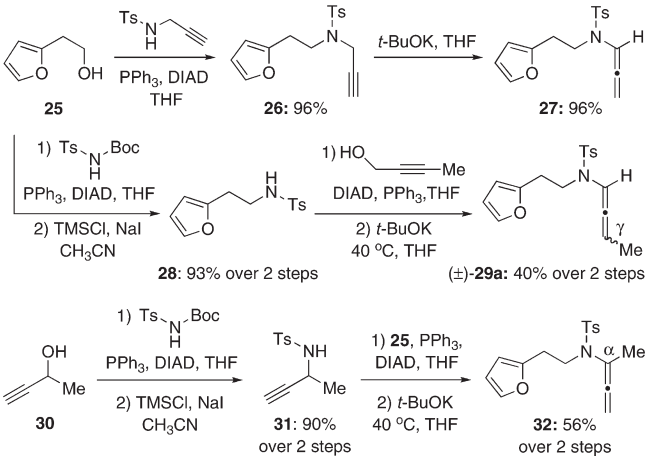
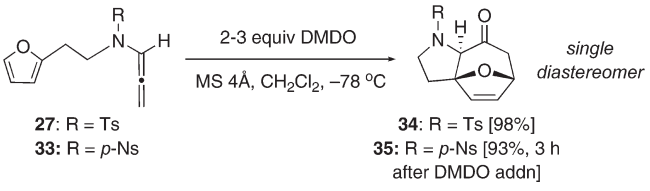


Figure 2. ^{1}H NMR of the [4 + 3] cycloadduct **20**.

Scheme 5. Synthesis of *N*-Sulfonyl Allenamides



Scheme 6. Intramolecular [4 + 3] Cycloaddition



allenamides to investigate the difference in reactivity of *N*-sulfonyl oxyallyl cations and perhaps improve overall selectivity in the [4 + 3] cycloaddition. Having recently published a facile route to *N*-sulfonyl-substituted allenamides[17] featuring a Mitsunobu reaction, allenamide **27** could be prepared in two steps from alcohol **25** in excellent yield. [Scheme 5]. Alternatively, γ-substituted allenamide (±)-**29a** and α-substituted allenamide **32** could be obtained from alcohols **25** and **30**, respectively, utilizing a four-step sequence featuring two Mitsunobu reactions.[18] It is worth noting that all of the alcohols are commercially available, making it possible to quickly access a variety of substituted allenamides depending on the substituted alcohol.

Our initial examination of *N*-Ts-substituted allenamide **27** in the [4 + 3] cycloaddition revealed *N*-sulfonyl allenamides to be much more reactive toward epoxidation as the reaction took place readily at −78 °C giving cycloadduct **34** in almost quantitative yield [Scheme 6]. The more electron-deficient *N*-*p*-nitrobenzenesulfonyl-substituted allenamide **33** also afforded cycloadduct **35** in 93% yield requiring only slightly longer reaction time after addition of DMDO. This is in great contrast with the reactivity of *N*-carbamoyl-substituted allenamides in which DMDO epoxidation is much slower at temperatures below −45 °C and often results in competing oxidative ring opening of the furan.

We proceeded to examine the scope of the intramolecular [4 + 3] cycloaddition of *N*-sulfonyl-substituted allenamides [Table 1]. First, methyl substitution at the α- or γ-allenic position (entries 1 and 2, respectively) gave cycloadducts **36** and **37a** with the major isomer of **37a** shown as assigned via NOE experiments. Attempts with γ-phenyl-substituted allenamide (±)-**29b** (entries 3 and 4) gave mostly hydrolysis of the allenamide and oxidation of furan, perhaps resulting from a more stabilized and less reactive oxyallyl cation. However, a cyclohexyl substitution was well-tolerated (entry 6) giving cycloadduct **39** containing a spirocenter in 90% yield.

Various furan substitutions were also investigated (entries 7−10). Disubstituted furans with either benzyl- or silyl-ethers afforded highly functionalized cycloadducts **41a** and **41b**, respectively, in excellent yields. This suggests that even at low temperatures, epoxidation of the allenic double bond is still favored over oxidation of furan, which again contrasts with the reactivity of *N*-carbamoyl allenamides. However, when using a trisubstituted furan (see **42**) under the reaction conditions, epoxidation of furan and oxidative ring opening occurred exclusively regardless of the reaction temperature. These results provide an interesting comparison between the electron-donating ability of the *N*-sulfonyl into the allenic double bond with that of the electron-rich furan.

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Table 1. Scope of [4 + 3] Cycloadditions

entry	allenamides[a]	temp [°C]	cycloadducts[b]	yield [%][c]
1	**32**	–78	**36**	69
2	(±)-**29a:** R = Me	–78	**37a** (80:20)	93[d]
3	(±)-**29b:** R = Ph	–78	**37b**	<5[e]
4	(±)-**29b:** R = Ph	0	**37b**	<5[e]
6	**38**		**39**	90
7	**40a:** P = Bn	–78	**41a**	81
8	**40b:** P = TBS	–78	**41b**	97
9	**42**	–78	**43**	<5[e]
10	**42**	0	**43**	<5[e]
11	**44:** R = H	–78	**45**	<5[e]
12	**44:** R = H	0	**45**	45[f]
13	**46:** R = Me	–78	**47**	<5[e]
14	**46:** R = Me	0	**47**	64[g]
15	**48**	0	**49**	17[g]
16	**50**	–78	**51**	<5[e]
17	**50**	10	**51**	73[f]

[a] All reactions were carried out in CH_2Cl_2 at 0.05 M with MS 4 Å. [b] Single diastereomers unless otherwise noted. [c] Isolated yields. [d] Major isomer shown. [e] Mostly decomposition by hydrolysis or oxidation of furan. [f] dr = 75:25. [g] dr = 90:10.

The three-carbon tethered allenamides **44** and **46** showed significantly better results compared with the *N*-carbamoyl allenamides (*vide supra*). Not only were yields much higher with or without a *gem*-dimethyl group, but the overall diastereoselectivity also increased (entries 12 and 14). Furthermore, despite a large entropic barrier, the four-carbon tethered allenamide **48** did afford the desired cycloadduct **49**, albeit in a modest 17% yield. It is worth noting that higher temperatures were required for the longer tethers to overcome the entropic barrier needed for furan to orient itself with the oxyallyl cation before competing oxidation or hydrolysis took place. Finally, the cycloaddition proceeded with a simple butadiene giving cycloadduct **51** in 73% yield (entry 17). Higher temperature was also required in this case as the unreactive *S*-trans conformation likely dominates at −78 °C.

X-ray analysis of cycloadduct **35** unambiguously confirmed the [4 + 3] cycloaddition pathway with *N*-sulfonyl allenamides and provides a general mechanistic model of the cycloaddition as shown in Figure 3. Although two possible transition structures are at play, **52**-*endo* [or *compact*][19] and **52**-*exo* [or *extended*],[19] which could both provide the observed stereochemistry in the

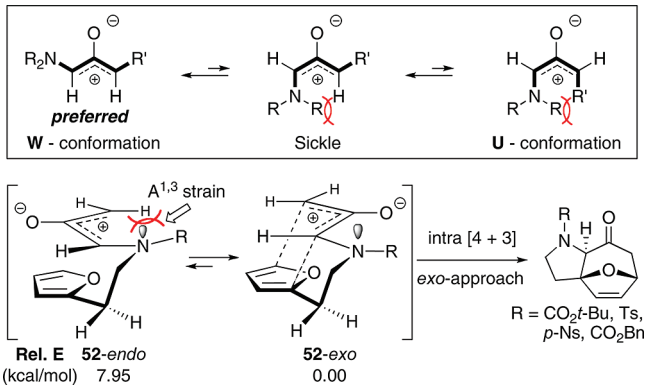
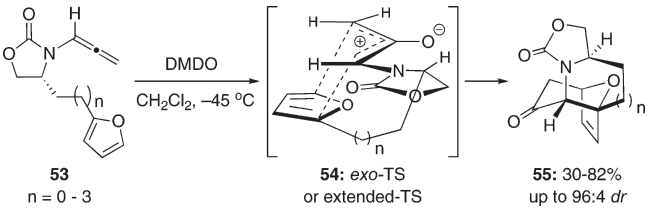
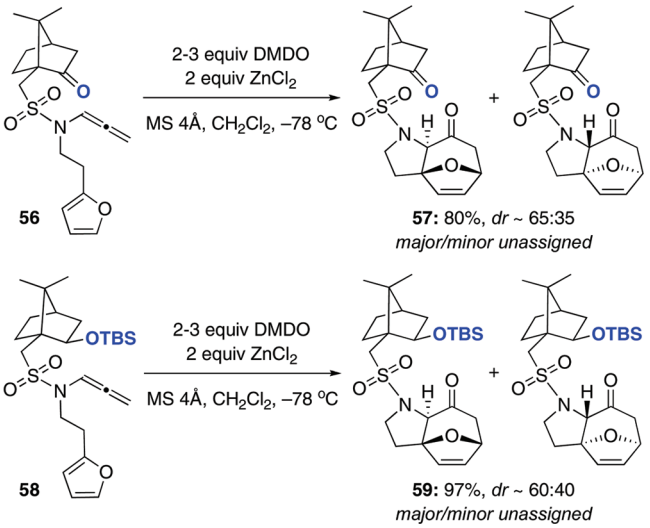


Figure 3. Proposed model for [4 + 3] cycloaddition.

Scheme 7. Previous Work on [4 + 3] Cycloaddition



Scheme 8. Cycloadditions of Camphor-Derived Allenamides



cycloadduct, the oxyallyl cation **52**-*endo* should experience more $A^{1,3}$ strain with the planar nitrogen substituents whereas **52**-*exo* possesses a more preferred W-conformation.[1,2] DFT calculations of the two possible transition state conformations also shows a tremendous preference for **52**-*exo*.[20] Thus, approach I in the intramolecular [4 + 3] cycloaddition of nitrogen-stabilized oxyallyl cations likely proceeds in an *exo* manner.

Achieving Diastereoselectivity in the [4 + 3] Cycloaddition. With the improved reactivity of *N*-sulfonyl-substituted allenamides in the intramolecular [4 + 3] cycloaddition, we decided to once again investigate the effect of a chiral auxiliary in the reaction. From our previous work, we were able to achieve

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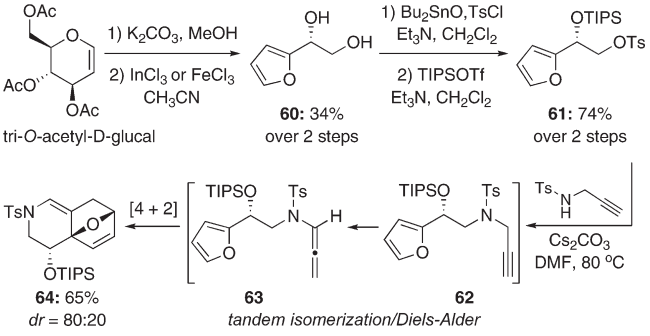
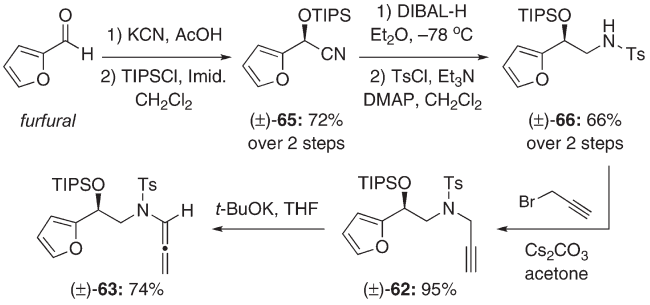
Scheme 9. Initial Route to Chiral Allenamide 63



Scheme 10. Revised Route to (±)-63: Showing One Enantiomer



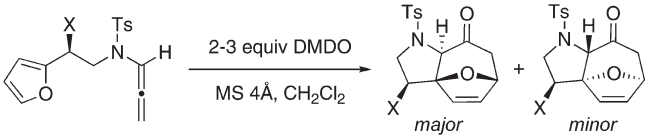
high diastereoselectivities and gain access to optically active cycloadducts containing seven- or eight-membered rings fused to the cycloheptane when using chiral oxazolidinone-substituted allenamides **53** [Scheme 7][11e] In the ensuing cycloaddition, the preferred W-conformation and a similar *exo* approach with chiral oxyallyl **54** would lead to the observed major diastereomer of **55**. However, the multistep synthesis required to make the cyclic allenamides as well as the potential difficulty in cleaving the auxiliary somewhat limited the utility of this approach.

We chose to investigate the chiral camphor-derived auxiliary for our *N*-sulfonyl-substituted allenamides for two reasons: 1) the possible coordinating effect of the ketone with a Lewis acid during the cycloaddition; 2) previously reported success in other cycloadditions using camphor auxiliaries.[21] As shown in Scheme 8, reaction of camphor-derived allenamide **56** in the presence of $ZnCl_2$ gave cycloadduct **57** in excellent yield but with only modest diastereoselectivity. Similar results were obtained upon conversion of the ketone to a silyl-ether on the auxiliary (**58** → **59**). Despite the improved reactivity of *N*-sulfonyl-substituted allenamides in the [4 + 3] cycloaddition, these results further support our previous conclusion that *N*-substituted auxiliaries are too far removed to provide asymmetric induction during the cycloaddition.

Knowing that the chiral auxiliary had little effect on the overall conformation during the cycloaddition, we chose to prepare allenamides containing a stereocenter on the tether in order to provide more of a conformational bias and perhaps lead to better selectivity [Scheme 9]. We chose to prepare diol **60** from the commercially available tri-*O*-acetyl-D-glucal using a previously reported protocol.[22] However, using either $FeCl_3 \cdot 6H_2O$ or $InCl_3 \cdot 3H_2O$, we found poor overall conversion under the reaction conditions. Selective protection of the primary alcohol with tosyl chloride in the presence of dibutyltin oxide[23] followed by protection of the secondary hydroxyl group provided tosylate **61** in good yield.[24] Interestingly, in an attempt to displace the tosylate with *N*-tosyl propargyl amine to obtain propargyl amide **62**, we instead obtained the [4 + 2] cycloadduct **64** in 65% yield, presumably through our previously reported tandem isomerization−cycloaddition sequence.[17] Although the [4 + 2] product was not desired, we were impressed by the overall yield for the three-step tandem sequence. Furthermore, we were encouraged by the diastereoselectivity observed, hoping for similar or better results in the [4 + 3] cycloaddition.

Using a revised route reported by Hashmi,[25] we were able to obtain the racemic propargyl amide (±)-**62** starting from furfural [Scheme 10]. Cyanohydrin formation followed by silyl protection of the resultant alcohol gave (±)-**65** in 72% yield. Reduction

Table 2. Diastereoselective [4 + 3] Cycloadditions



entry	allenamide[a]	X	temp [°C]	cycloadduct	yield [%][b]	major: minor
1	(±)-**63**	-OTIPS	−78	**67**	85	80:20
2	(±)-**63**	-OTIPS	0	**67**	86	75:25
3	(±)-**68**	-OTES	−78	**69**	97	83:17
4	(±)-**70**	-OPiv	−78	**71**	94	>95:5
5	(±)-**72**	-NBocp-Ns	−78	**73**	<5	
6	(±)-**72**	-NBocp-Ns	0	**73**	49	>95:5

[a] All reactions were carried out at 0.05 M with 50 mg MS 4 Å. [b] Isolated yields.

of the nitrile to a primary amine followed by tosylation then provided sulfonamide (±)-**66** in good overall yield. Finally, propargylation and subsequent isomerization using our protocol afforded the desired allenamide (±)-**63**. It is worth noting that Hashmi's synthesis was also done asymmetrically using enzyme catalysis for the cyanohydrin formation.[25,26] We are also aware of the fact that O'Doherty has documented an array of beautiful and practical asymmetric protocols for accessing diols and amino alcohols related to **60** and **66** that we could adopt in future applications.[27]

Other derivatives were also prepared in order to investigate their effect on the diastereoselectivity in the [4 + 3] cycloaddition. As shown in Table 2, our first attempt using TIPS-protected allenamide (±)-**63** under our standard conditions gave the desired cycloadduct in 85% yield with an 80:20 diastereomeric ratio, similar to that of the [4 + 2] product. The yield remained the same at a higher reaction temperature, although a slight decrease in selectivity was observed (entry 2). Interestingly, the smaller TES group gave a slight increase in selectivity and yield (entry 3).

While we were pleased with the reasonable selectivity observed using silyl-protecting groups, we reasoned that we might be able to achieve even better diastereoselectivity using a pivalate protecting group because the shorter oxygen−carbon bond could provide a stronger conformational bias during the ensuing

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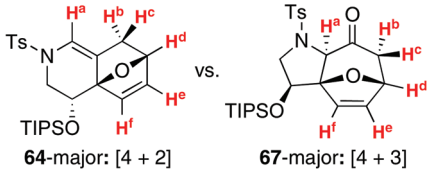
Table 3. Comparison of [4 + 2] and [4 + 3] Cycloadducts



δ ppm (500 MHz)	Δδ ppm	δ ppm (500 MHz)
6.58 (s, H^a)	3.16	3.42 (s, H^a)
1.91 (dd, H^b, J = 1.5,14.0 Hz)	0.48	2.39 (d, H^b, J = 15.0 Hz)
2.52 (ddd, H^c, J = 1.0, 4.5,14.0 Hz)	0.66	3.18 (dd, H^c, J = 5.0, 15.0 Hz)
5.05 (d, H^d, J = 1.5, 4.5 Hz)	0.03	5.08 (d, H^d, J = 5.0 Hz)
6.27 (dd, H^e, J = 1.5, 5.5 Hz)	0.07	6.34 (d, H^e, J = 6.0 Hz)
6.22 (d, H^f, J = 6.0 Hz)	0.05	6.17 (d, H^f, J = 6.0 Hz)

cycloaddition. To our delight, the pivalate-protected allenamide (±)-**70** afforded the desired cycloadduct not only in excellent yield but also with excellent diastereoselectivity (entry 4). Furthermore, while reaction of nitrogen-substituted allenamide (±)-**72** failed at −78 °C, giving only oxidative ring-opening and hydrolysis products, the desired cycloadduct **73** could also be obtained with excellent selectivity and reasonable yield at higher temperature (entry 6). We reasoned that the steric bulk of the substituents on the nitrogen atom may actually hinder the ensuing cycloaddition, thus allowing the competing oxidative ring-opening pathway to dominate, especially at low temperatures.

Spectroscopic Comparisons of [4 + 2] and [4 + 3] Cycloadducts and Mechanistic Pathways. An interesting comparison can be made between [4 + 2] and [4 + 3] cycloadducts derived from TIPS-protected allenamide (±)-**63**. As shown in Table 3, the two cycloadducts have similar key ^{1}H NMR resonances with the largest difference obviously being the H^a proton on an sp^2 versus sp^3 carbon. However, an interesting dichotomy arises when comparing the major isomers of [4 + 2] and [4 + 3] cycloadducts (**64**-major and **67**-major, respectively). The major isomer from the [4 + 2] cycloaddition possesses an *anti* relationship between the silyl-ether and the oxa-bicyclic bridge, whereas that of the [4 + 3] cycloadduct possesses a *syn* relationship as assigned via NOE experiments.

A working model was proposed based on the stereochemical assignments and our previous mechanistic understanding of the [4 + 2] and [4 + 3] pathways [Figure 4]. In the [4 + 2] pathway, the most stable conformation would place the large silyl-ether substituent in a pseudoequatorial position away from the ensuing cycloaddition thus leading to the observed isomer. For the [4 + 3] pathway, if we maintain the preferred W-conformation of the oxyallyl-cation, we can envision two possible *exo*-approaches. While *exo*-**I** would suffer from steric interaction of the large silyl-ether pointing into the ensuing cycloaddition thereby leading to the minor isomer, *exo*-**II** places the silyl-ether away from the cycloaddition and would lead to the observed major isomer.

The ability to access both [4 + 2] and [4 + 3] cycloadducts through divergent pathways highlights yet another synthetic utility of *N*-sulfonyl allenamides [Scheme 11]. Not only do *N*-sulfonyl-substituted allenamides show improved reactivity compared to *N*-carbamoyl-substituted allenamides, but their facile preparation from a variety of commercially available starting materials also provides a practical approach to accessing a diverse array of complex heterocyclic scaffolds via thermal or electrophilic activation conditions.

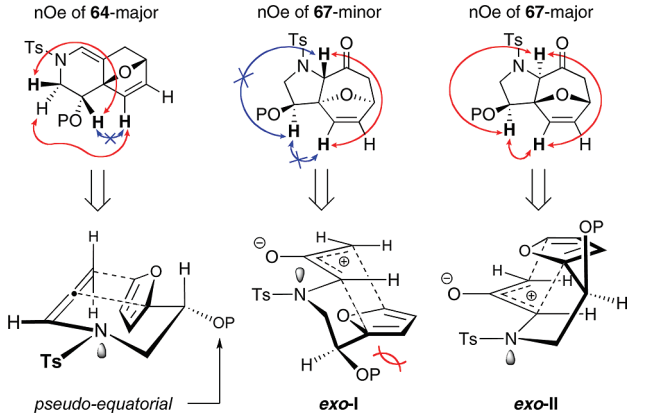
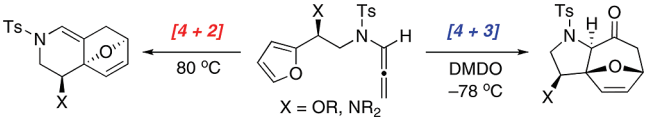


Figure 4. NOE experiments and proposed model.

Scheme 11. Divergent Reactivity of *N*-Sulfonyl Allenamides



CONCLUSION

We have described here our efforts toward achieving a practical and diastereoselective intramolecular [4 + 3] cycloaddition of nitrogen-stabilized oxyallyl cations with tethered dienes. Selectivity is found to depend greatly on the tethering length as well as the stability of the oxyallyl cation intermediate, whether generated from *N*-carbamoyl- or *N*-sulfonyl-substituted allenamides. Oxyallyl cations derived from the *N*-sulfonyl-substituted allenamides show overall improved reactivity in the cycloaddition, allowing for greater diversity in substrate scope. While the use of chiral auxiliaries provided minimal diastereoselectivity in the cycloaddition, high diastereoselectivity can be achieved with a stereocenter present on the tether. These studies provide further support for the synthetic utility of allenamides and promising potential for future development in intramolecular [4 + 3] cycloadditions of nitrogen-stabilized oxyallyl cations.

EXPERIMENTAL SECTION

General Experimental Methods. All reactions were performed in flame-dried glassware under nitrogen atmosphere. Solvents were distilled prior to use. ^{1}H and ^{13}C NMR spectra were obtained on 400 or 500 MHz spectrometers using $CDCl_3$ with TMS or residual solvent as standard unless otherwise noted. Infrared spectra were obtained in $CHCl_3$ or neat. Optical rotations were measured on a digital polarimeter, using a 1 mL cell with a 1 dm path length. For low (MS) and high (HRMS) resolution, m/z ratios are reported as values in atomic mass units. Mass analysis was done in either APCI mode or EI mode. All spectral data obtained for new compounds are reported here.

General Procedure for Isomerizaton of Propargyl Amides to Allenamides. To a flame-dried 25 mL RB flask filled were added propargyl amide **26** (245 mg, 0.8 mmol) and anhydrous THF (0.3 M)

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under N_2. The solution was cooled to 0 °C, and *t*-BuOK (20 mol % from 1 M solution in THF) was added. The resulting mixture was warmed to room temperature or the reported reaction temperature and stirred for 2−6 h. The reaction was monitored by TLC and after completion was filtered through Celite or a small bed of silica gel with ethyl acetate and concentrated under reduced pressure. The crude residue was purified via silica gel flash column chromatography (isocratic eluent: EtOAc in hexanes) to provide the desired allenamide **27** (235 mg, 96%) as a colorless oil.

Allenamide **21** (178 mg, 0.51 mmol) was prepared in 85% yield according to the general procedure. R_f = 0.65 [1:9 EtOAc/hexanes]; $[\alpha]^{23}_D$ −45.4° [*c* 1.0, CH_2Cl_2]; pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) (due to rotamers, many of the signals were not well-resolved and/or line-broadened) δ 0.79 (d, 3H, *J* = 7.0 Hz), 0.87−0.91 (m, 6H), 0.92−0.98 (m, 1H), 1.00−1.08 (m, 1H), 1.10 (t, 1H, *J* = 7.0 Hz), 1.33−1.40 (m, 1H), 1.44−1.53 (m, 1H), 1.64−1.71 (m, 2H), 1.85−1.96 (m, 2H), 2.24−2.29 (m, 1H), 2.62 (t, 1H, *J* = 7.5 Hz), 3.26 (brs, 1H), 3.35−3.49 (m, 2H), 4.63 (td, 1H, *J* = 4.0, 10.5 Hz), [extra resonance due to rotamer, 4.56 (td, *J* = 4.0, 10.5 Hz)] 5.31 (brs, 2H), 5.99 (brs, 1H), 6.27 (brs, 1H), due to rotamers, α-H on allenamide split into two signals: 7.01 (t, 0.5H, *J* = 6.0 Hz) and 7.17 (t, 0.5H, *J* = 6.0 Hz), 7.29 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) not recorded to due to rotamers; IR (neat) cm^{-1} 2952s, 2930 m, 1703s, 1457 m, 1236 m; MS (ESI) *m*/*e* (% relative intensity) 369.4 (5) $(M + Na + H)^+$, 369.4 (80) $(M + Na)^+$, 346.4 (5) $(M + H)^+$, 310.4 (100); HRMS (ESI) *m*/*e* calcd for $C_{21}H_{31}NO_3^+$ $(M + Na)^+$ 368.2197, found 368.2203.

Allenamide **23** (1.01 g, 2.8 mmol) was prepared in 89% yield according to the general procedure. R_f = 0.80 [1:4 EtOAc/hexanes]; $[\alpha]^{23}_D$ −44.4° [*c* 1.0, CH_2Cl_2]; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (due to rotamers, many of the signals were not well-resolved and/or line-broadened) δ 0.78 (d, 3H, *J* = 7.2 Hz), 0.90 (dd, 6H, *J* = 2.4, 7.2 Hz), 1.05 (qd, 2H, *J* = 3.2, 12.8 Hz), 1.26−1.29 (m, 1H), 1.35−1.40 (m, 1H), 1.44−1.49 (m, 1H), 1.55−1.64 (m, 4H), 1.65−1.72 (m, 2H), 1.88−1.94 (m, 1H), 2.05 (d, 1H, *J* = 12.8 Hz), 2.63 (t, 2H, *J* = 7.6 Hz), 3.32−3.46 (m, 2H), 4.63 (td, 1H, *J* = 4.4, 10.4 Hz), 5.30−5.34 (m, 2H), 5.96 (d, 1H, *J* = 2.4 Hz), 6.26 (brs, 1H), due to rotamers, α-H on allenamide split into two signals: 7.01 (t, 0.5H, *J* = 6.2 Hz) and 7.17 (t, 0.5H, *J* = 6.2 Hz), 7.28 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) not recorded to due to rotamers; IR (neat) cm^{-1} 2953 m, 1698s, 1457 m, 1401s, 1302 m; MS (ESI) *m*/*e* (% relative intensity) 383.4 (10) $(M + Na + H)^+$, 382.4 (100) $(M + Na)^+$, 360.4 (20) $(M + H)^+$; HRMS (ESI) *m*/*e* calcd for $C_{22}H_{33}NO_3^+$ $(M + Na)^+$ 382.2353, found 382.2364.

Allenamide **32** (40 mg, 0.13 mmol) was prepared in 40% yield according to the general procedure at 40 °C. R_f = 0.42 [1:5 EtOAc/hexanes]; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99 (t, 3H, *J* = 3.2 Hz), 2.41 (s, 3H), 2.87 (t, 2H, *J* = 7.2 Hz), 3.39 (t, 2H, *J* = 7.2 Hz), 4.66 (qt, 2H, *J* = 3.2 Hz), 6.09 (dd, 1H, *J* = 0.4, 3.2 Hz), 6.27 (dd, 1H, *J* = 2.0, 3.2 Hz), 7.26 (brs, 1H), 7.27 (d, 2H, *J* = 8.4 Hz), 7.64 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 21.7, 48.9, 81.6, 106.6, 107.3, 110.4, 128.0, 129.4, 134.2, 141.5, 143.6, 152.5, 207.1; IR (neat) cm^{-1} 2925 m, 1597 m, 1348s, 1159s, 1092 m; MS (ESI) *m*/*e* (% relative intensity) 340.9 (10) $(M + Na)^+$, 339.8 (100), 318.9 (10) $(M + H)^+$, 317.9 (60) $(M)^+$; HRMS (ESI) *m*/*e* calcd for $C_{17}H_{19}NO_3S^+$ $(M + Na)^+$ 340.1159, found 340.1163.

Allenamide **40a** (90 mg, 0.205 mmol) was prepared in 75% yield according to the general procedure. R_f = 0.30 [1:5 EtOAc/hexanes]; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 2.83 (t, 2H, *J* = 7.6 Hz), 2.88 (t, 2H, *J* = 7.2 Hz), 3.36 (t, 2H, *J* = 7.6 Hz), 3.69 (t, 2H, *J* = 7.2 Hz), 4.52 (s, 2H), 5.30 (d, 2H, *J* = 6.0 Hz), 5.93 (s, 2H), 6.83 (t, 1H, *J* = 6.0 Hz), 7.24−7.32 (m, 7H), 7.68 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 27.3, 29.0, 45.4, 68.5, 73.1, 88.0, 100.2, 106.7, 107.1, 127.3, 127.7, 127.8, 128.5, 129.9, 135.6, 138.4, 143.9, 150.8, 152.0, 201.3; IR (neat) cm^{-1} 2861w, 1597w, 1453 m, 1353s, 1161s; MS (ESI) *m*/*e* (% relative intensity) 461.2 (10) $(M + Na + H)^+$, 460.2 (100) $(M + Na)^+$, 438.2 (10) $(M + H)^+$; HRMS (ESI) *m*/*e* calcd for $C_{25}H_{27}NO_4S^+$ $(M + Na)^+$ 460.1553, found 460.1551.

Allenamide **44** (170 mg, 0.49 mmol) was prepared in 68% yield from the corresponding propargyl amide according to the general procedure. R_f = 0.45 [1:5 EtOAc/hexanes]; white solid; mp = 64−65 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.96 (s, 6H), 2.42 (s, 3H), 2.61 (s, 2H), 2.98 (s, 2H), 5.17 (d, 2H, *J* = 6.5 Hz), 6.03 (d, 1H, *J* = 3.0 Hz), 6.28 (dd, 1H, *J* = 1.5, 2.5 Hz), 6.74 (t, 1H, *J* = 6.5 Hz), 7.29 (d, 1H, *J* = 1.5 Hz), 7.31 (d, 2H, *J* = 8.0 Hz), 7.66 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 25.6, 36.3, 39.1, 56.0, 88.0, 102.5, 107.8, 110.3, 127.7, 129.7, 134.8, 141.2, 143.8, 153.6, 203.1; IR (neat) cm^{-1} 2925 m, 2189w, 1659w, 1459 m, 1166s; MS (ESI) *m*/*e* (% relative intensity) 341.3 (15) $(M + Na + H)^+$, 340.2 (100) $(M + Na)^+$, 318.3 (5) $(M + H)^+$; HRMS (ESI) *m*/*e* calcd for $C_{17}H_{19}NO_3S^+$ $(M + Na)^+$ 340.0978, found 340.0980.

Allenamide **48** (296 mg, 0.89 mmol) was prepared in 99% yield from the corresponding propargyl amide according to the general procedure. R_f = 0.47 [1:3 EtOAc/hexanes]; pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.57 (sept, 2H, *J* = 7.0 Hz), 1.65 (sept, 2H, *J* = 7.5 Hz), 2.42 (s, 3H), 2.61 (t, 2H, *J* = 7.0 Hz), 3.10 (t, 2H, *J* = 7.0 Hz), 5.25 (d, 2H, *J* = 6.5 Hz), 5.96 (dd, 1H, *J* = 0.5, 8.0 Hz), 6.26 (dd, 1H, *J* = 2.0, 8.0 Hz), 6.81 (t, 1H, *J* = 6.0 Hz), 7.28 (d, 1H, *J* = 1.5 Hz), 7.30 (d, 2H, *J* = 8.0 Hz), 7.67 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 25.1, 27.4, 27.6, 46.4, 87.6, 100.3, 105.1, 110.2, 127.3, 129.9, 135.6, 140.9, 143.8, 155.9, 201.6; IR (thin film) cm^{-1} 3260w, 2926 m, 1597w, 1347s, 1160s; MS (ESI) *m*/*e* (% relative intensity) 355.3 (10) $(M + Na + H)^+$, 354.3 (100) $(M + Na)^+$, 332.3 (10) $(M + H)^+$; HRMS (ESI) *m*/*e* calcd for $C_{18}H_{21}NO_3S^+$ $(M + Na)^+$ 354.1135, found 354.1142.

Allenamide **56** (70 mg, 0.19 mmol) was prepared in 70% yield from the corresponding propargyl amide according to the general procedure. R_f = 0.51 [1:2 EtOAc/hexanes]; $[\alpha]^{23}_D$ +14.2° [*c* 0.55, CH_2Cl_2]; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87, (s, 3H), 1.13 (s, 3H), 1.42 (ddd, 1H, *J* = 4.0, 5.6, 13.2 Hz), 1.65 (ddd, 1H, *J* = 4.4, 5.2, 14.0 Hz), 1.93 (d, 1H, *J* = 18.4 Hz), 2.01−2.07 (m, 1H), 2.10 (t, 1H, *J* = 4.4 Hz), 2.38 (dt, 1H, *J* = 4.0, 18.4 Hz), 2.45−2.52 (m, 1H), 2.81 (d, 1H, *J* = 14.8 Hz), 2.95 (t, 2H, *J* = 7.6 Hz), 3.38 (d, 1H, *J* = 14.4 Hz), 3.62 (sept, 1H, *J* = 7.6 Hz), 3.67 (sept, 1H, *J* = 7.6 Hz), 5.45 (d, 2H, *J* = 6.0 Hz), 6.10 (d, 1H, *J* = 3.6 Hz), 6.28 (t, 1H, *J* = 2.4 Hz), 6.74 (t, 1H, *J* = 6.4 Hz), 7.31 (dd, 1H, *J* = 1.2, 2.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 20.1, 25.4, 27.0, 27.6, 42.7, 43.0, 45.6, 47.9, 48.0, 58.5, 88.2, 99.8, 106.7, 110.4, 141.6, 152.3, 200.8, 214.9; IR (thin film) cm^{-1} 2921 m, 1742s, 1350s, 1235 m, 1089s; MS (ESI) *m*/*e* (% relative intensity) 386.8 (10) $(M + Na)^+$, 385.9 (100), 363.9 (20) $(M)^+$; HRMS (ESI) *m*/*e* calcd for $C_{19}H_{25}NO_4S^+$ $(M + Na)^+$ 386.1397, found 386.1394.

Allenamide **58** (107 mg, 0.22 mmol) was prepared in 97% yield from the corresponding propargyl amide according to the general procedure. R_f = 0.43 [1:10 EtOAc/hexanes]; $[\alpha]^{23}_D$ −22.8° [*c* 0.54, CH_2Cl_2]; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.06 (s, 3H), 0.11 (s, 3H), 0.84 (s, 3H), 0.87 (s, 9H), 0.99 (s, 3H), 1.06−1.12 (m, 1H), 1.39 (ddd, 1H, *J* = 3.6, 9.6, 11.2 Hz), 1.68−1.75 (m, 4H), 1.98 (td, 1H, *J* = 3.2, 11.6 Hz), 2.63 (d, 1H, *J* = 13.6 Hz), 2.90 (t, 2H, *J* = 7.6 Hz), 3.48 (d, 1H, *J* = 13.2 Hz), 3.56 (sept, 1H, *J* = 6.4 Hz), 3.60 (sept, 1H, *J* = 6.8 Hz), 4.01 (dd, 1H, *J* = 3.6, 6.8 Hz), 5.42 (d, 2H, *J* = 6.0 Hz), 6.08 (d, 1H, *J* = 0.8, 3.2 Hz), 6.28 (dd, 1H, *J* = 2.0, 3.2 Hz), 6.74 (t, 1H, *J* = 6.0 Hz), 7.31 (dd, 1H, *J* = 0.8, 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.8, −3.7, 17.9, 20.3, 20.9, 26.1, 27.4, 27.7, 29.3, 42.5, 44.7, 45.3, 48.7, 49.1, 50.2, 76.3, 88.0, 100.1, 106.6, 110.5, 141.6, 152.5, 200.7; IR (thin film) cm^{-1} 2928 m, 1595w, 1358s, 1151s, 1083s; MS (ESI) *m*/*e* (% relative intensity) 503.5 (15) $(M + Na + H)^+$, 502.5 (100) $(M + Na)^+$; HRMS (ESI) *m*/*e* calcd for $C_{25}H_{41}NO_4SSi^+$ $(M + Na)^+$ 502.2418, found 502.2401.

Allenamide (±)-**63** (153 mg, 0.32 mmol) was prepared in 61% yield according to the general procedure. R_f = 0.36 [1:8 EtOAc/hexanes]; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (d, 9H, *J* = 5.6 Hz), 1.01−1.07 (m, 12H), 2.41 (s, 3H), 3.30 (dd, 1H, *J* = 7.2, 13.6 Hz), 3.45

(dd, 1H, J = 6.8, 13.6 Hz), 5.08 (t, 2H, J = 7.2 Hz), 5.24 (d, 2H, J = 6.0 Hz), 6.26 (dd, 1H, J = 3.2 Hz), 6.29−6.31 (m, 1H), 6.68 (t, 1H, J = 6.4 Hz), 7.29 (d, 2H, J = 8.0 Hz), 7.34 (dd, 1H, J = 0.8, 1.2 Hz), 7.66 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 17.9, 18.0, 21.7, 51.7, 67.1, 88.2, 101.0, 107.8, 110.2, 127.4, 129.8, 135.2, 141.9, 143.8, 154.5, 201.4; IR (neat) cm^{-1} 2943 m, 2866w, 1462w, 1359s, 1164s; MS (ESI) m/e (% relative intensity) 499.2 (5) $(M + Na + H)^+$, 498.2 (25) $(M + Na)^+$, 476.2 (100) $(M + H)^+$; HRMS (ESI) m/e calcd for $C_{25}H_{37}NO_4SSi^+$ $(M + H)^+$ 476.2286, found 476.2269.

Allenamide (±)-**68** (115 mg, 0.26 mmol) was prepared in 82% yield according to the general procedure. R_f = 0.35 [1:8 EtOAc/hexanes]; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.57 (qt, 6H, J = 7.6 Hz), 0.90 (t, 9H, J = 8.0 Hz), 2.41 (s, 3H), 3.37 (AB of ABX, 2H, $J_{AX} = J_{BX}$ = 6.8, J_{AB} = 13.6 Hz), 4.96 (t, 1H, J = 6.8 Hz), 5.27 (d, 2H, J = 6.4 Hz), 6.26 (d, 1H, J = 3.2 Hz), 6.30 (dd, 1H, J = 1.6, 3.2 Hz), 6.73 (t, 1H, J = 6.4 Hz), 7.29 (d, 2H, J = 8.0 Hz), 7.37 (d, 1H, J = 1.6 Hz), 7.67 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.7, 6.8, 21.7, 51.5, 66.7, 88.1, 100.9, 107.5, 110.3, 127.4, 129.8, 135.2, 142.0, 143.8, 154.4, 201.5; IR (neat) cm^{-1} 2940 m, 1460w, 1355s, 1159s, 1090s; MS (ESI) m/e (% relative intensity) 457.2 (15) $(M + Na + H)^+$, 456.1 (50) $(M + Na)^+$, 434.2 (100) $(M + H)^+$; HRMS (ESI) m/e calcd for $C_{22}H_{31}NO_4SSi^+$ $(M + Na)^+$ 456.1636, found 456.1634.

Allenamide (±)-**70** (90 mg, 0.22 mmol) was prepared in 52% yield according to the general procedure. R_f = 0.31 [1:8 EtOAc/hexanes]; white solid; mp = 47−49 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (s, 9H), 2.42 (s, 3H), 3.31(dd, 1H, J = 4.0, 14.0 Hz), 3.84 (dd, 1H, J = 9.2, 14.0 Hz), 5.29 (dd, 1H, J = 6.4, 10.0 Hz), 5.41 (dd, 1H, J = 6.4, 10.4 Hz), 6.05 (dd, 1H, J = 4.4, 9.2 Hz), 6.32 (dd, 1H, J = 2.0, 3.2 Hz), 6.34 (d, 1H, J = 3.6 Hz), 6.76 (t, 1H, J = 6.4 Hz), 7.31 (d, 2H, J = 8.4 Hz), 7.36 (dd, 1H, J = 0.8, 1.6 Hz), 7.68 (d, 2H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 27.2, 39.0, 48.2, 65.2, 88.5, 100.4, 109.1, 110.5, 127.4, 129.9, 135.0, 142.8, 144.0, 150.3, 177.6, 201.6; IR (neat) cm^{-1} 2972w, 1728s, 1357s, 1166s, 1146s; MS (ESI) m/e (% relative intensity) 426.1 (20) $(M + Na)^+$, 421.2 (100), 404.2 (5) $(M + H)^+$; HRMS (ESI) m/e calcd for $C_{21}H_{25}NO_5S^+$ $(M + Na)^+$ 426.1346, found 426.1337.

Allenamide (±)-**72** (65 mg, 0.107 mmol) was prepared in 59% yield according to the general procedure. R_f = 0.32 [1:8 EtOAc/hexanes]; orange foam solid; mp = 73−75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 9H), 2.44 (s, 3H), 3.53 (dd, 1H, J = 4.0, 14.0 Hz), 4.24 (dd, 1H, J = 9.6, 14.0 Hz), 5.35 (dd, 1H, J = 6.0, 10.4 Hz), 5.47 (dd, 1H, J = 6.0, 10.4 Hz), 5.92 (dd, 1H, J = 4.4, 9.2 Hz), 6.36 (s, 2H), 6.90 (t, 1H, J = 6.0 Hz), 7.34 (d, 2H, J = 8.4 Hz), 7.36 (brs, 1H), 7.67 (d, 2H, J = 8.4 Hz), 8.25 (d, 2H, J = 8.8 Hz), 8.37 (d, 2H, J = 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 27.9, 46.6, 52.8, 85.8, 89.1, 100.1, 108.1, 110.8, 123.9, 127.4, 130.1, 130.3, 134.5, 142.0, 144.4, 145.6, 149.6, 150.1, 150.5, 201.3; IR (neat) cm^{-1} 3154w, 1730s, 1597 m, 1531s, 1148s; MS (ESI) m/e (% relative intensity) 627.1 (25) $(M + Na + H)^+$, 626.1 (80) $(M + Na)^+$, 621.2 (100), 604.2 (5) $(M + H)^+$; HRMS (ESI) m/e calcd for $C_{27}H_{29}N_3O_9S_2^+$ $(M + Na)^+$ 626.1238, found 626.1208.

Allenamide **38** (110 mg, 0.296 mmol) was prepared in 44% yield (77% brsm) from amide **28** and (2-iodovinylidene)cyclohexane according to our previously reported Cu(I) cross-coupling procedure.[28] R_f = 0.56 [1:2 EtOAc/hexanes]; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47−1.52 (m, 3H), 1.54 (s, 2H), 1.58−1.65 (m, 2H), 2.09 (t, 3H, J = 5.0 Hz), 2.41 (s, 3H), 2.86 (t, 2H, J = 8.0 Hz), 3.33 (t, 2H, J = 8.0 Hz), 6.03 (d, 1H, J = 3.0 Hz), 6.26 (t, 1H, J = 2.5 Hz), 6.58 (brs, 1H), 7.28 (brs, 1H), 7.29 (d, 2H, J = 8.5 Hz), 7.69 (d, 2H, J = 8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 25.9, 26.8, 27.3, 32.8, 45.3, 96.8, 106.3, 110.3, 116.1, 127.3, 129.7, 135.6, 141.4, 143.6, 152.6, 189.0; IR (neat) cm^{-1} 2929 m, 1447w, 1348 m, 1163s; MS (ESI) m/e (% relative intensity) 394.9 (10) $(M + Na)^+$, 393.9 (100), 372.9 (10) $(M + H)^+$, 371.9 (60) $(M)^+$; HRMS (ESI) m/e calcd for $C_{21}H_{25}NO_3S^+$ $(M + H)^+$ 372.1628, found 372.1625.

General Procedure for the Intramolecular [4 + 3] Cycloaddition of Allenamides. To a solution of allenamide (±)-**70** (40 mg, 0.10 mmol) and 50 mg of 4 Å molecular sieves in CH_2Cl_2 (2 mL) was added DMDO (2.8 mL, 0.07 M in acetone, 2 equiv) as a chilled solution (at −78 °C) via syringe pump over ∼1−2 h. The syringe pump was cooled by dry ice at all times during the addition. After the addition, the solution was filtered through Celite with ethyl acetate and concentrated under reduced pressure. The resulting crude residue was purified via silica gel flash column chromatography (isocratic eluent: EtOAc in hexanes) to provide the desired cycloadduct **71** (39 mg, 0.093 mmol, 94% yield, >95:5 dr). R_f = 0.11 [1:3 EtOAc/hexanes]; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (s, 9H), 2.41 (s, 3H), 2.42 (d, 1H, J = 16.0 Hz), 3.13 (dd, 1H, J = 5.6, 16.0 Hz), 3.52 (d, 1H, J = 12.8 Hz), 3.56 (s, 1H), 4.02 (dd, 1H, J = 4.0, 12.8 Hz), 5.07 (d, 1H, J = 4.0 Hz), 5.11 (d, 1H, J = 6.4 Hz), 6.05 (dd, 1H, J = 0.4, 6.0 Hz), 6.42 (dd, 1H, J = 1.6, 6.0 Hz), 7.33 (d, 2H, J = 8.0 Hz), 7.81 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 26.8, 27.1, 38.6, 44.2, 55.6, 69.1, 78.5, 93.6, 128.1, 128.2, 129.8, 134.1, 137.3, 144.0, 176.8, 200.4; IR (thin film) cm^{-1} 2976 m, 1733s, 1597 m, 1240s, 1140s; MS (ESI) m/e (% relative intensity) 443.2 (10) $(M + Na + H)^+$, 442.1 (100) $(M + Na)^+$, 420.1 (40) $(M + H)^+$; HRMS (ESI) m/e calcd for $C_{21}H_{25}NO_6S^+$ $(M + H)^+$ 420.1476, found 420.1490.

Cycloadduct **20** (40 mg, 0.115 mmol) was isolated in 78% yield from allenamide **19** as a 1:1 mixture of diastereomers according to the general procedure. R_f = 0.15 [1:2 EtOAc/hexanes]; $[\alpha]^{23}_D$ −469.1° [c 0.13, CH_2Cl_2]; white solid; ^{1}H NMR (500 MHz, $CDCl_3$) (due to rotamers, many of the signals were not well-resolved and/or line-broadened) δ 0.79 (d, 3H, J = 7.0 Hz), 0.89 (d, 6H, J = 6.5 Hz); 0.80−1.08 (m, 3H), 1.26−1.34 (m, 1H), 1.45−1.50 (m, 1H), 1.65 (d, 2H, J = 10.0 Hz), 1.92−1.96 (m, 1H), 2.10 (dd, 1H, J = 6.0, 13.0 Hz), 2.14−2.20 (m, 1H), 2.41 (ddd, 1H, J = 1.0, 4.0, 16.0 Hz), 2.93 (ddd, 1H, J = 2.5, 9.5, 16.0 Hz), 3.52 (td, 1H, J = 6.0, 11.5 Hz), 3.90 (brs, 1H), 4.05 (brs, 1H), 4.58 (td, 1H, J = 4.0, 11.0 Hz), 5.03 (d, 1H, J = 6.5 Hz), 6.27 (d, 1H, J = 6.0 Hz), 6.45 (dt, 1H, J = 1.5, 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) not recorded to due to rotamers; IR (thin film) cm^{-1} 2954s, 2870s, 1731s, 1694s, 1416 m; MS (ESI) m/e (% relative intensity) 371.3 (15) $(M + Na + H)^+$, 370.3 (100) $(M + Na)^+$; HRMS (ESI) m/e calcd for $C_{20}H_{29}NO_4^+$ $(M + Na)^+$ 370.1989, found 370.1999.

Cycloadduct **22** (14 mg, 0.038 mmol) was isolated in 26% yield (60:40 mixture of diastereomers with respect to the ring fusion) from allenamide **21** according to the general procedure. Major: R_f = 0.18 [1:2 EtOAc/hexanes]; colorless oil; 1:1 mixture with respect to the auxiliary (due to rotamers, many of the signals were not well-resolved and/or line-broadened). ^{1}H NMR (500 MHz, $CDCl_3$) [extra resonances from rotamers reported in brackets] δ 0.77 (d, 1.5H, J = 7.0 Hz), [0.81, (d, 1.5H, J = 7.0 Hz)], 0.82−0.92 (m, 6H); 0.95−1.08 (m, 2H), 1.24−1.32 (m, 2H), 1.41−1.46 (m, 1H), 1.58−1.68 (m, 3H), 1.76−1.82 (m, 1H), 1.86−1.98 (m, 2H), 2.02−2.18 (m, 2H), 2.45 (dd, 1H, J = 7.5, 16.0 Hz), 2.85 (dd, 1H, J = 5.0, 16.0 Hz), 3.24 (brs, 1H), 3.70−3.86 (m, 2H), 4.52 (m, 1H), 5.01 (d, 1H, J = 5.0 Hz), 6.17 (dd, 1H, J = 6.0, 15.0 Hz), 6.34 (td, 1H, J = 1.5, 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) not recorded to due to rotamers. IR (thin film) cm^{-1} 2949s, 1725s, 1705s, 1425 m, 1355 m; MS (ESI) m/e (% relative intensity) 385.4 (15) $(M + Na + H)^+$, 384.4 (100) $(M + Na)^+$; HRMS (ESI) m/e calcd for $C_{21}H_{31}NO_4^+$ $(M + Na)^+$ 384.2146, found 384.2146. Minor: R_f = 0.24 [1:2 EtOAc/hexanes]; colorless oil; 1:1 mixture with respect to the auxiliary. ^{1}H NMR (400 MHz, $CDCl_3$) (due to rotamers, many of the signals were not well-resolved and/or line-broadened) [extra resonances from rotamers reported in brackets] δ 0.75 (d, 1.5H, J = 6.8 Hz), [0.80 (d, 1.5H, J = 6.8 Hz)], 0.86−0.93 (m, 6H); 0.95−1.08 (m, 2H), 1.31−1.48 (m, 2H), 1.62−1.29 (m, 3H), 1.78 (dd, 1H, J = 4.6, 13.2 Hz), 1.84−1.94 (m, 2H), 2.02−2.10 (m, 2H), 2.38 (dd, 1H, J = 4.6, 14.4 Hz), 2.80 (dq, 1H, J = 3.2, 11.6 Hz), 3.27 (dt, 1H, J = 4.6, 14.4 Hz) 3.46 (d, 1H, J = 5.6 Hz), 4.05−4.18 (m, 1H), 4.55 (td, 0.5H,

J = 4.5, 11.2 Hz), [4.48 (td, 0.5H, J = 4.5, 11.2 Hz)], 5.01−5.04 (m, 1H), 5.91 (t, 1H, J = 6.0 Hz), 6.33 (dt, 1H, J = 2.0, 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) not recorded to due to rotamers; IR (thin film) cm^{-1} 2946s, 1727s, 1703s, 1424 m, 1356 m; MS (ESI) m/e (% relative intensity) 385.4 (15) $(M + Na + H)^+$, 384.4 (100) $(M + Na)^+$, 360.5 (15) $(M + H)^+$, 360.5 (20) $(M-H)^+$; HRMS (ESI) m/e calcd for $C_{21}H_{31}NO_4^+$ $(M + Na)^+$ 384.2146, found 384.2140.

Cycloadduct **34** (41 mg, 0.128 mmol) was obtained in 98% yield from allenamide **27** according to the general procedure. R_f = 0.17 [1:2 EtOAc/hexanes]; white solid; mp = 157−158 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.89−1.96 (m, 1H), 2.08 (ddd, 1H, J = 2.0, 5.5, 13.5 Hz), 2.40 (d, 1H, J = 16.0 Hz), 2.43 (s, 3H), 3.03 (dd, 1H, J = 6.5, 16.0), 3.61 (s, 1H), 3.62−3.67 (m, 2H), 5.04 (d, 1H, J = 6.5 Hz), 6.09 (d, 1H, J = 6.0 Hz), 6.40 (dd, 1H, J = 1.5, 6.0 Hz), 7.34 (d, 2H, J = 8.0 Hz), 7.83 (d, 2H, J = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 31.9, 44.2, 48.9, 71.4, 77.6, 92.8, 128.0, 129.8, 131.7, 134.9, 137.0, 143.8, 201.4; IR (neat) cm^{-1} 2950 m, 1705s, 1465w, 1325 m, 1155s; MS (ESI) m/e (% relative intensity) 342.8 (10) $(M + Na)^+$, 341.9 (100), 319.9 (20) $(M)^+$; HRMS (ESI) m/e calcd for $C_{16}H_{17}NO_4S^+$ $(M + Na)^+$ 342.0771, found 342.0764.

Cycloadduct **35** (33 mg, 0.084 mmol) was obtained in 93% yield from allenamide **33** according to the general procedure. R_f = 0.14 [1:2 EtOAc/hexanes]; white solid; mp = 194−195 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.17−2.21 (m, 2H), 2.41 (dd, 1H, J = 0.8, 16.4 Hz), 2.96 (ddd, 1H, J = 0.8, 6.8, 16.8 Hz), 3.61 (td, 1H, J = 7.2, 10.0 Hz), 3.85−3.90 (m, 1H), 3.94 (s, 1H), 5.06 (dd, 1H, J = 0.8, 6.8 Hz), 6.21 (d, 1H, J = 6.0 Hz), 6.47 (dd, 1H, J = 2.4, 6.0 Hz), 8.16 (d, 2H, J = 8.8 Hz), 8.37 (d, 2H, J = 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.9, 44.0, 49.1, 71.6, 77.3, 92.8, 124.3, 129.0, 131.9, 137.4, 145.2, 150.2, 201.7; IR (neat) cm^{-1} 2961 m, 2923w, 1599 m, 1258 m, 1013s; MS (ESI) m/e (% relative intensity) 373.8 (10) $(M + Na)^+$, 372.8 (100), 350.8 (5) $(M)^+$; HRMS (ESI) m/e calcd for $C_{15}H_{14}N_2O_6S^+$ $(M + Na)^+$ 373.0465, found 373.0451.

Cycloadduct **36** (23 mg, 0.069 mmol) was obtained in 69% yield from allenamide **32** according to the general procedure. R_f = 0.15 [1:2 EtOAc/hexanes]; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.97 (s, 3H), 2.17 (ddd, 1H, J = 2.0, 8.0, 13.5 Hz), 2.31 (d, 1H, J = 16.0 Hz), 2.30−2.35 (m, 1H), 2.41 (s, 3H), 2.83 (dd, 1H, J = 5.5, 15.5 Hz), 3.68 (td, 1H, J = 2.0, 9.5 Hz), 3.99 (qt, 1H, J = 9.0 Hz), 4.94 (d, 1H, J = 5.5 Hz), 6.04 (d, 1H, J = 6.0 Hz), 6.33 (dd, 1H, J = 1.5, 6.0 Hz), 7.28 (d, 2H, J = 8.0 Hz), 7.70 (d, 2H, J = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.0, 21.7, 29.3, 43.6, 47.6, 74.4, 77.5, 95.2, 127.5, 129.7, 130.5, 137.1, 138.2, 143.4, 201.8; IR (thin film) cm^{-1} 2925 m, 1718s, 1460w, 1334 m, 1158s; MS (ESI) m/e (% relative intensity) 356.8 (15) $(M + Na)^+$, 355.8 (100), 333.9 (10) $(M)^+$; HRMS (ESI) m/e calcd for $C_{17}H_{19}NO_4S^+$ $(M + Na)^+$ 356.0927, found 356.0934.

Cycloadduct **37a** (15 mg, 0.045 mmol) was obtained in 95% yield as ~80:20 inseparable mixture from allenamide (±)-**29a** according to the general procedure. R_f = 0.10 [1:2 EtOAc/hexanes]; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) *Major* δ 1.0 (d, 3H, J = 7.0 Hz), 1.91 (q, 1H, J = 10.0 Hz), 2.13 (ddd, 1H, J = 2.0, 7.0, 13.5 Hz), 2.43 (s, 3H), 3.10 (s, 1H), 3.23 (quint, 1H, J = 7.0 Hz), 3.44 (td, 1H, J = 2.0, 10.0 Hz), 3.86 (qd, 1H, J = 1.5, 10.0 Hz), 4.88 (d, 1H, J = 5.0 Hz), 6.05 (d, 1H, J = 6.0 Hz), 6.36 (dd, 1H, J = 1.5, 6.0 Hz), 7.35 (d, 2H, J = 8.5 Hz), 7.81 (d, 2H, J = 8.5 Hz); Select resonances for minor δ 1.37 (d, 3H, J = 7.0 Hz), 2.13 (dd, 1H, J = 6.0, 13.5 Hz), 2.45 (s, 3H), 3.14 (s, 1H), 3.55 (td, 1H, J = 6.0, 11.0 Hz), 3.68 (t, 1H, J = 10.0 Hz), 4.22 (ddd, 1H, J = 5.5, 8.0, 13.5 Hz), 4.65 (brs, 1H), 6.11 (d, 1H, J = 6.0 Hz), 6.46 (dd, 1H, J = 1.5, 6.0 Hz), 7.87 (d, 2H, J = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.3, 21.7, 27.8, 30.7, 48.7, 70.1, 82.7, 93.3, 128.2, 129.9, 132.1, 133.3, 135.8, 144.0, 203.7; IR (thin film) cm^{-1} 2916s, 2848s, 1717s, 1349 m, 1163s; MS (ESI) m/e (% relative intensity) 356.8 (10) $(M + Na)^+$, 355.8 (100), 333.9 (20) $(M)^+$; HRMS (ESI) m/e calcd for $C_{17}H_{19}NO_4S^+$ $(M + Na)^+$ 356.0927, found 356.0937.

Cycloadduct **39** (28 mg, 0.072 mmol) was obtained in 90% yield from allenamide **38** according to the general procedure. R_f = 0.25 [1:2 EtOAc/hexanes]; light brown solid; mp = 134−135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16−1.20 (m, 1H), 1.36−1.48 (m, 3H), 1.56−1.66 (m, 2H), 1.69−1.86 (m, 3H), 1.89−2.10 (m, 2H), 2.15 (ddd, 1H, J = 4.4, 8.4, 13.2 Hz), 2.43 (s, 3H), 3.19 (s, 1H), 3.50 (td, 1H, J = 1.2, 10.4 Hz), 3.80 (td, 1H, J = 7.2, 10.4 Hz), 4.82 (s, 1H), 6.03 (d, 1H, J = 6.0 Hz), 6.40 (dd, 1H, J = 0.8, 6.0 Hz), 7.34 (d, 2H, J = 8.0 Hz), 7.84 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 21.8, 22.1, 25.6, 29.8, 31.1, 33.0, 49.2, 56.2, 69.6, 84.3, 93.1, 128.3, 129.8, 131.9, 133.3, 136.2, 143.9, 206.3; IR (neat) cm^{-1} 2921 m, 1721s, 1464 m, 1333 m, 1165 m; MS (ESI) m/e (% relative intensity) 410.9 (10) $(M + Na)^+$, 409.8 (100), 387.9 (20) $(M)^+$; HRMS (ESI) m/e calcd for $C_{21}H_{25}NO_4S^+$ $(M + Na)^+$ 410.1397, found 410.1403.

Cycloadduct **41a** (25 mg, 0.055 mmol) was obtained in 81% yield from allenamide **40a** according to the general procedure. R_f = 0.22 [1:2 EtOAc/hexanes]; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.91 (q, 1H, J = 9.6 Hz), 2.04−2.08 (m, 1H), 2.09 (q, 2H, J = 5.6 Hz), 2.43 (s, 3H), 2.52 (d, 1H, J = 16.0 Hz), 2.82 (d, 1H, J = 16.0 Hz), 3.55−3.64 (m, 5H), 4.48 (s, 2H), 5.97 (d, 1H, J = 6.0 Hz), 6.31 (d, 1H, J = 6.0 Hz), 7.28−7.36 (m, 7H), 7.84 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 32.2, 37.1, 48.9, 49.3, 65.6, 70.1, 73.3, 85.9, 92.7, 127.8, 127.9, 128.1, 128.6, 129.8, 130.9, 135.0, 138.3, 139.7, 143.8, 202.0; IR (thin film) cm^{-1} 2925 m, 1719s, 1352 m, 1267 m, 1165s; MS (ESI) m/e (% relative intensity) 477.2 (10) $(M + Na)^+$, 476.2 (100), 454.2 (10) $(M)^+$; HRMS (ESI) m/e calcd for $C_{25}H_{27}NO_5S^+$ $(M + H)^+$ 454.1683, found 454.1684.

Cycloadduct **41b** (33 mg, 0.068 mmol) was obtained in 97% yield from allenamide **40b** according to the general procedure. R_f = 0.10 [1:6 EtOAc/hexanes]; white solid; mp = 106−107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.03 (s, 3H), 0.04 (s, 3H), 0.87 (s, 9H), 1.87−1.95 (m, 1H), 2.00 (td, 2H, J = 3.6, 6.4 Hz), 2.08 (ddd, 1H, J = 2.4, 5.2, 13.2 Hz), 2.44 (s, 3H), 2.54 (d, 1H, J = 16.0 Hz), 2.82 (dd, 1H, J = 0.4, 16.0 Hz), 3.61−3.65 (m, 2H), 3.74 (t, 2H, J = 6.4 Hz), 5.96 (d, 1H, J = 5.6 Hz), 6.33 (d, 1H, J = 6.0 Hz), 7.33 (dd, 2H, J = 0.8, 8.8 Hz), 7.84 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.2, −5.1, 18.4, 21.8, 26.1, 32.3, 40.0, 48.9, 49.4, 58.6, 70.2, 86.0, 92.6, 128.1, 129.8, 130.7, 135.2, 140.0, 143.8, 202.1; IR (neat) cm^{-1} 2883 m, 1735s, 1507w, 1365 m, 1216 m; MS (ESI) m/e (% relative intensity) 500.8 (20) $(M + Na)^+$, 499.8 (100), 477.9 (5) $(M)^+$; HRMS (ESI) m/e calcd for $C_{24}H_{35}NO_5SSi^+$ $(M + Na)^+$ 500.1898, found 500.1906.

Cycloadduct **45** (14 mg, 0.042 mmol) was obtained in 45% yield as a 3:1 mixture of diastereomers from allenamide **44** according to the general procedure. Minor isomer was found to epimerize upon column chromatography. R_f = 0.15 [1:2 EtOAc/hexanes]; white solid; mp = 184−185 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51 (td, 1H, J = 5.0, 14.0 Hz), 1.68 (dquint, 1H, J = 2.5, 13.0 Hz), 1.99 (d, 1H, J = 14.0 Hz), 2.09 (qd, 1H, J = 2.5, 13.0 Hz), 2.17 (quartet of triplets, 1H, J = 3.5, 13.5 Hz), 2.42 (d, 1H, J = 16.0 Hz), 2.43 (s, 3H), 2.72 (s, 1H), 3.54 (dd, 1H, J = 5.0, 15.5 Hz), 3.93 (dd, 1H, J = 3.0, 11.5 Hz), 5.11 (d, 1H, J = 4.5 Hz), 5.80 (d, 1H, J = 6.0 Hz), 6.34 (dd, 1H, J = 2.0, 6.0 Hz), 7.35 (d, 2H, J = 8.0 Hz), 7.70 (d, 2H, J = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.2, 21.7, 30.6, 46.3, 47.4, 71.4, 79.9, 85.1, 128.6, 129.8, 131.9, 132.9, 137.2, 144.1, 202.1; IR (neat) cm^{-1} 2971 m, 1738s, 1337 m, 1158s, 1098 m; MS (ESI) m/e (% relative intensity) 356.1 (100) $(M + Na + H)^+$, 334.1 (95) $(M + H)^+$; HRMS (ESI) m/e calcd for $C_{17}H_{19}NO_4S^+$ $(M + H)^+$ 334.1108, found 334.1115.

Cycloadduct **47** (28 mg, 0.072 mmol) was obtained in 90% yield from allenamide **46** according to the general procedure. R_f = 0.25 [1:2 EtOAc/hexanes]; white solid; mp = 155−156 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.91 (s, 3H), 1.36 (s, 3H), 1.42 (d, 1H, J = 14.5 Hz), 1.82 (dd, 1H, J = 2.0, 14.5 Hz), 1.89 (d, 1H, J = 11.5 Hz), 2.43 (s, 3H), 2.44 (d, 1H, J = 13.5 Hz), 2.71 (s, 1H), 3.52 (dd, 1H, J = 2.0, 12.0 Hz), 3.55 (dd, 1H, J = 4.5, 14.0 Hz), 5.11 (d, 1H, J = 4.5 Hz), 5.72 (d, 1H, J = 6.0 Hz),

6.30 (dd, 1H, J = 1.5, 6.0 Hz), 7.34 (d, 2H, J = 8.0 Hz), 7.70 (d, 2H, J = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 25.8, 29.8, 30.8, 43.2, 46.7, 59.1, 71.5, 80.1, 86.1, 128.4, 129.8, 133.0, 133.8, 136.7, 143.9, 202.2; IR (neat) cm^{-1} 2923 m, 1709s, 1327 m, 1162s, 1095s; MS (ESI) m/e (% relative intensity) 385.2 (10) $(M + Na + H)^+$, 384.1 (100) $(M + Na)^+$; HRMS (ESI) m/e calcd for $C_{19}H_{23}NO_4S^+$ $(M + H)^+$ 362.1421, found 362.1408.

Cycloadduct **49** (7 mg, 0.020 mmol) was obtained in 17% yield from allenamide **48** according to the general procedure. R_f = 0.17 [1:3 EtOAc/hexanes]; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.71 (br d, 2H, J = 14.0 Hz), 1.84−1.95 (m, 2H), 2.02 (dd, 1H, J = 6.0, 14.5 Hz), 2.22 (t, 1H, J = 14.0 Hz), 2.38 (d, 1H, J = 18.0 Hz), 2.41 (s, 3H), 2.75−2.80 (m, 1H), 3.58 (d, 1H, J = 15.0 Hz), 4.38 (s, 1H), 4.98 (d, 1H, J = 6.5 Hz), 6.26 (d, 1H, J = 5.5 Hz), 6.33 (d, 1H, J = 6.0 Hz), 7.27 (d, 2H, J = 8.0 Hz), 7.73 (d, 2H, J = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 21.8, 30.6, 33.5, 46.5, 47.3, 70.3, 76.7, 89.8, 128.1, 129.3, 133.7, 137.3, 137.5, 143.3, 205.1; IR (thin film) cm^{-1} 2926 m, 1723s, 1330s, 1265 m, 1153s; MS (ESI) m/e (% relative intensity) 371.3 (10) $(M + Na + H)^+$, 370.3 (100) $(M + Na)^+$; HRMS (ESI) m/e calcd for $C_{18}H_{21}NO_4S^+$ $(M + Na)^+$ 370.1084, found 370.1101.

Cycloadduct **51** (24 mg, 0.078 mmol) was obtained in 73% yield as a 3:1 mixture of diastereomers from allenamide **50** according to the general procedure. Major: R_f = 0.20 [1:3 EtOAc/hexanes]; white solid; mp = 83−84 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.67−1.72 (m, 1H), 1.99 (quintet of doublets, 1H, J = 3.0, 7.0 Hz), 2.31−2.36 (m, 1H), 2.43 (s, 3H), 2.45 (d, 1H, J = 15.0 Hz), 2.54−2.59 (m, 1H), 2.68 (d, 1H, J = 5.0 Hz) 2.70 (dd, 1H, J = 2.0, 5.0 Hz), 2.97−3.00 (m, 1H), 3.27 (q, 1H, J = 9.0 Hz), 3.44 (td, 1H, J = 3.0, 8.0 Hz), 4.91 (d, 1H, J = 9.0 Hz), 5.48 (ddd, 1H, J = 1.0, 4.5, 11.0 Hz), 5.84 (ddd, 1H, J = 1.5, 2.5, 7.5 Hz), 7.31 (d, 2H, J = 8.5 Hz), 7.75 (d, 2H, J = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.4, 21.7, 31.6, 42.4, 43.3, 46.3, 67.5, 127.8, 129.6, 129.8, 129.9, 135.5, 143.7, 206.4; IR (neat) cm^{-1} 2917s, 1726s, 1340 m, 1154s, 1105 m; MS (ESI) m/e (% relative intensity) 329.1 (10) $(M + Na + H)^+$, 328.1 (55) $(M + Na)^+$, 306.1 (100) $(M + H)^+$; HRMS (ESI) m/e calcd for $C_{16}H_{19}NO_3S^+$ $(M + H)^+$ 306.1159, found 306.1147. Minor: R_f = 0.16 [1:3 EtOAc/hexanes]; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.63−1.70 (m, 2H), 2.08 (dt, 1H, J = 5.5, 11.5 Hz), 2.13−2.16 (m, 1H), 2.43 (s, 3H), 2.53−2.62 (m, 4H), 3.15 (ddd, 1H, J = 5.5, 6.0, 7.0 Hz), 3.73 (dd, 1H, J = 8.0, 10.5 Hz), 4.43 (d, 1H, J = 11.5 Hz), 5.84 (ddd, 1H, J = 1.5, 3.0, 11.0 Hz), 6.02 (quintet of doublets, 1H, J = 2.5, 6.0 Hz), 7.31 (d, 2H, J = 8.0 Hz), 7.88 (d, 2H, J = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 23.9, 32.3, 40.7, 43.2, 48.3, 72.0, 127.9, 129.7, 131.0, 132.1, 136.9, 143.6, 205.8; IR (thin film) cm^{-1} 2849 m, 1723s, 1335 m, 1140s, 1098 m; MS (ESI) m/e (% relative intensity) 328.1 (10) $(M + Na)^+$, 306.1 (100) $(M + H)^+$; HRMS (ESI) m/e calcd for $C_{16}H_{19}NO_3S^+$ $(M + H)^+$ 306.1159, found 306.1151.

Cycloadduct **57** (25 mg, 0.065 mmol) was obtained in 80% yield as a 65:35 inseparable mixture of diastereomers from allenamide **56** according to the general procedure. R_f = 0.24 [1:1 EtOAc/hexanes]; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) Major δ 0.91 (s, 3H), 1.13 (s, 3H), 1.42 (td, 1H, J = 4.0, 9.5 Hz), 1.67−1.75 (m, 1H), 1.93 (d, 1H, J = 18.0 Hz), 2.01−2.07 (m, 1H), 2.09 (t, 1H, J = 5.0 Hz), 2.11−2.15 (m, 1H), 2.28 (td, 1H, J = 8.5, 13.0 Hz), 2.36−2.42 (m, 1H), 2.41 (dd, 1H, J = 5.0, 17.5 Hz), 2.45−2.54 (m, 1H), 2.96 (dd, 1H, J = 7.5, 17.5 Hz), 3.17 (d, 1H, J = 15.0 Hz), 3.48−3.56 (m, 1H), 3.60 (s, 1H), 3.90 (d, 1H, J = 15.0 Hz), 4.10 (dd, 1H, J = 8.5, 10.5 Hz), 4.26 (s, 1H), 5.05 (d, 1H, J = 7.5 Hz), 6.28 (d, 1H, J = 6.0 Hz), 6.48 (dd, 1H, J = 1.5, 6.0 Hz); Select resonances for minor δ 1.11 (s, 3H), 1.91 (d, 1H, J = 18.0 Hz), 2.99 (dd, 1H, J = 7.0, 17.0 Hz), 4.03 (dd, 1H, J = 8.5, 10.5 Hz), 4.22 (s, 1H), 6.27 (d, 1H, J = 6.5 Hz), 6.46 (dd, 1H, J = 2.0, 6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) not obtained for inseparable mixture; IR (thin film) cm^{-1} 2959 m, 1739s, 1415w, 1332s, 1144s; MS (ESI) m/e (% relative intensity) 403.1 (10) $(M + Na + H)^+$, 402.2 (100) $(M + Na)^+$, 380.2 (10) $(M + H)^+$; HRMS (ESI) m/e calcd for $C_{19}H_{25}NO_5S^+$ $(M + Na)^+$ 402.1346, found 402.1351.

Cycloadduct **59** (25 mg, 0.065 mmol) was obtained in 97% yield as a 60:40 inseparable mixture of diastereomers from allenamide **58** according to the general procedure. R_f = 0.50 [1:5 EtOAc/hexanes]; pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) Major δ 0.07 (s, 3H), 0.19 (s, 3H), 0.89 (s, 9H), 0.90 (s, 3H), 1.03 (s, 3H), 1.05−1.10 (m, 1H), 1.35−1.41 (m, 1H), 1.67−1.78 (m, 4H), 1.92−1.94 (m, 1H), 2.00−2.10 (m, 2H), 2.24 (td, 1H, J = 8.0, 12.8 Hz), 2.40 (d, 1H, J = 17.2 Hz), 2.95 (dd, 1H, J = 7.6, 17.2 Hz), 3.35−3.42 (m, 1H), 3.48 (d, 1H, J = 13.6 Hz), 3.59 (d, 1H, J = 13.6 Hz), 4.00−4.07 (m, 2H), 4.32 (s, 1H), 5.04 (d, 1H, J = 7.2 Hz),6.29 (d, 1H, J = 5.6 Hz), 6.46−6.48 (m, 1H); Select resonances for minor δ 0.05 (s, 3H), 0.90 (s, 3H), 0.87 (s, 9H), 0.91 (s, 3H), 1.25 (s, 3H), 2.39 (d, 1H, J = 17.6 Hz), 2.94 (dd, 1H, J = 7.6, 17.6 Hz), 3.45 (d, 1H, J = 14.0 Hz), 3.73 (d, 1H, J = 14.4 Hz), 4.17 (dd, 1H, J = 8.0, 11.6 Hz), 4.27 (s, 1H), 6.27 (d, 1H, J = 5.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) not obtained for inseparable mixture; IR (thin film) cm^{-1} 2955 m, 1737s, 1329s, 1248 m, 1099 m; MS (ESI) m/e (% relative intensity) 519.5 (20) $(M + Na + H)^+$, 518.5 (100) $(M + Na)^+$; HRMS (ESI) m/e calcd for $C_{25}H_{41}NO_5SSi^+$ $(M + Na)^+$ 518.2367, found 518.2383.

Cycloadduct **67** (35 mg, 0.071 mmol) was obtained in 85% yield as a 4:1 mixture of diastereomers from allenamide (±)-**63** according to the general procedure. Major: R_f = 0.19 [1:4 EtOAc/hexanes]; white solid; mp = 97−98 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.91−0.95 (m, 3H), 0.90 (d, 18H, J = 8.0 Hz), 2.39 (d, 1H, J = 15.0 Hz), 2.40 (s, 3H), 3.18 (dd, 1H, J = 5.0, 15.0 Hz), 3.33 (d, 1H, J = 11.0 Hz), 3.42 (s, 1H), 4.04 (dd, 1H, J = 4.0, 11.5 Hz), 4.30 (d, 1H, J = 4.0 Hz), 5.08 (d, 1H, J = 5.0 Hz), 6.17 (d, 1H, J = 6.0 Hz), 6.34 (d, 1H, J = 6.0 Hz), 7.31 (d, 2H, J = 8.0 Hz), 7.80 (d, 2H, J = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1, 17.9, 18.0, 21.6, 44.4, 59.3, 68.4, 72.5, 78.8, 95.7, 128.1, 128.9, 129.8, 133.5, 136.5, 143.8, 200.9; IR (neat) cm^{-1} 2944 m, 1721s, 1462 m, 1352s, 1165s; MS (ESI) m/e (% relative intensity) 515.2 (5) $(M + Na + H)^+$, 509.2 (100), 492.2 (75) $(M + H)^+$; HRMS (ESI) m/e calcd for $C_{25}H_{37}NO_5SSi^+$ $(M + H)^+$ 492.2235, found 492.2236. Minor: R_f = 0.09 [1:4 EtOAc/hexanes]; white solid; mp = 126−128 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89−0.97 (m, 3H), 1.00 (s, 18H), 2.40 (d, 1H, J = 17.0 Hz), 2.43 (s, 3H), 3.01 (dd, 1H, J = 6.5, 17.0 Hz), 3.40 (t, 1H, J = 10.5 Hz), 3.81 (dd, 1H, J = 7.5, 10.5 Hz), 3.83 (s, 1H), 4.19 (dd, 1H, J = 7.5, 9.5 Hz), 5.13 (d, 1H, J = 6.5 Hz), 6.10 (d, 1H, J = 6.0 Hz), 6.47 (dd, 1H, J = 1.5, 6.0 Hz), 7.33 (d, 2H, J = 8.0 Hz), 7.83 (d, 2H, J = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.3, 18.0, 18.1, 21.7, 44.4, 53.5, 69.2, 70.4, 77.3, 91.8, 127.9, 129.8, 131.0, 135.8, 138.0, 144.0, 201.4; IR (neat) cm^{-1} 2918s, 1724s, 1460 m, 1347s, 1116s; MS (ESI) m/e (% relative intensity) 514.2 (20) $(M + Na)^+$, 509.2 (100), 492.2 (75) $(M + H)^+$; HRMS (ESI) m/e calcd for $C_{25}H_{37}NO_5SSi^+$ $(M + H)^+$ 492.2235, found 492.2231.

Cycloadduct **69** (35 mg, 0.071 mmol) was obtained in 85% yield as a 4:1 mixture of diastereomers from allenamide (±)-**68** according to the general procedure. Major: R_f = 0.24 [1:3 EtOAc/hexanes]; white solid; mp = 73−74 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.44 (qd, 6H, J = 3.5, 7.5 Hz), 0.79 (t, 9H, J = 7.5 Hz), 2.39 (d, 1H, J = 15.5 Hz), 2.41 (s, 3H), 3.14 (dd, 1H, J = 5.0, 15.5 Hz), 3.32 (d, 1H, J = 11.5 Hz), 3.42 (s, 1H), 3.99 (dd, 1H, J = 4.0, 11.5 Hz), 4.12 (d, 1H, J = 3.5 Hz), 5.06 (d, 1H, J = 5.5 Hz), 6.11 (d, 1H, J = 6.0 Hz), 6.34 (dd, 1H, J = 1.5, 6.0 Hz), 7.32 (d, 2H, J = 8.0 Hz), 7.79 (d, 2H, J = 8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.6, 6.7, 21.6, 44.4, 59.2, 68.3, 71.7, 78.7, 95.5, 128.1, 128.8, 129.6, 133.5, 136.7, 143.7, 200.9; IR (neat) cm^{-1} 2866 m, 1719s, 1415w, 1350s, 1166s; MS (ESI) m/e (% relative intensity) 473.2 (10) $(M + Na + H)^+$, 467.2 (80), 450.2 (100) $(M + H)^+$; HRMS (ESI) m/e calcd for $C_{22}H_{31}NO_5SSi^+$ $(M + H)^+$ 450.1765, found 450.1750. Minor: R_f = 0.12 [1:3 EtOAc/hexanes]; white solid; mp = 129−131 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.56 (q, 6H, J = 8.0 Hz), 0.90 (t, 9H, J = 8.0 Hz), 2.40 (d, 1H, J = 17.0 Hz), 2.44 (s, 3H), 3.00 (dd, 1H, J = 6.5, 17.0 Hz), 3.38 (t, 1H, J = 10.5 Hz), 3.77 (dd, 1H, J = 7.5, 10.5 Hz), 3.85 (s, 1H), 4.07 (dd, 1H, J = 7.5, 9.5 Hz), 5.14 (d, 1H, J = 6.5 Hz), 6.08

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(d, 1H, J = 6.0 Hz), 6.48 (dd, 1H, J = 1.5, 6.0 Hz), 7.34 (d, 2H, J = 8.0 Hz), 7.83 (d, 2H, J = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 0.2, 4.7, 6.7, 21.8, 44.4, 53.3, 69.1, 70.1, 91.7, 127.9, 129.8, 130.8, 135.9, 138.3, 144.0, 201.3; IR (neat) cm^{-1} 2849 m, 1725s, 1462 m, 1352s, 1163s; MS (ESI) m/e (% relative intensity) 472.2 (30) $(M + Na)^+$, 467.2 (80), 451.2 (20) $(M + 2H)^+$, 450.2 (100) $(M + H)^+$; HRMS (ESI) m/e calcd for $C_{22}H_{31}NO_5SSi^+$ $(M + H)^+$ 450.1765, found 450.1756.

Cycloadduct **73** (15 mg, 0.024 mmol) was obtained in 49% yield with >95:5 dr from allenamide (±)-**72** according to the general procedure. R_f = 0.11 [1:3 EtOAc/hexanes]; yellow solid; mp = 104−106 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.35 (s, 9H), 2.46 (s, 3H), 2.47 (d, 1H, J = 16.5 Hz), 3.07 (dd, 1H, J = 6.5, 16.5 Hz), 3.72 (dd, 1H, J = 9.0, 10.5 Hz), 3.82 (s, 1H), 4.43 (dd, 1H, J = 9.0, 10.5 Hz), 4.93 (t, 1H J = 9.0 Hz), 5.10 (d, 1H, J = 6.5 Hz), 6.20 (d, 1H, J = 6.0 Hz), 6.48 (dd, 1H, J = 2.0, 6.0 Hz), 7.38 (d, 2H, J = 8.0 Hz), 7.89 (d, 2H, J = 8.5 Hz), 8.08 (d, 2H, J = 8.5 Hz), 8.32 (d, 2H, J = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 0.2, 21.8, 27.9, 44.4, 49.3, 56.2, 69.5, 77.7, 86.6, 91.7, 124.0, 128.3, 129.5, 130.0, 131.7, 134.5, 137.8, 144.5, 146.0, 150.4, 200.1; IR (neat) cm^{-1} 2928w, 1732s, 1717s, 1350s, 1265 m, 1147s; MS (ESI) m/e (% relative intensity) 644.4 (5) $(M + Na + 2H)^+$, 643.4 (20) $(M + Na + H)^+$, 642.4 (100) $(M + Na)^+$; HRMS (ESI) m/e calcd for $C_{27}H_{29}N_3O_{10}S_2^+$ $(M + Na)^+$ 642.1187, found 642.1213.

A solution of tosylate **61** (50 mg, 0.11 mmol), *N*-tosyl propargyl amine (36 mg, 0.17 mmol), and Cs_2CO_3 (45 mg, 0.13 mmol) in DMF (0.11 mL) was heated to 80 °C overnight. The solution was then filtered through Celite with ethyl acetate and concentrated under reduced pressure. The resulting crude residue was purified via silica gel flash column chromatography (isocratic eluent: EtOAc in hexanes) to provide the desired cycloadduct **64** (35 mg, 0.074 mmol) in 65% yield as ~80:20 mixture of diastereomers. R_f = 0.20 [1:10 EtOAc/hexanes]; colorless oil; Major isomer reported. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.91−0.96 (m, 3H), 0.97 (s, 18H), 1.91 (dd, 1H, J = 1.5, 14.0 Hz), 2.42 (s, 3H), 2.52 (ddd, 1H, J = 1.0, 4.5, 14.0 Hz), 2.85−2.90 (m, 1H), 3.79−3.96 (m, 2H), 5.05 (d, 1H, J = 1.5, 4.5 Hz), 6.22 (d, 1H, J = 6.0 Hz), 6.27 (dd, 1H, J = 1.5, 5.5 Hz), 6.58 (s, 1H), 7.30 (d, 2H, J = 8.0 Hz), 7.67 (d, 2H, J = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 12.3, 18.0, 18.1, 21.7, 31.0, 48.0, 65.9, 78.3, 89.4, 117.3, 119.2, 127.3, 130.0, 133.0, 134.9, 135.2, 144.0; ^{1}H NMR (500 MHz, C_6D_6) δ 1.02 (sept, 3H, J = 6.5 Hz), 1.05 (d, 18H, J = 6.5 Hz), 1.40 (dd, 1H, J = 1.0, 14.0 Hz), 1.80 (s, 3H), 2.12 (ddd, 1H, J = 1.0, 4.0, 14.0 Hz), 2.93 (dd, 1H, J = 11.5, 12.0 Hz), 4.17 (dd, 1H, J = 5.0, 11.0 Hz), 4.26 (ddd, 1H, J = 0.5, 5.0, 12.0 Hz), 4.54 (dd, 1H, J = 1.5, 4.5 Hz), 5.72 (d, 1H, J = 6.0 Hz), 6.01 (d, 1H, J = 5.5 Hz), 6.68 (d, 2H, J = 8.0 Hz), 6.74 (s, 1H), 7.69 (d, 2H, J = 8.0 Hz); IR (thin film) cm^{-1} 2943 m, 2866 m, 1735w, 1357 m, 1165s; MS (ESI) m/e (% relative intensity) 498.2 (10) $(M + Na)^+$, 477.2 (20) $(M + 2H)^+$, 476.2 (100) $(M + H)^+$; HRMS (ESI) m/e calcd for $C_{25}H_{37}NO_4SSi^+$ $(M + H)^+$ 476.2286, found 476.2266.

Compound (±)-**65** (12 g, 42.94 mmol) was prepared in 72% yield over two steps according to the procedure reported by Hashmi.[25] R_f = 0.63 [1:4 EtOAc/hexanes]; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (d, 9H, J = 6.8 Hz), 1.09 (d, 9H, J = 6.8 Hz), 1.13−1.22 (m, 3H), 5.63 (s, 1H), 6.38 (dd, 1H, J = 2.0, 3.6 Hz), 6.52 (dd, 1H, J = 0.8, 3.6 Hz), 7.42 (dd, 1H, J = 0.8, 2.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.1, 17.7, 17.8, 58.4, 109.3, 110.8, 117.4, 143.7, 148.0; IR (neat) cm^{-1} 2945s, 2868 m, 1719w, 1463s, 1091s; MS (ESI) m/e (% relative intensity) 302.3 (100) $(M + Na)^+$, 253 (20) $(M - CN)^+$; HRMS (ESI) m/e calcd for $C_{15}H_{25}NO_2Si^+$ $(M + Na)^+$ 302.1547, found 302.1557.

Compound (±)-**66** (3.09 g, 7.06 mmol) was prepared in 66% yield over two steps according to the procedure reported by Hashmi.[25] R_f = 0.47 [1:4 EtOAc/hexanes]; white solid; mp = 41−42 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (d, 9H, J = 5.6 Hz), 0.95−1.03 (m, 12H), 2.42 (s, 3H), 3.22 (dt, 1H, J = 6.0, 12.0 Hz), 3.30 (dt, 1H, J = 6.0, 12.0 Hz), 4.63 (t, 1H, J = 6.0 Hz), 4.85 (t, 1H, J = 6.0 Hz), 6.22 (d, 1H, J = 3.2 Hz), 6.29 (dd, 1H, J = 1.2, 2.4 Hz), 7.29 (d, 2H, J = 8.0 Hz), 7.30 (brs, 1H), 7.70 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.3, 17.9, 18.0, 21.7, 48.2, 67.3, 108.0, 110.4, 127.3, 129.9, 137.0, 142.2, 143.6, 153.8; IR (neat) cm^{-1} 3289 m, 2944 m, 2865 m, 1738w, 1326s, 1160s; MS (ESI) m/e (% relative intensity) 461.4 (15) $(M + Na + H)^+$, 460.4 (100) $(M + Na)^+$; HRMS (ESI) m/e calcd for $C_{22}H_{35}NO_4SSi^+$ $(M + Na)^+$ 460.1949, found 460.1934.

Amide (±)-**62** (2.8 g, 5.88 mmol) was prepared in 95% yield according to the procedure reported by Hashmi.[25] R_f = 0.51 [1:4 EtOAc/hexanes]; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97 (d, 9H, J = 6.0 Hz), 1.02−1.05 (m, 3H), 1.03 (d, 9H, J = 6.0 Hz), 1.98 (t, 1H, J = 2.4 Hz), 2.41 (s, 3H), 3.40 (dd, 1H, J = 7.2, 14.4 Hz), 3.52 (ddd, 1H, J = 0.8, 6.4, 14.4 Hz), 3.62 (dd, 1H, J = 2.4, 18.4 Hz), 4.19 (ddd, 1H, J = 0.8, 2.4, 18.4 Hz), 5.08 (t, 1H, J = 6.8 Hz), 6.30 (dd, 1H, J = 0.8, 3.2 Hz), 6.32 (dd, 1H, J = 2.0, 3.2 Hz), 7.27 (d, 2H, J = 8.0 Hz), 7.37 (dd, 1H, J = 0.8, 2.0 Hz), 7.71 (d, 2H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 17.9, 18.1, 21.7, 38.5, 51.5, 68.4, 73.6, 77.4, 108.3, 110.5, 128.0, 129.6, 136.2, 142.1, 143.6, 154.5; IR (neat) cm^{-1} 3285 m, 2928 m, 2854 m, 1348s, 1159s; MS (ESI) m/e (% relative intensity) 499.2 (5) $(M + Na + H)^+$, 498.2 (30) $(M + Na)^+$, 493.3 (100); HRMS (ESI) m/e calcd for $C_{25}H_{37}NO_4SSi^+$ $(M + Na)^+$ 498.2105, found 498.2124.

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H NMR, ^{13}C NMR spectra, and X-ray structural data. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

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■ REFERENCES

(1) For excellent reviews on heteroatom-substituted oxyallyl cations, see: (a) Harmata, M. *Adv. Synth. Catal.* **2006**, *348*, 2297. (b) Harmata, M. *Recent Res. Dev. Org. Chem.* **1997**, *1*, 523. Also see:(c) Katritzky, A. R.; Dennis, N. *Chem. Rev.* **1989**, *89*, 827.

(2) For general reviews on [4 + 3] cycloadditions, see: (a) Harmata, M. *Chem. Commun.* **2010**, *46*, 8886 and 8904. (b) Battiste, M. A.; Pelphrey, P. M.; Wright, D. L. *Chem.—Eur. J.* **2006**, *12*, 3438. (c) Antoline, J. E.; Hsung, R. P. *ChemTracts* **2005**, *18*, 562. (d) Hartung, I. V.; Hoffmann, H. M. R. *Angew. Chem., Int. Ed.* **2004**, *43*, 1934. (e) Harmata, M.; Rashatasakhon, P. *Tetrahedron* **2003**, *59*, 2371. (f) Harmata, M. *Acc. Chem. Res.* **2001**, *34*, 595. Also see:(g) Davies, H. M. L. In *Advances in Cycloaddition*; Harmata, M., Ed.; JAI Press: Greenwich, CT, 1998; Vol. 5, p 119. (h) West, F. G. In *Advances in Cycloaddition*; Lautens, M., Ed.; JAI Press: Greenwich: 1997; Vol. 4, p 1. (i) Rigby, J. H.; Pigge, F. C. *Org. React.* **1997**, *51*, 351. (j) Harmata, M. *Tetrahedron* **1997**, *53*, 6235.

(3) For leading examples of oxygen-substituted oxyallyl cations, see: (a) Sáez, J. A.; Arnó, M.; Domingo, L. R. *Tetrahedron* **2005**, *61*, 7538. (b) Harmata, M.; Kahraman, M.; Adenu, G.; Barnes, C. L. *Heterocycles* **2004**, *62*, 583. (c) Sáez, J. A.; Arnó, M.; Domingo, L. R. *Org. Lett.* **2003**, *5*, 4117. (d) Funk, R. L.; Aungst, R. A. *Org. Lett.* **2001**, *3*, 3553. (e) Harmata, M.; Sharma, U. *Org. Lett.* **2000**, *2*, 2703. (f) Lee, K.; Cha, J. K. *Org. Lett.* **1999**, *1*, 523. (g) Masuya, K.; Domon, K.; Tanino, K.; Kuwajima, I. *J. Am. Chem. Soc.* **1998**, *120*, 1724. (h) Harmata, M.;

Elomari, S.; Barnes, C. J. *J. Am. Chem. Soc.* **1996**, *118*, 2860 and references therein.

(4) For examples of sulfur-substituted oxyallyl cations, see: (a) Hardinger, S. A.; Bayne, C.; Kantorowski, E.; McClellan, L. L.; Nuesse, M.-A. *J. Org. Chem.* **1995**, *60*, 1104. (b) Harmata, M.; Gamlath, C. B. *J. Org. Chem.* **1988**, *53*, 6156.

(5) For examples of halogen-substituted oxyallyl cations, see: (a) Harmata, M.; Wacharasindhu, S. *Org. Lett.* **2005**, *7*, 2563. (b) Lee, K.; Cha, J. K. *Org. Lett.* **1999**, *1*, 523.

(6) For oxidopyridinium ions: (a) Peece, K. M.; Gin, D. Y. *Org. Lett.* **2005**, *7*, 3323. (b) Sung, M. J.; Lee, H. I.; Chong, Y.; Cha, J. K. *Org. Lett.* **1999**, *1*, 2017. (c) Dennis, N.; Ibrahim, B.; Katritzky, A. R. *J. Chem. Soc., Perkin Trans.* **1976**, *1*, 2307. For phthalamide-substituted systems: (d) Walters, M. A.; Arcand, H. R. *J. Org. Chem.* **1996**, *61*, 1478 and references therein.

(7) For leading examples of nitrogen-stabilized oxyallyl cations in [4 + 3] cycloadditions, see: (a) Walters, M. A.; Arcand, H. R.; Lawrie, D. J. *Tetrahedron Lett.* **1995**, *36*, 23. (b) Walters, M. A.; Arcand, H. R. *J. Org. Chem.* **1996**, *61*, 1478.(c) Arcand, H. R. *Investigation of the reactivity of nitrogen-substituted oxyallyl cations (asymmetry, stereoselective)*. Ph.D. Thesis, Dartmouth College, 1996. (d) MaGee, D. I.; Godineau, E.; Thornton, P. D.; Walters, M. A.; Sponholtz, D. J. *Eur. J. Org. Chem.* **2006**, 3667. (e) Myers, A. G.; Barbay, J. K. *Org. Lett.* **2001**, *3*, 425.

(8) Xiong, H.; Hsung, R. P.; Berry, C. R.; Rameshkumar, C. *J. Am. Chem. Soc.* **2001**, *123*, 7174.

(9) For leading reviews on allenamides, see: (a) Hsung, R. P.; Wei, L.-L.; Xiong, H. *Acc. Chem. Res.* **2003**, *36*, 773. (b) Standen, P. E.; Kimber, M. C. *Curr. Opin. Drug Discovery Dev.* **2010**, *13*, 645. Also see: (c) Tracey, M. R.; Hsung, R. P.; Antoline, J.; Kurtz, K. C. M.; Shen, L.; Slafer, B. W.; Zhang, Y. In *Science of Synthesis, Houben-Weyl Methods of Molecular Transformations*; Weinreb, S. M. , Ed. Georg Thieme Verlag KG: Stuttgart, 2005; Chapter 21.4. (d) Deagostino, A.; Prandi, C.; Tabasso, S.; Venturello, P. *Molecules* **2010**, *15*, 2667.

(10) (a) Lohse, A. G.; Krenske, E.; Houk, K. N.; Hsung, R. P. *Org. Lett.* **2010**, *12*, 5506. (b) Antoline, J. E.; Hsung, R. P. *Synlett* **2008**, 739.

(11) For our work on nitrogen-stabilized oxyallyl cations in intermolecular [4 + 3] cycloadditions with furans and pyrroles, see: (a) Krenske, E. K.; Houk, K. N.; Lohse, A. G.; Antoline, J. E.; Hsung, R. P. *Chem. Sci.* **2010**, *1*, 387. (b) Antoline, J. E.; Hsung, R. P.; Huang, J.; Song, Z.; Li, G. *Org. Lett.* **2007**, *9*, 1275. (c) Rameshkumar, C.; Xiong, H.; Tracey, M. R.; Berry, C. R.; Yao, L. J.; Hsung, R. P. *J. Org. Chem.* **2002**, *67*, 1339. For our work in intramolecular [4 + 3] cycloadditions, see:(d) Rameshkumar, C.; Hsung, R. P. *Angew. Chem., Int. Ed.* **2004**, *43*, 615. (e) Xiong, H.; Huang, J.; Ghosh, S.; Hsung, R. P. *J. Am. Chem. Soc.* **2003**, *125*, 12694. For a recent account on intramolecular [4 + 3] cycloadditions of allenyl dienes employing $PtCl_2$ as a catalyst, see:(f) Trillo, B.; López, F.; Gulías, M.; Castedo, L.; Mascareñas, J. L. *Angew. Chem., Int. Ed.* **2007**, *47*, 951.

(12) For recent diastereoselective [4 + 3] cycloadditions, see: (a) Chung, W. K.; Lam, S. K.; Lo, B.; Liu, L. L.; Wong, W.-T.; Chiu, P. *J. Am. Chem. Soc.* **2009**, *131*, 4556. (b) Craft, D. T.; Gung, B. W. *Tetrahedron Lett.* **2008**, *49*, 5931. Davies, H. M. L.; Dai, X. *J. Am. Chem. Soc.* **2004**, *126*, 2693. (c) Prié, G.; Prévost, N.; Twin, H.; Fernandes, S. A.; Hayes, J. F.; Shipman, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 6517. (d) Grainger, R. S.; Owoare, R. B.; Tisselli, P.; Steed, J. W. *J. Org. Chem.* **2003**, *68*, 7899. (e) Montanã, A. M.; Grima, P. M. *Tetrahedron* **2002**, *58*, 4769. (f) Beck, H.; Stark, C. B. W.; Hoffman, H. M. R. *Org. Lett.* **2000**, *2*, 883 and ref 11 cited within. (g) Harmata, M.; Rashatasakhon, P. *Synlett* **2000**, 1419. (h) Cho, S. Y.; Lee, J. C.; Cha, J. K. *J. Org. Chem.* **1999**, *64*, 3394. (i) Harmata, M.; Jones, D. E.; Kahraman, M.; Sharma, U.; Barnes, C. L. *Tetrahedron Lett.* **1999**, *40*, 1831. (j) Kende, A. S.; Huang, H. *Tetrahedron Lett.* **1997**, *38*, 3353. (k) Harmata, M.; Jones, D. E. *J. Org. Chem.* **1997**, *62*, 4885.

(13) Huang, J.; Hsung, R. P. *J. Am. Chem. Soc.* **2005**, *127*, 50.

(14) For an account on asymmetric [4 + 3] cycloadditions that predated ours, see: (a) Harmata, M.; Ghosh, S. K.; Hong, X.; Wacharasindu, S.; Kirchhoefer, P. *J. Am. Chem. Soc.* **2003**, *125*, 2058. For an enantioselective formal [4 + 3] cycloaddition, see:(b) Dai, X.; Davies, H. M. L. *Adv. Synth. Catal.* **2006**, *348*, 2449.

(15) For some examples, see: (a) Grainger, R. S.; Owoare, R. B. *Org. Lett.* **2004**, *6*, 2961. (b) Vidal, P. M.; Proemmel, S.; Beil, W.; Wartchow, R.; Hoffmann, H. M. R. *Org. Lett.* **2004**, *6*, 4155. (c) Gillingham, D. G.; Kataoka, O.; Garber, S. B.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 12288. (d) Hoegermeier, J.; Reissig, H. -U.; Bruedgam, I.; Hartl, H. *Adv. Synth. Catal.* **2004**, *346*, 1868. (e) Lautens, M.; Fagnou, K.; Yang, D. *J. Am. Chem. Soc.* **2003**, *125*, 14884.

(16) Due to rotamers, many of the signals were not well resolved and/or line-broadened, and we were unable to obtain ^{13}C NMR data.

(17) Lohse, A. G.; Hsung, R. P. *Org. Lett.* **2009**, *11*, 3430.

(18) The base-promoted isomerization of allenamides with α- or γ-substituents require higher temperatures and longer reactions times.

(19) For a review on Hoffmann's notation, see: (a) Hoffmann, H. M. R. *Angew. Chem.* **1973**, *85*, 877; *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 819. See also:(b) Hoffmann, H. M. R.; Joy, D. R. *J. Chem. Soc. B* **1968**, 1182.

(20) DFT calculations were performed at the B3LYP/6-31G (d) level using *Spartan '10 Release 1.0.1v4*; Wave function Inc.: Irvine, CA 92612.

(21) Webster, R.; Lautens, M. *Org. Lett.* **2009**, *11*, 4688.

(22) (a) Sobhana Babu, B.; Balasubramanian, K. K. *J. Org. Chem.* **2000**, *65*, 4198. (b) Porzelle, A.; Gordon, V. A.; Williams, C. M. *Synlett* **2007**, 1619.

(23) Martinelli, M. J.; Nayyar, N. K.; Moher, E. D.; Dhokte, U. P.; Pawlak, J. M.; Vaidyanathan, R. *Org. Lett.* **1999**, *1*, 447.

(24) Because of the instability of the tosylate, it was carried on without further purification.

(25) Hashmi, A. S. K.; Ata, F.; Haufe, P.; Rominger, F. *Tetrahedron* **2009**, *65*, 1919.

(26) For reviews on enzyme catalysis with furfural, see: (a) Gregory, R. J. H. *Chem. Rev.* **1999**, *99*, 3649. (b) Wajant, H.; Effenberger, F. *Biol. Chem.* **1996**, *377*, 611.

(27) For leading references, see: (a) Bushey, M. L.; Haukaas, M. H.; O'Doherty, G. A. *J. Org. Chem.* **1999**, *64*, 2984. (b) Harris, J. M.; Keranen, M. D.; O'Doherty, G. A. *J. Org. Chem.* **1999**, *64*, 2982. Also see: (c) Taniguchi, T.; Nakamura, K.; Ogasawara, K. *Synlett* **1996**, 971. (d) Taniguchi, T.; Ohnishi, H.; Ogasawara, K. *Chem. Commun.* **1996**, 1477.

(28) Shen, L.; Hsung, R. P.; Zhang, Y.; Antoline, J. E.; Zhang, X. *Org. Lett.* **2005**, *7*, 3081.