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Generation of Functionalized Azepinone Derivatives via a (4 + 3)-Cycloaddition of Vinyl Ketenes and α-Imino Carbenes Derived from *N*-Sulfonyl-triazoles

Harrison M. Hill, Zachary D. Tucker, Kevin X. Rodriguez, Katelyn A. Wendt, and Brandon L. Ashfeld*

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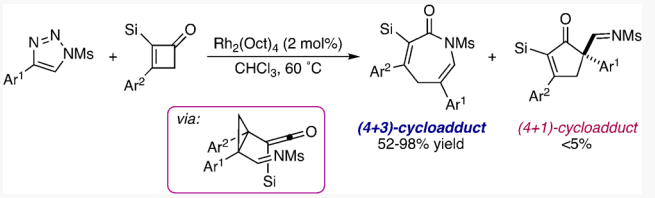
ABSTRACT: An intermolecular Rh^{II}-catalyzed, formal (4 + 3)-cycloaddition between vinyl ketenes and *N*-sulfonyl-1,2,3-triazoles for the construction of azepinone products is described. Employing vinyl ketenes as a 1,4-dipolar surrogate, instead of the more commonly used dienyl moieties, allows for the intermolecular and selective formation of azepinone products over a potential (3 + 2)-cycloadduct under mild reaction conditions allows for the generation of azepinone products in up to 98% yield.



Discovered in 1909, the Dimroth rearrangement marked the ring-opening tautomerization of select 1,2,3-triazoles to yield the corresponding α-diazo imine.[1] By exploiting this dynamic equilibrium, the ability to access metal-stabilized carbenes by employing masked, benchtop materials has led to the development of exquisite new methods in carbo- and heterocycle construction.[2−5] Early studies revealed that the triazole *N*-substituent was critical in shifting this equilibrium to the ring-opened diazo congener, highlighting an important structural parameter for the use of these substrates in synthesis.[1,6] In general, *N*-sulfonyl triazoles **1** proved superior compared to their *N*-alkyl counterparts at enabling adequate generation of the corresponding α-diazo imine **2**, which upon exposure to a transition metal complex (e.g., Rh^{II}, Cu^{II}, etc.) provides the metal-stabilized α-imino carbene **3** (Figure 1a).[7,8]

In recent years, α-imino carbenes **3** have played a central role in the development of transannulations,[8−10] cyclopropanations,[11,12] C−H functionalizations,[13] azomethine ylides in (3 + 2)-cycloadditions, and various other transformations leading to high value synthetic building blocks.[14] For example, a report from the Fokin group in 2013 illustrated the capability of Rh-stabilized carbenes derived from sulfonyl triazoles in N−H and O−H insertions to provide *Z*-dienamines with exceptional control of olefin stereochemistry (Figure 1b).[15] Additionally, Gevorgyan and co-workers demonstrated the utility of Co-stabilized carbenes derived from pyridotriazoles in a transannulation assembly of imino thiazolopyridines with isothiocyanates. Recent efforts have also shown that synthetically challenging medium- and large-membered heterocycles are accessible via (5 + 2)- and (4 + 3)-cycloadditions exploiting metallocarbenes derived from *N*-sulfonyl triazoles.[4,16]

Recently, *N*-tosyl triazoles were shown to participate in Rh-catalyzed (4 + 3)-cycloadditions to provide access to the challenging 7-membered heterocycles. However, (4 + 3)-cycloadditions involving triazoles are often complicated by competitive (3 + 2)-cycloadditions leading to 5-membered nitrogen heterocycles. For example, in 2014 Tang and co-workers[4] reported the Rh^{II}-catalyzed (4 + 3)-cyclization of *N*-tosyl triazole and 1,3-dienes to provide the desired azepines, albeit at relatively high reaction temperatures (Figure 2a). Over the course of their study, they found that the substitution pattern and olefin geometry of the 1,3-diene played a critical role in whether the (4 + 3)-cycloadduct or the dihydropyrrole resulting from a (3 + 2)-cycloaddition was observed. For example, *trans*-1,3-dienes bearing aryl substituents at C1 or C2 favored azepine formation, whereas *cis*-1,3-dienes with C1-alkyl substituents led to selective formation of the (3 + 2)-cycloadducts. In a related study, Sarpong and co-workers[17] reported a highly diastereoselective and chemoselective, Rh^{II}-catalyzed, intramolecular (4 + 3)-cycloaddition for the formation of fused bicyclic azepines, but under substantially more mild conditions as compared to the study above (Figure 2b). Azepine formation presumably occurs via an initial Rh^{II}-catalyzed cyclopropanation of the 1,3-diene followed by an *aza*-Cope rearrangement that is commensurate with divinyl cyclopropane rearrangements[18−21] to give the resulting *N*-heterocycle. While the work from Tang and Sarpong demonstrated the capabilities of accessing the azepine scaffold, selectivity appeared dependent upon the structural attributes of the 1,3-diene component.

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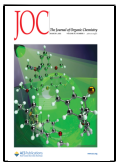

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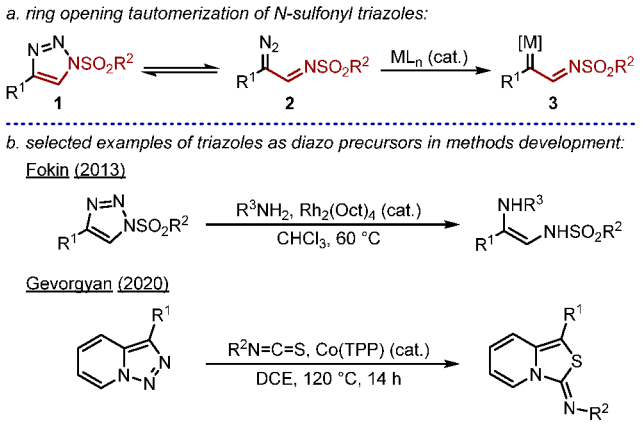

Figure 1. Ring opening of triazole **1** to α-imino diazo compound **2** and subsequent rhodium carbenoid formation. Select reactions utilizing triazole starting materials. (a) Stereoselective formation of diamine products. (b) Formation of imino-thiazolopyridine products.

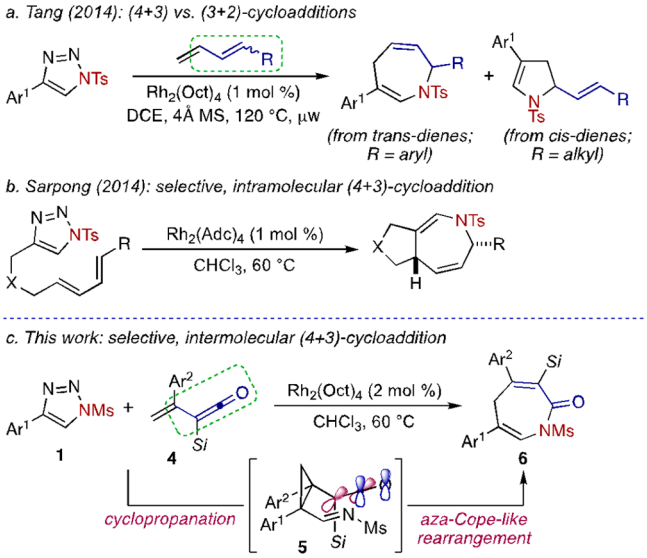

Figure 2. (4 + 3)-Cycloadditions employing *N*-sulfonyl-triazoles: (a) Intermolecular (4 + 3)-cycloaddition reaction with substituted dienes; (b) Selective intramolecular (4 + 3)-cycloadditions; (c) This work: employing vinyl ketenes in place of 1,3-dienes.

Inspired by these seminal contributions, we sought to address this challenge of selective azepine formation through the use of an alternative 1,4-dipole surrogate wherein the reliance on olefin geometry is avoided and formation of the 7-membered ring is accelerated so as to avoid often forcing conditions. We speculated that the use of vinyl ketenes as 1,4-dipole surrogates, in place of a 1,3-diene, would yield a selective, intermolecular, Rh^{II}-catalyzed (4 + 3)-cycloaddition under conditions comparable to the intramolecular variant explored above. Over the course of our previous studies on the development of (4 + 1)-cycloadditions employing vinyl ketenes and vinyl isocyanates, we observed a substantial rate enhancement in the penultimate vinyl cyclopropane rearrangement leading to cyclopentenone and pyrrolidinone formation, respectively.[22,23] Based on our subsequent mechanistic studies[24] and related transformations[25,26] in the literature, we surmised that the observed rate enhancement was due to the highly polarized nature of the ketene/isocyanate and the presence of the orthogonal p-orbitals on the sp-hybridized central cumulene carbon leading to improved orbital overlap in the transition state. Therefore, we envisioned a similar rate enhancement upon exposure of *N*-methanesulfonyl triazole **1** to a Rh^{II}-catalyst and vinyl ketene **4**, whereupon the polarized ketene functionality present in the intermediate cyclopropyl ketene **5** would promote an *aza*-[3,3]-rearrangement to yield azepinone **6** (Figure 2c).

Of the common medium-sized *N*-heterocyclic compounds, the benzodiazepine, azepine, and azepinone scaffolds are of particular interest to synthetic and medicinal chemists due to their prevalence in biologically active small molecules.[14,16,17,27−30] A number of biologically relevant natural products and designed small molecules bearing the azepine, azepinone, and benzodiazepine frameworks, such as glantamine, cephalotaxine, and sclerotigenin, have shown promise as treatments for anxiety[31] and Alzheimer's disease,[32] while others have demonstrated antibacterial activity[33−36] and insecticidal properties (Figure 3).[37,38] The prevalence of this motif in small molecules that have exhibited a wide array of translational potential has inspired the continued growth of new and efficient methods for their assembly.

We began our study by examining the Rh^{II}-catalyzed cycloaddition of *N*-tosyl triazole **1a** and vinyl ketene precursor cyclobutenone **7a** (Scheme 1). While treatment with Rh$_2$(OAc)$_4$ (2 mol %) at 60 °C led to a mere 16% of azepine **6a**, we were encouraged to find that no evidence of the corresponding (4 + 1)-cycloadduct emerged. It is noteworthy that extended reaction times and elevated temperatures led to an increasingly complex mixture of products. Interestingly, when the chiral catalyst Rh$_2$(*S*-TCPTTL)$_4$ was employed, we observed substantially improved reactivity, but the combined yield of 87% comprised **6a** and **8a** in a 1:1.35 ratio. It is worth noting that the intermediate imine-bearing (4 + 1) cycloadduct proved unstable to the purification conditions and was therefore characterized as the amine. Encouraged by the selectivity we observed with the vinyl ketene **4a** in the presence of Rh$_2$(OAc)$_4$, we embarked on a closer evaluation of the reaction parameters.

A key consideration when employing *N*-sulfonyl triazoles in metallocarbene-mediated transformations is the accessibility of diazo intermediate **2** and the role the *N*-sulfonyl group plays in the position of this equilibrium. Exchanging the *N*-tosyl triazole **1a** for the *N*-mesyl derivative **1b** led to an improved yield in the formation of azepinone **6b** in the presence of Rh$_2$(OAc)$_4$ (Table 1, entry 1). While the Rh^{II} complex Rh$_2$(esp)$_2$ failed to provide either **6b** or **8**, a slight improvement in the yield of **6b** was observed in the presence of Rh$_2$(Oct)$_4$ (entries 2 and 3). Increasing the reaction temperature to either 80 °C or 100 °C failed to significantly improve the yield of **6b**. While alternating the α-silyl group on

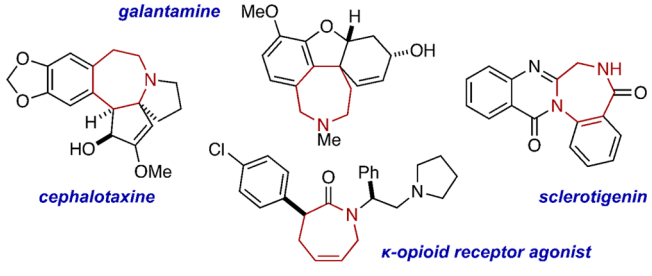

Figure 3. Azepine and azepinone natural products and therapeutics.

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Scheme 1. Initial Findings

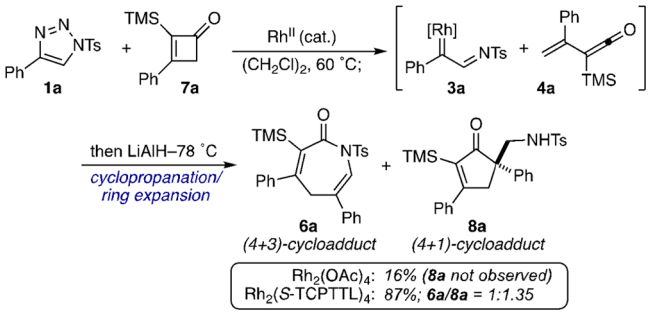
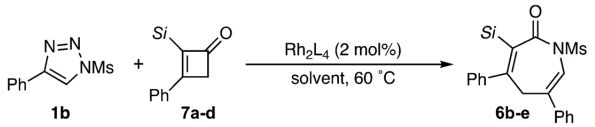


Table 1. Optimization of Reaction Conditions[a]



entry	catalyst	solvent	7	yield(%)
1	$Rh_2(OAc)_4$	$(CH_2Cl)_2$	TMS (**7a**)	40 (**6b**)
2	$Rh_2(esp)_2$	$(CH_2Cl)_2$	TMS (**7a**)	0 (**6b**)
3	$Rh_2(Oct)_4$	$(CH_2Cl)_2$	TMS (**7a**)	45 (**6b**)[b]
4	$Rh_2(Oct)_4$	$(CH_2Cl)_2$	TES (**7b**)	31 (**6c**)
5	$Rh_2(Oct)_4$	$(CH_2Cl)_2$	TIPS (**7c**)	23 (**6d**)
6	$Rh_2(Oct)_4$	$(CH_2Cl)_2$	TBS (**7d**)	50 (**6e**)
7	$Rh_2(Oct)_4$	THF	TBS (**7d**)	0 (**6e**)
8	$Rh_2(Oct)_4$	MeCN	TBS (**7d**)	0 (**6e**)
9	$Rh_2(Oct)_4$	DMF	TBS (**7d**)	0 (**6e**)
10	$Rh_2(Oct)_4$	CH_2Cl_2	TBS (**7d**)	46 (**6e**)
11	$Rh_2(Oct)_4$	PhMe	TBS (**7d**)	26 (**6e**)
12	*$Rh_2(Oct)_4$*	*$CHCl_3$*	*TBS (**7d**)*	*83 (**6e**)*
13	$Rh_2(Oct)_4$	$CHCl_3$	TBS (**7d**)	81 (**6e**)[c]

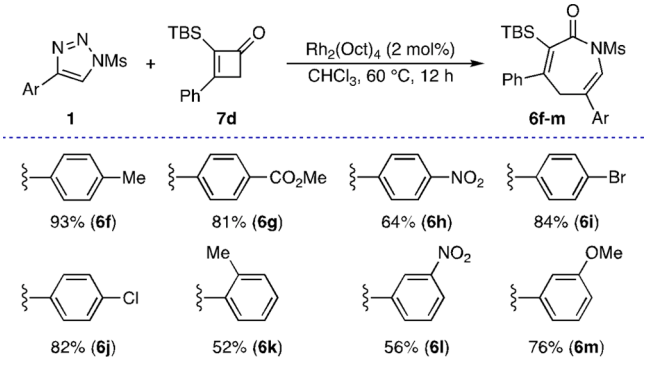
[a]Conditions: **1b** (1.0 equiv), **7** (3.0 equiv), and Rh_2L_4 (2 mol %) at 0.1 M. [b]At 80 °C, **6b** was obtained in 36% yield. [c]Reaction run on 1 mmol scale. Less than 5% of the (4 + 1)-cycloadduct **8** was observed in each case.

cyclobutenone **7** from TMS to either TES or TIPS led to the formation of azepinones **6c** and **6d** in 31% and 23% yields, respectively, employing the α-TBS cyclobutenone **7d** resulted in a 50% yield of **6e** (entries 4–6). Finally, a survey of different solvents revealed that polar, coordinating solvents, such as THF, MeCN, and DMF, failed to provide the cycloadduct, while nonpolar solvents such as CH_2Cl_2 and PhMe gave **6e** in 46% and 26% yields, respectively (entries 7–11). However, performing the reaction in $CHCl_3$ with cyclobutenone **7d** in the presence of $Rh_2(Oct)_4$ led to selective formation of the target azepinone **6e** in 83% yield (entry 12). It is noteworthy that the *N*-nosyl and *N*-SO_2(2,6-$MeOC_6H_4$) derivatives were also investigated under these optimized reaction conditions, but failed to provide **6b** in greater than trace yield with either triazole. Speculating that perhaps trace amounts of HCl present in the $CHCl_3$ used was responsible for the improved yield, we replicated the experiment conducted in CH_2Cl_2 with 5% aqueous HCl (entry 10). However, cycloadduct **6b** was obtained in a diminished 41% yield compared to what was observed in the absence of HCl (46%), indicating that this potential contaminant of $CHCl_3$ was not responsible for the increase in yield. With our optimized conditions in hand, we then turned our attention toward examining the impact of structural variations of the aryl rings in triazole **1** and cyclobutenone **7**.

In general, the (4 + 3)-cycloaddition of various *N*-mesyl triazoles **1** with cyclobutenone **7d** under our optimized conditions led to good to excellent yields of the corresponding azepinones (Table 2). Substitution of the *para*-position of the aryl group was well tolerated, providing cycloadducts **6f–j** in 64–91% yields. Although the presence of an electron-withdrawing ester, bromide, or chloride at the 4-position of the aryl ring in **1** gave the corresponding cycloadducts in 81–84% yields, introduction of a nitro group at that position resulted in a slightly diminished yield of 64% for cycloadduct **6h**. Similarly, methyl substitution at the more sterically demanding *ortho*-position led to a moderate decrease in yield (**6k**), as did the presence of a 3-nitro group (**6l**). In contrast, the electron-donating methoxy group at the 3-position gave cycloadduct **6m** in 76% yield. It is worth noting that *N*-sulfonyl triazoles bearing alkyl (^{n}Bu) and vinyl (isoprenyl) substituents in place of the phenyl ring at the 4-position of the triazole resulted in quantitative recovery of the parent heterocycle. This is likely a consequence of the relative inaccessibility of α-imino diazo compound **2** in the absence of a donor stabilizing aryl substituent at the α-position, thereby leading to the parent triazole as the favored isomer.

The evaluation of various 3-aryl substituted cyclobutenones **7** in the (4 + 3)-cycloaddition with triazole **1b** revealed a general tolerance for both electron-withdrawing and electron-donating substituents to provide the corresponding cycloadducts **6n–u** in moderate to excellent yields (Table 3). Substitution at the 4-position of the aryl ring gave cycloadducts **6n–q** in 38–98% yield for alkyl, aryl, alkoxy, and chloride substituents. While naphthalene-substituted cyclobutenone provided cycloadduct **6r** in 56% yield, *ortho*-methyl substitution failed to provide the anticipated cycloadduct. A comparison of cycloadditions to provide azepinones **6k** and **6s** would seem to indicate that while steric encumbrance at the *ortho*-position hinders cycloadduct formation, the effect is substantially more pronounced in the intermediate vinyl ketene component. Additionally, both methoxy and nitro substitution at the 3-position of the aryl ring led to a reduced yield of the cycloadduct. This result also contrasts with the significant difference in yield observed between the comparable

Table 2. Variations of the *N*-Sulfonyl Triazole 1[a]



[a]Conditions: **1** (1.0 equiv), **7d** (3.0 equiv), and $Rh_2(Oct)_4$ (2 mol %) in $CHCl_3$ (0.1 M). Less than 5% of the (4 + 1)-cycloadduct **8** was observed in each case.

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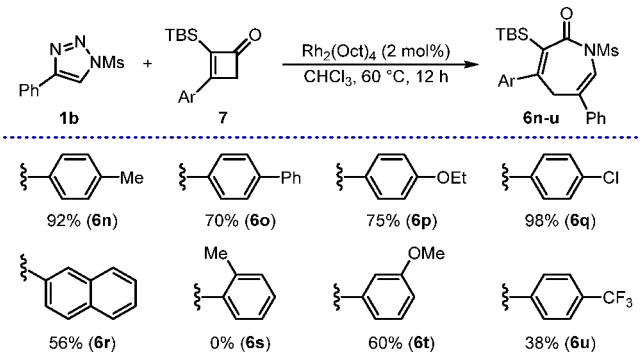
Table 3. Variations of the Cyclobutenone 7[a]



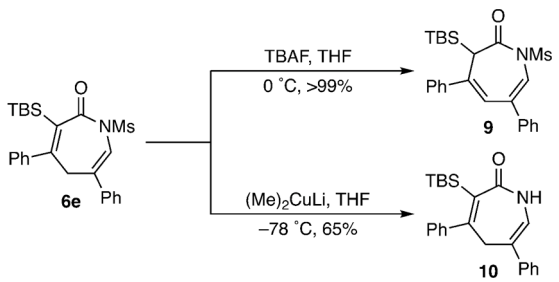
[a]Conditions: **1b** (1.0 equiv), **7** (3.0 equiv), and $Rh_2(Oct)_4$ (2 mol %) in $CHCl_3$ (0.1 M). Less than 5% of the (4 + 1)-cycloadduct **8** was observed in each case.

substitution pattern on the triazole, as illustrated in the formation of cycloadducts **6l** and **6m**.

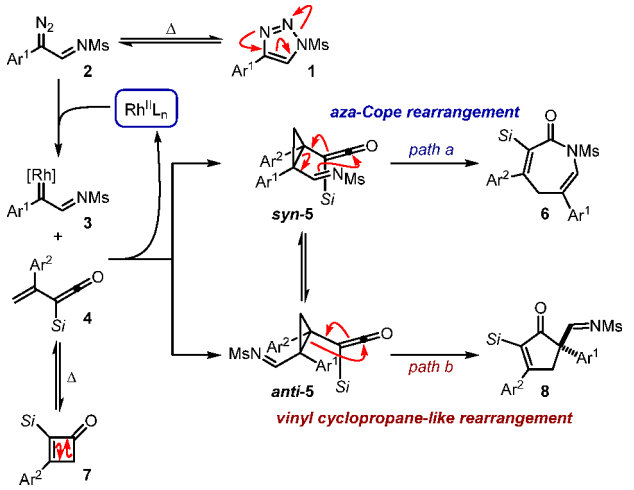
As we sought to demonstrate the synthetic utility of azepinones **6**, we discovered rather intriguing and unanticipated reactivity related to this heterocyclic motif. For example, attempts to proto-desilylate azepinone **6e** by employing TBAF did not lead to removal of the α-TBS group, but rather resulted in olefin isomerization to generate the vinylogous enamine **9** in quantitative yield (Scheme 2). We hypothesize that this unexpected olefin isomerization could possibly result from γ-deprotonation followed by subsequent α-reprotonation. Perhaps even more surprising, the addition of Me_2CuLi to **6e** did not provide the anticipated conjugate addition product, but instead yielded desulfonylated lactam **10** in 65% yield. We postulate that this unexpected transformation can be attributed to trace water in our THF in the presence of $(Me)_2CuLi$ resulting in the loss of the mesyl group on **6e** via an analogous mechanism observed when deprotecting *N*-tosyl protected sulfonyl triazoles.[39] That said, the mechanisms described above are purely speculative. These results provide a template for the development of further transformations starting from the azepinone building block for the construction of more functionally diverse heterocyclic scaffolds.

Based on the composite results of this study, our previous work on the development of cycloadditions with vinyl ketenes and vinyl isocyanates with metallocarbenes, and related studies involving metallocarbenes derived from *N*-sulfonyl triazoles, a possible mechanism for the formation of azepinones **6** is shown in Scheme 3. A heat-driven, electrocyclic ring-opening of cyclobutenone **7** generates vinyl ketene **4**, and generation of α-imino diazo compound **2** from triazole **1** precedes diazo

Scheme 2. Selected Transformations Involving Azepinone 6e



Scheme 3. Possible Mechanism for Azepinone Formation



decomposition in the presence of $Rh_2(Oct)_4$ to yield metallocarbene **3**. The key cyclopropanation of vinyl ketene **4** may lead to two diastereomeric cyclopropyl ketene intermediates ***syn*-5** and ***anti*-5**. An *aza*-Cope-like rearrangement of ***syn*-5** leads to azepinone **6** whereas a vinyl cyclopropane-like ring expansion from ***anti*-5** yields cyclopentenone **8**. Given the often highly diastereoselective outcomes of cyclopropanations involving donor−acceptor diazo compounds,[4,17,22−24] it is conceivable that the high degree of selectivity observed for the formation of azepinone **6** results from a similarly diastereoselective cyclopropanation event to provide primarily ***syn*-5**. However, competing pathways involving isomerization of ***anti*-5** to ***syn*-5**, or a reversion of cyclopentenone **8** to azepinone **6** under the reaction conditions, are not without precedent. Unfortunately, all attempts to isolate or visualize the intermediate cyclopropyl ketene by NMR were unsuccessful owing to the rapid formation of **6** under the reaction conditions. Our previous success in isolating cyclopropyl ketenes derived from diazo oxindoles, combined with the rapid seven-membered ring formation, presumably as a result of the highly polarized nature of the ketene moiety in **5**, would seem to suggest that our inability to observe ***anti*-5** is a result of a highly diastereoselective cyclopropanation that ultimately minimized competitive formation of cyclopentenone **8**. Additionally, the comparatively low level of product selectivity when the chiral catalyst $Rh_2(S\text{-TCPTTL})_4$ was employed is consistent with our earlier discovery that this catalyst favored the corresponding *anti*-diastereomer with diazo oxindoles, thereby implicating the diastereoselectivity of the cyclopropanation in product distribution.

In conclusion, we have developed an intermolecular Rh^{II}-catalyzed formal (4 + 3)-cycloaddition of vinyl ketenes and α-imino carbenes derived from *N*-sulfonyl-1,2,3-triazoles for the synthesis of an azepinone framework that bears a diverse array of translational potential. This intermolecular reaction circumnavigates issues observed in analogous reports investigating (4 + 3)-cycloaddition reactions with *N*-sulfonyl triazoles associated with competitive (3 + 2)-cycloadditions as a result of structural attributes of diene moieties by utilizing vinyl ketenes as a 1,4-dipolar surrogate. The reaction mechanism likely involves an initial diastereoselective cyclopropanation of the vinyl ketene moiety which then generates azepinone products through a rapid *aza*-Cope-like rearrangement under

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milder reaction conditions than the previously established protocols. Efforts to develop a protocol for the selective generation of the 5-membered cyclopentenone are currently under investigation and will be reported in due course.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, solvents and reagents were reagent grade and used without purification. Acetonitrile (MeCN), methylene chloride (CH_2Cl_2), diethyl ether (Et_2O), dimethylformamide (DMF), tetrahydrofuran (THF), and toluene (PhMe) were passed through a column of molecular sieves and stored under argon. Aldehydes, if liquid, were distilled under vacuum and stored under nitrogen. Triazoles **1** and cyclobutenones **7a–d** were synthesized *via* reported methods.[22,40,41] ^{1}H nuclear magnetic resonance (NMR) spectra were obtained at 400 or 500 MHz, $^{13}C\{^1H\}$ NMR were obtained at 100 or 125 MHz. Chemical shifts are reported in parts per million (ppm, δ) and referenced from the solvent. Coupling constants are reported in hertz (Hz). Spectral splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; comp, complex; app, apparent; and br, broad. High- and low-resolution electrospray ionization (ESI) measurements were made with a micro time-of-flight mass spectrometer (microTOF-MS) JEOL JMS-AX505HA. Analytical thin layer chromatography (TLC) was performed using EMD 250 μm 60 F254 silica gel plates, visualized with UV light, and stained with *p*-anisaldehyde, ceric ammonium nitrate, or potassium permanganate solutions. Flash column chromatography was performed according to Still's procedure (Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923) using Silicycle SiliaFlash P60 40–63 μm 60 Å silica gel.

General Procedure for the Synthesis of Silyl-Protected Alkynes. A solution of ^{n}BuLi (1.2 equiv) was added dropwise to a solution of phenylacetylene derivative (1.0 equiv) in THF (0.30 M) under an inert atmosphere at −78 °C. The resulting solution was allowed to stir for 30 min, and then *tert*-butyldimethylsilyl chloride (1.2 equiv) was added dropwise. The reaction was then allowed to warm to room temperature by removal of the dry ice/acetone bath and stirred for an additional 2 h. The crude mixture was diluted with H_2O (15 mL), the layers were separated, and the aqueous phase was extracted with Et_2O (3 × 15 mL). The combined organic extracts were washed sequentially with saturated aqueous $NaHCO_3$ (3 × 15 mL) and saturated aqueous NaCl (3 × 15 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The resulting silyl-protected alkynes were carried forward without further purification.

General Procedure for the (2 + 2)-Cyclization and Reductive Dechlorination. A solution of trichloroacetylchloride (1.2 equiv) in Et_2O (0.30 M) was added slowly to a refluxing solution of silyl-protected alkyne (1.0 equiv) and Zn/Cu (3.0 equiv) in Et_2O (0.46 M) over 3 h and then stirred for an additional 15 h. The mixture was cooled to room temperature by removal of the oil bath, and the heterogeneous mixture was filtered through a pad of Celite eluting with Et_2O (30 mL). The filtrate was washed sequentially with saturated aqueous $NaHCO_3$, H_2O, and saturated aqueous NaCl (30 mL each). Then the organic extract was dried (Na_2SO_4) and concentrated under reduced pressure. The crude 4,4-dichlorocyclobutenone was utilized without further purification.

A solution of crude 4,4-dichlorocyclobutenone (1.0 equiv) in ethanol (0.3 M) was added slowly to a mixture of zinc (5.8 equiv), *N,N,N′,N′*-tetramethylethylenediamine (5.8 equiv), and acetic acid (5.8 equiv) in ethanol (0.2 M) at 0 °C over 20 min. The reaction mixture was allowed to warm to room temperature by removal of the ice bath, stirred for 3 h, then diluted with 1:1 hexanes/Et_2O (20 mL), and filtered through a pad of Celite. The filtrate was washed sequentially with saturated aqueous $NaHCO_3$, H_2O, and saturated aqueous NaCl, dried (Na_2SO_4), and concentrated under reduced pressure [note: rotary evaporator bath temperature not to exceed 40 °C]. The crude mixture was purified by flash chromatography eluting with hexanes/EtOAc (98:2) to provide the title α-silylcyclobutenones **7**. [Note: cyclobutenones were stored in a 4 °C refrigerator until needed. Prolonged storage required repurification prior to use.]

*2-(tert-Butyldimethylsilyl)-3-(p-tolyl)cyclobut-2-en-1-one (**7e**).* The synthesis of **7e** began from 1-ethynyl-4-methylbenzene. The (2 + 2)-cyclization and reductive dichlorination were conducted on a 2.5 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (98:2) to provide 191 mg (28%) of **7e** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.2 Hz, 2H), 3.70 (s, 2H), 2.43 (s, 3H), 0.97 (s, 9H), 0.29 (s, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 191.7, 178.0, 146.6, 142.5, 129.6, 129.5, 112.8, 111.6, 52.4, 26.9, 21.9, 18, −4.7. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{25}OSi$ 273.1675; Found 273.1669.

*3-([1,1′-Biphenyl]-4-yl)-2-(tert-butyldimethylsilyl)cyclobut-2-en-1-one (**7f**).* The synthesis of **7f** began from 4-ethynyl-1,1′-biphenyl. The (2 + 2)-cyclization and reductive dichlorination were conducted on a 1.4 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (98:2) to provide 205 mg (44%) of **7f** as a yellow oil. ^{1}H NMR (500 MHz $CDCl_3$) δ 8.09 (d, J = 0.7 Hz, 1H), 7.96–7.84 (m, 4H), 7.80 (dd, J = 8.6, 1.8 Hz, 1H), 7.64–7.53 (m, 2H), 3.85 (s, 7H), 1.01 (s, 9H), 0.35 (s, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 191.7, 177.8, 148.2, 134.7, 133.1, 131.2, 130.5, 129.3, 128.5, 128.4, 128.2, 128.1, 127.2, 125.5, 77.5, 77.2, 77.0, 52.6, 27.0, 26.9, 26.9, 18.2, −4.6. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{27}OSi$ 335.1831; Found 335.1826

*2-(tert-Butyldimethylsilyl)-3-(4-ethoxyphenyl)cyclobut-2-en-1-one (**7g**).* The synthesis of **7g** began from 1-ethoxy-4-ethynylbenzene. The (2 + 2)-cyclization and reductive dichlorination were conducted on a 1.1 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (98:2) to provide 131 mg (39%) **7g** as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 8.9 Hz, 2H), 6.97 (d, J = 8.9 Hz, 2H), 4.11 (q, J = 6.9 Hz, 2H), 3.68 (s, 2H), 1.46 (t, J = 6.9 Hz, 3H), 0.96 (s, 9H), 0.29 (s, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 191.5, 177.2, 161.7, 144.2, 131.5, 126.1, 114.5, 63.8, 52.0, 26.7, 18.0, −4.9. HRMS (ESI) m/z: [M + H]+ Calcd for $C_{18}H_{26}O_2Si$ 303.1780; Found 303.1775

*2-(tert-Butyldimethylsilyl)-3-(4-chlorophenyl)cyclobut-2-en-1-one (**7h**).* The synthesis of **7h** began from 1-chloro-4-ethynylbenzene. The (2 + 2)-cyclization and reductive dichlorination were conducted on a 2.5 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (98:2) to provide 151 mg (26%) of **7h** as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.6 Hz, 2H), 7.45 (d, J = 8.6 Hz, 2H), 3.71 (s, 2H), 0.95 (s, 9H), 0.27 (s, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 181.0, 172.5, 163.7, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 126.4, 120.7, 114.1, 43.4, 40.2, 27.8, 26.9, −2.8. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{22}ClOSi$ 293.1128; Found 293.1123

*2-(tert-butyldimethylsilyl)-3-(naphthalen-2-yl)cyclobut-2-en-1-one (**7i**).* The synthesis of **7i** began from 2-ethynylnaphthalene. The (2 + 2)-cyclization and reductive dichlorination were conducted on a 1.2 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (98:2) to provide 150 mg (41%) of **7i** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, J = 2.7 Hz, 3H), 7.68–7.63 (d, J = 2.7 Hz, 2 H), 7.49 (t, J = 7.5 Hz, 1H), 7.41 (t, J = 7.5 Hz, 1H), 3.77 (s, 2H), 1.00 (s, 9H), 0.33 (s, 6H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 191.6, 177.4, 147.6, 144.4, 140.0, 132.5, 130.0, 129.2, 129.0, 128.5, 127.7, 127.5, 127.4, 127.3, 127.2, 77.5, 77.3, 77.0, 52.5, 27.0, 26.9, 26.9, 18.2, −4.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{25}OSi$ 309.1675; Found 309.1669

*2-(tert-Butyldimethylsilyl)-3-(3-methoxyphenyl)cyclobut-2-en-1-one (**7j**).* The synthesis of **7j** began from 1-ethynyl-3-methoxybenzene. The (2 + 2)-cyclization and reductive dichlorination were conducted on a 2 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (98:2) to provide 191 mg (28%) of **7j** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (t, J = 7.9 Hz, 1H), 7.22 (d, J = 7.9 Hz, 1H), 7.18 (s, 1H), 7.03 (ddd, J = 8.3, 2.6, 1.0 Hz, 1H), 3.85 (s, 3H), 3.71 (s, 2H), 0.97 (s, 9H), 0.29 (s, 6H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 191.6, 178.0, 159.9, 134.9, 129.9, 122.1, 117.8, 114.0, 77.5, 77.3, 77.0, 65.6, 55.7, 52.6, 44.5, 41.0, 29.2, 27.0, 26.9, 26.8, 26.1, 18.1, −4.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{25}O_2Si$ 289.1624; Found 289.1618

*2-(tert-Butyldimethylsilyl)-3-(4-(trifluoromethyl)phenyl)cyclobut-2-en-1-one (**7k**).* The synthesis of **7k** began from 1-ethynyl-4-

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trifluoromethylbenzene. The (2 + 2)-cyclization and reductive dichlorination were conducted on a 0.5 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (98:2) to provide 51 mg (31%) of **7k** as a yellow oil ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, J = 8.8 Hz, 2H), 7.43 (d, J = 8.8 Hz, 2H), 3.55 (s, 2H), 0.91 (s, 9H), 0.14 (d, J = 8.3 Hz, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 208.6, 206.1 149.4, 128.8, 127.1, 126.0, 61.1, 55.4, 31.4, 26.8, −7.1; HRMS (ESI) m/z: $[M + H]^+$ Calc'd for $C_{17}H_{22}F_3OSi$ 327.1392; Found 327.1387

Synthesis of 4,6-Diphenyl-1-tosyl-3-(trimethylsilyl)-1,5-dihydro-2H-azepin-2-one ***6a*** *and 4-Methyl-N-((2-oxo-1,4-diphenyl-3-(trimethylsilyl)cyclopent-3-en-1-yl)methyl)benzenesulfonamide* ***8a***. To a flame-dried 2-dram vial equipped with a magnetic stir bar were added cyclobuteneone **7a** (59 mg, 0.27 mmol, 2.0 equiv) and triazole **1a** (40 mg, 0.13 mmol, 1 equiv). The vessel was sealed with a rubber septum, evacuated, and refilled with nitrogen three times then was charged with $(CH_2Cl)_2$ (2.6 mL, 0.05M). To the stirring solution was added Rh_2(S-TCPTTL)$_4$ (4.5 mg, 0.003 mmol, 2 mol %), then the vessel was sealed with a screw cap, and the reaction mixture was immediately brought to 75 °C via a preheated mineral oil bath. The reaction was monitored by TLC, and upon consumption of **1** (3 h) the reaction was cooled to room temperature by removal from the oil bath and concentrated under reduced pressure. The crude reaction mixture was then reconstituted in THF (2.6 mL, 0.05 M) and cooled to −78 °C with a dry ice/acetone bath. To the stirring solution was added $LiAlH_4$ (7.4 mg, 0.20 mmol, 1.5 equiv), which was allowed to come to room temperature over 15 h. The mixture was then cooled to −78 °C with a dry ice/acetone bath, treated with 0.25 mL of MeOH, and allowed to warm to room temperature via removal from the cooling bath. The crude reaction mixture was diluted with H_2O (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic fractions were washed with saturated aqueous NaCl (2 × 10 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography eluting with hexanes/EtOAc (10:1) with 1% NEt_3 to hexanes/EtOAc (4:1) to provide 21.3 mg (34% yield) of **6a** as a yellow oil and 21.4 mg (38% yield) of **8a** as a yellow film (mixture of silyated and desilyated isomers). **6a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.0 Hz, 2H), 7.47−7.37 (m, 5H), 7.34 (d, J = 8.0 Hz, 2H), 7.22−7.12 (m, 3H), 6.88 (d, J = 8.0 Hz, 2H), 3.31 (s, 2H), 2.44 (s, 3H), −0.24 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 171.1, 163.6, 145.0, 142.0, 137.7, 136.7, 136.4, 129.4, 128.9, 128.8, 128.3, 128.2, 127.0, 126.4, 121.4, 116.4, 38.7, 21.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{28}H_{30}NO_3SSi$ 488.1716; Found 488.1710. **8a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67−7.52 (m, 2H), 7.44−7.27 (m, 7H), 7.25−7.15 (m, 6H), 4.73 (d, J = 7.2 Hz, 1H), 3.70 (s, 2H), 3.37−3.26 (d, J = 16.7 Hz, 1H), 3.00 (d, J = 16.7 Hz, 1H), 2.42 (s, 3H), 0.00 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 143.7, 140.2, 139.4, 130.0, 130.0, 129.6, 129.2, 129.1, 128.9, 128.3, 128.2, 128.0, 128.0, 127.4, 127.2, 127.2, 127.0, 126.7, 85.5, 67.3, 55.9, 51.7, 45.9, 45.9, 21.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{28}H_{32}NO_3SSi$ 490.1872; Found 490.1867.

General Procedure for Formal (4 + 3)-Cycloaddition of 3a−3v. To a flame-dried 2-dram vial equipped with a magnetic stir bar were added **7** (3 equiv) and $CHCl_3$ (0.2 M) followed by heating to 90 °C via preheated mineral bath for 30 min. To a separate flame-dried 2-dram vial equipped with a magnetic stir bar were added **1** (1 equiv) and $Rh_2(Oct)_4$ (2.0 mol %) in $CHCl_3$ (0.2 M), and to this solution was added the solution of **7** via syringe followed by heating at 60 °C for 12 h. The reaction was monitored by TLC, and upon consumption of **1** (∼12 h) the reaction was cooled to room temperature by removal from the oil bath. The crude reaction mixture was then concentrated under reduced pressure. The residue was purified by column chromatography with silica gel eluting with hexanes/ethyl acetate (8:2).

3-(tert-Butyldimethylsilyl)-1-(methylsulfonyl)-4,6-diphenyl-1,5-dihydro-2H-azepin-2-one ***(6e)***. The cycloaddition of **6e** was conducted on a 0.10 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (8:2) to provide 37.7 mg (83%) of the title compound as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (m, 6H), 7.22 (m, 2H), 7.00−6.94 (d, 2H), 6.92 (s, 1H), 3.54 (s, 3H), 3.41 (s, 2H), 0.85 (s, 9H), −0.22 (s, 6H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 172.5, 165.0, 141.9, 137.2, 137.0, 133.1, 128.8, 128.3, 128.1, 128.1, 127.3, 126.3, 125.2, 120.5, 77.3, 77.0, 76.7, 60.4, 43.1, 40.1, 27.6, 18.4, 14.2, 0.0, −3.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{32}NO_3SSi$ 454.1872; Found 454.1867.

3-(tert-Butyldimethylsilyl)-1-(methylsulfonyl)-4,6-diphenyl-1,5-dihydro-2H-azepin-2-one ***(6e)***. The scaled up cycloaddition of **6e** was conducted on a 1 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (8:2) to provide 0.367 g (81%) of the title compound as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (m, 6H), 7.22 (m, 2H), 7.00−6.94 (d, 2H), 6.92 (s, 1H), 3.54 (s, 3H), 3.41 (s, 2H), 0.85 (s, 9H), −0.22 (s, 6H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 172.5, 165.0, 141.9, 137.2, 137.0, 133.1, 128.8, 128.3, 128.1, 128.1, 127.3, 126.3, 125.2, 120.5, 77.3, 77.0, 76.7, 60.4, 43.1, 40.1, 27.6, 18.4, 14.2, 0.0, −3.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{32}NO_3SSi$ 454.1872; Found 454.1867

3-(tert-Butyldimethylsilyl)-1-(methylsulfonyl)-4-phenyl-6-(p-tolyl)-1,5-dihydro-2H-azepin-2-one ***(6f)***. The cycloaddition of **6f** was conducted on a 0.10 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (8:2) to provide 24.4 mg (52%) of the title compound as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.11 (m, 8 H), 6.96 (d, J = 7.2, 2 H), 6.89 (s, 1 H) 3.53 (s, 3 H), 3.39 (s, 2 H), 2.35 (s, 3 H), 0.85 (s, 3 H), −0.23 (s, 6 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 177.7, 149.8, 144.6, 138.9, 137.1, 136.6, 134.9, 134.5, 134.0, 133.8, 133.0, 132.6, 132.4, 132.0, 131.8, 131.7, 128.6, 128.4, 124.5, 111.0, 50.8, 35.9, 31.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{26}H_{34}NO_3SSi$ 468.2029; Found 468.2023.

4-(6-(tert-Butyldimethylsilyl)-1-(methylsulfonyl)-7-oxo-5-phenyl-4,7-dihydro-1H-azepin-3-yl)benzoate ***(6g)***. The cycloaddition of **6g** was conducted on a 0.10 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (8:2) to provide 41.5 mg (81%) of the title compound as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.6 Hz, 2 H), 7.34 (d, J = 8.7 Hz), 7.22 (m, 3 H), 7.05 (s, 1 H), 6.94 (d, J = 8.1 Hz, 2 H), 3.92 (s, 3 H), 3.55 (s, 3 H), 3.43 (s, 2 H), 0.86 (s, 3 H), −0.22 (s, 6 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 172.3, 166.6, 164.5, 141.6, 135.4, 133.3, 130.1, 129.7, 128.2, 128.1 127.3, 126.0, 122.2, 52.2, 43.3, 39.9, 27.7, 18.4; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{33}NO_5SSiNa$ 534.1746; Found 534.1741.

3-(tert-Butyldimethylsilyl)-1-(methylsulfonyl)-4-(3-nitrophenyl)-6-phenyl-1,5-dihydro-2H-azepin-2-one ***(6h)***. The cycloaddition of **6h** was conducted on a 0.10 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (8:2) to provide 32 mg (64%) of the title compound as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (ddd, J = 8.2, 2.2, 1.0 Hz, 1H), 8.29 (t, J = 2.2 Hz, 1H), 7.84 (ddd, J = 7.8, 1.9, 1.1 Hz, 1H), 7.73 (t, J = 8.0 Hz, 1H), 7.64 (qt, J = 7.0, 3.3 Hz, 1H), 7.55−7.49 (m, 2H), 7.47−7.42 (m, 2H), 7.42−7.36 (m, 1H), 7.28 (s, 1H), 7.22−7.13 (m, 2H), 3.78 (s, 3H), 3.65 (s, 2H), 1.08 (s, 9H), −0.04 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 172.0, 164.1, 148.6, 141.4, 139.1, 133.7, 133.6, 131.8, 129.9, 128.4, 128.3, 127.2, 122.9, 122.8, 121.0, 43.3, 40.0, 27.7, 18.4, −3.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{30}N_2NaO_5SSi$ 521.1542; Found 521.1537

6-(4-Bromophenyl)-3-(tert-butyldimethylsilyl)-1-(methylsulfonyl)-4-phenyl-1,5-dihydro-2H-azepin-2-one ***(6i)***. The cycloaddition of **6i** was conducted on a 0.10 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (8:2) to provide 45 mg (84%) of the title compound as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 8.7 Hz, 2 H), 7.25 (m, 3 H), 7.14 (d, J = 8.7 Hz, 2 H), 6.94 (m, 3 H), 3.54 (s, 3 H), 3.37 (s, 2 H), 0.84 (s, 9 H), −0.23 (s, 6 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 172.3, 164.6, 141.7, 136.2, 135.6, 133.3, 131.9, 128.2, 127.7, 127.3, 122.4, 120.9, 43.2, 39.9, 27.6, 18.4, −3.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{31}BrNO_3SSi$ 532.0977; Found 532.0972 and 534.0954.

3-(tert-Butyldimethylsilyl)-6-(4-chlorophenyl)-1-(methylsulfonyl)-4-phenyl-1,5-dihydro-2H-azepin-2-one ***(6j)***. The cycloaddition of **6j** was conducted on a 0.10 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (8:2) to provide 40 mg

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(82%) of the title compound as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.0 Hz, 1 H), 7.58 (J = 8.0 Hz, 2 H), 7.32 (m, 6 H), 7.18 (d, J = 8.0, 2 H), 7.05, (td, J = 7.6, 1 H), 6.98 (m, 1 H), 5.18 (m, 1 H), 4.90 (d, J = 4.0, 1 H), 4.79 (m, 2 H), 3.68 (dd, J = 8.0, 4 H), 2.36 (s, 3 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 143.9, 143.2, 142.2, 141.6, 138.1, 134.6, 130.4, 129.3, 128.8, 128.6, 128.5, 128.3, 127.6, 125.7, 125.6, 124.3, 115.8, 115.6, 71.0, 55.7, 21.4; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{25}H_{31}ClNO_3SSi$ 488.1482; Found 488.1477.

*3-(tert-Butyldimethylsilyl)-1-(methylsulfonyl)-4-phenyl-6-(o-tolyl)-1,5-dihydro-2H-azepin-2-one (**6k**).* The cycloaddition of **6k** was conducted on a 0.10 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (8:2) to provide 43.6 mg (93%) of the title compound as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.11 (m, 8 H), 6.96 (d, J = 7.2, 2 H), 6.89 (s, 1 H) 3.53 (s, 3 H), 3.39 (s, 2 H), 2.35 (s, 3 H), 0.85 (s, 3 H), −0.23 (s, 6 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 177.7, 149.8, 144.6, 138.9, 137.1, 136.6, 134.9, 134.5, 134.0, 133.8, 133.0, 132.6, 132.4, 132.0, 131.8, 131.7, 128.6, 128.4, 124.5, 111.0, 50.8, 35.9, 31.6; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{26}H_{34}NO_3SSi$ 468.2029; Found 468.2023.

*3-(tert-Butyldimethylsilyl)-1-(methylsulfonyl)-6-(3-nitrophenyl)-4-phenyl-1,5-dihydro-2H-azepin-2-one (**6l**).* The cycloaddition of **6l** was conducted on a 0.10 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (8:2) to provide 28 mg (56%) of the title compound as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (ddd, J = 8.2, 2.3, 1.1 Hz, 1H), 8.08 (t, J = 2.3 Hz, 1H), 7.67−7.59 (m, 1H), 7.52 (t, J = 8.2 Hz, 1H), 7.33−7.27 (m, 2H), 7.24 (m, 1H), 7.07 (s, 1H), 7.01−6.92 (m, 2H), 3.57 (s, 3H), 3.44 (s, 2H), 0.87 (s, 9H), −0.21 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 172.0, 164.1, 148.6, 141.4, 139.2, 133.7, 133.6, 131.8, 129.9, 128.4, 128.4, 127.2, 122.9, 122.9, 121.0, 43.4, 40.1, 29.7, 27.7, 27.4, 21.1, 18.4, 14.2, −3.1; HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{25}H_{30}N_2O_5SSiNa$ 521.1542; Found 521.1537.

*3-(tert-Butyldimethylsilyl)-6-(3-methoxyphenyl)-1-(methylsulfonyl)-4-phenyl-1,5-dihydro-2H-azepin-2-one (**6m**).* The cycloaddition of **6m** was conducted on a 0.10 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (8:2) to provide 37 mg (76%) of the title compound as a pale green oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26−7.22 (m, 5 H), 6.99 (dd, J = 7.9, 1.8 Hz, 2 H), 6.90 (d, J = 7.9 Hz, 1 H), 6.85 (dd, J = 8.3, 1.9 Hz, 1 H), 6.76 (t, J = 1.9 Hz, 1 H), 3.72 (s, 3 H), 3.53 (s, 3 H), 3.39 (s, 2 H), 0.85 (s, 9 H), −0.21 (s, 6 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 172.5, 164.9, 159.8, 141.9, 138.7, 136.9, 133.1, 129.8, 128.1, 127.5, 120.7, 118.8, 113.9, 111.8, 55.2, 43.1, 40.2, 27.6, 18.4, −3.0; HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{26}H_{33}NO_4SSiNa$ 506.1797; Found 506.1792.

*3-(tert-Butyldimethylsilyl)-1-(methylsulfonyl)-6-phenyl-4-(p-tolyl)-1,5-dihydro-2H-azepin-2-one (**6n**).* The cycloaddition of **6n** was conducted on a 0.10 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (8:2) to provide 43 mg (92%) of the title compound as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.27 (m, 5H), 7.02 (d, J = 7.7 Hz, 2H), 6.91 (s, 1H), 6.84 (d, J = 7.7 Hz, 2H), 3.53 (s, 3H), 3.40 (s, 2H), 2.31 (s, 3H), 0.85 (s, 9H), −0.21 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 172.6, 165.2, 139.1, 137.9, 137.3, 137.1, 132.9, 128.8, 128.7, 128.3, 127.3, 126.3, 120.4, 43.1, 40.2, 27.7, 21.2, 18.4; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{26}H_{34}NO_3SSi$ 468.2029; Found 468.2023.

*4-([1,1′-Biphenyl]-4-yl)-3-(tert-butyldimethylsilyl)-1-(methylsulfonyl)-6-phenyl-1,5-dihydro-2H-azepin-2-one (**6o**).* The cycloaddition of **6o** was conducted on a 0.10 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (8:2) to provide 37 mg (70%) of the title compound as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (m, 2H), 7.68 (m, 2H), 7.48 (m, 4H), 7.32 (s, 5H), 7.01 (dd, J = 8.4, 1.8 Hz, 1H), 6.96 (s, 1H), 3.56 (s, 3H), 3.49 (s, 2H), 0.86 (s, 9H), −0.25 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 172.6, 164.9, 141.7, 139.2, 137.3, 133.5, 133.1, 132.7, 132.6, 132.5, 128.9, 128.4, 128.2, 128.1, 127.8, 127.6, 126.7, 126.5, 126.3, 126.1, 126.0, 125.4, 125.1, 120.5, 43.2, 40.1, 27.7, 27.4, 19.2, 18.5, −2.94, −3.71; HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{31}H_{35}NO_3SSiNa$ 552.2005; Found 552.1999.

*3-(tert-Butyldimethylsilyl)-4-(4-ethoxyphenyl)-1-(methylsulfonyl)-6-phenyl-1,5-dihydro-2H-azepin-2-one (**6p**).* The cycloaddition of **6p** was conducted on a 0.10 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (8:2) to provide 37 mg (75%) of the title compound as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.24 (m, 5H), 6.90 (s, 1H), 6.87 (d, J = 8.7 Hz, 2H), 6.73 (d, J = 8.7 Hz, 2H), 3.99 (q, J = 7.0 Hz, 2H), 3.53 (s, 3H), 3.40 (s, 2H), 1.39 (t, J = 7.0 Hz, 3H), 0.85 (s, 9H), −0.19 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, CDCl3) δ 172.6, 165.0, 158.8, 137.3, 137.1, 134.3, 132.8, 128.8, 128.3, 126.2, 120.4, 113.9, 63.4, 43.1, 40.4, 27.7, 18.5, 14.7, −2.9; HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{27}H_{35}NO_4SSiNa$ 520.1954; Found 520.1948.

*3-(tert-Butyldimethylsilyl)-4-(4-chlorophenyl)-1-(methylsulfonyl)-6-phenyl-1,5-dihydro-2H-azepin-2-one (**6q**).* The cycloaddition of 6q was conducted on a 0.10 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (8:2) to provide 48 mg (98%) of the title compound as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J = 1.9 Hz, 1H), 7.23−7.16 (m, 1H), 6.92 (s, 1H), 6.89 (d, J = 8.3 Hz, 1H), 3.54 (s, 2H), 3.38 (s, 1H), 0.86 (s, 6H), −0.20 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 172.8, 165.6, 143.2, 137.6, 137.5, 129.0, 128.5, 128.3, 127.5, 126.6, 126.5, 120.6, 43.3, 35.5, 33.7, 29.9, 27.9, 22.4, 14.1, −2.9, −2.9; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{25}H_{31}ClNO_3SSi$ 488.1482; Found 488.1477

*3-(tert-Butyldimethylsilyl)-1-(methylsulfonyl)-4-(naphthalen-2-yl)-6-phenyl-1,5-dihydro-2H-azepin-2-one (**6r**).* The cycloaddition of **6r** was conducted on a 0.10 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (8:2) to provide 28 mg (56%) of the title compound as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8.3 Hz, 4H), 7.53 (d, J = 8.3 Hz, 4H), 7.47−7.42 (t, J = 4H), 7.05 (d, J = 8.3 Hz, 2H), 6.97 (s, 1H), 3.57 (s, 3H), 3.48 (s, 2H), 0.91 (s, 9H), −0.15 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 172.58, 164.9, 153.9, 141.7, 139.2, 137.3, 137.2, 133.5, 133.1, 132.7, 132.5, 128.9, 128.4, 128.2, 128.0, 127.8, 127.6, 126.7, 126.5, 126.3, 126.1, 126.0, 125.4, 125.0, 120.5, 43.2, 40.1, 27.7, 27.4, 18.5, −3.7; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{29}H_{34}NO_3SSi$ 504.2029; Found 504.2023.

*3-(tert-Butyldimethylsilyl)-4-(3-methoxyphenyl)-1-(methylsulfonyl)-6-phenyl-1,5-dihydro-2H-azepin-2-one (**6t**).* The cycloaddition of **6t** was conducted on a 0.10 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (8:2) to provide 29 mg (60%) of the title compound as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 5H), 7.12 (t, J = 8.3 Hz, 1H), 6.91 (s, 1H), 6.78 (ddd, J = 8.3, 2.6, 1.0 Hz, 1H), 6.62−6.54 (d, J = 8.3 Hz, 1H), 6.38 (s, 1H), 3.54 (s, 3H), 3.50 (s, 3H), 3.41 (s, 2H), 0.87 (s, 9H), −0.19 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 196.16, 172.57, 164.81, 159.13, 143.16, 137.43, 137.40, 132.95, 129.21, 128.89, 128.38, 126.44, 120.44, 119.74, 114.55, 111.82, 54.94, 43.13, 40.13, 27.68, −3.20; HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{26}H_{33}NO_4SSiNa$ 506.1797; Found 506.1792.

*3-(tert-Butyldimethylsilyl)-1-(methylsulfonyl)-6-phenyl-4-(4-(trifluoromethyl)phenyl)-1,5-dihydro-2H-azepin-2-one (**6u**).* The cycloaddition of 6u was conducted on a 0.05 mmol scale and purified by flash chromatography eluting with hexanes/EtOAc (8:2) to provide 10 mg (38%) of the title compound as a pale yellow oil. ^{1}H NMR (400 MHz, CDCl3) δ 7.90 (s, 1H), 7.79 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 8.4 Hz, 2H), 7.65 (m, 1H), 7.07 (d, J = 10.9 Hz, 2H), 7.00 (d, J = 6.8 Hz, 2H), 3.63 (s, 3H), 3.52 (s, 2H), 0.99 (s, 9H), −0.11 (s, 6H); ^{13}C{^{1}H} NMR (125 MHz, CDCl3) δ 163.7, 159.2, 136.2, 129.5, 129.3, 129.1, 128.5, 128.1, 127.5, 127.3, 126.8, 52.2, 42.1, 41.9, 26.9, 14.3, −3.6; HRMS (ESI) m/z: [M + H]+ Calcd for $C_{26}H_{31}F_3NO_3SSi$ 522.1746; Found 522.1741.

*3-(tert-Butyldimethylsilyl)-1-(methylsulfonyl)-4,6-diphenyl-1,3-dihydro-2H-azepin-2-one **9**.* To a flame-dried 2-dram vial equipped with a magnetic stir bar was added **6e** (0.05 mmol, 23 mg). The vessel was sealed with a rubber septum, evacuated, and refilled with nitrogen three times and then was charged with THF (0.13 mL). The solution was cooled to 0 °C via an ice−water bath, and then a solution of TBAF (0.1 mmol, 26 mg) in THF (0.13 mL) was added dropwise. After 3 h, the mixture was allowed to warm to room temperature

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overnight via removal from the cooling bath. The crude reaction mixture was diluted with H_2O (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic fractions were washed with saturated aqueous NaCl (2 × 10 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The reaction provided 23 mg (>99%) of the title compound as a pale yellow oil without the need for purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (dd, J = 4.9, 1.9 Hz, 6H), 7.40−7.35 (m, 4H), 6.10 (s, 2H), 4.06 (s, 1H), 2.67 (s, 3H), 0.83 (s, 9H), −0.19 (s 3H) −0.28 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 206.4, 179.5, 138.8, 135.5, 134.9, 130.1, 129.6, 129.5, 129.3, 128.8, 128.5, 128.4, 128.2, 128.0, 127.9, 127.7, 122.3, 53.2, 41.5, 29.7, 27.4, 25.6, 17.7, −4.90, −4.94; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{25}H_{32}NO_3SSi$ 454.1872; Found 454.1867.

3-(tert-Butyldimethylsilyl)-4,6-diphenyl-1,5-dihydro-2H-azepin-2-one ***10***. To a flame-dried 2-dram vial equipped with a magnetic stir bar was added **6e** (0.05 mmol, 23 mg). The vessel was sealed with a rubber septum, evacuated, and refilled with nitrogen three times and then charged with THF (0.13 mL), followed by cooling to −78 °C via a dry ice/acetone bath. In a separate flame-dried vial, Me_2CuLi was generated by adding MeLi (0.093 mL of a 1.6 M solution in diethyl ether) to CuI (0.15 mmol, 14 mg) in 0.13 mL of THF at −78 °C. Then, the solution of Me_2CuLi was added dropwise. After 3 h, the mixture was allowed to warm to 0 °C by removal of the dry/ice acetone bath and placement into an ice−water bath. After 12 h, the crude reaction mixture was diluted with H_2O (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic fractions were washed with saturated aqueous NaCl (2 × 10 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude reaction mixture was purified by flash chromatography eluting with 8:2 hexanes/EtOAc, providing 23 mg (65%) of the title compound as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, J = 6.1 Hz, 3H), 7.24−7.18 (m, 5H), 7.04−6.97 (m, 2H), 6.50 (s, 1H), 3.36 (s, 2H), 0.88 (s, 9H), −0.28 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 138.0, 128.7, 127.9, 127.5, 127.4, 127.3, 125.7, 122.0, 40.5, 29.7, 27.9, 18.5, −3.1; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{24}H_{30}NOSi$ 376.2097; Found 376.2091.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c03002.

^{1}H and ^{13}C{^{1}H} NMR spectra for all new compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Brandon L. Ashfeld − *Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, Indiana 46556, United States;* orcid.org/0000-0002-4552-2705; Email: bashfeld@nd.edu

Authors

Harrison M. Hill − *Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, Indiana 46556, United States*

Zachary D. Tucker − *Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, Indiana 46556, United States*

Kevin X. Rodriguez − *Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, Indiana 46556, United States*

Katelyn A. Wendt − *Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, Indiana 46556, United States*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.1c03002

Notes

The authors declare no competing financial interest.

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