The Emergence of Allenamides in Organic Synthesis

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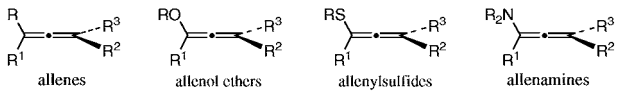
ABSTRACT

This Account highlights recent studies describing utility of allenamides in stereoselective inter- and intramolecular synthetic methodologies. It is written to raise interest in the chemistry of allenamides.

1. Introduction

1.1. An Overview. Allenes represent a versatile functional group that can be utilized as a useful building block in a variety of synthetic transformations, leading to complex structures that are useful for constructing natural and unnatural products.[1] Subgroups of allenes are those substituted at the terminal carbon with a heteroatom such as oxygen, sulfur, or nitrogen. Despite the synthetic potential of allenes, heteroatom-substituted allenes, and in particular allenamines, have received relatively little attention.[1]



Conceptually, allenamines should be synthetically useful because they are electron-rich and can be readily activated in the presence of an electrophile [$E^{\oplus}$]. More significantly, the nitrogen atom can donate its lone pair toward the allenic moiety to render transformations involving additions of electrophiles [$E^{\oplus}$] and nucleophiles [Nu^{y}] highly regioselective, which is a challenge in general with reactions involving allenes [Figure 1].

There are a few literature examples of synthetic transformations involving allenamines, suggesting that allenamines can be useful in organic synthesis. These examples, as highlighted in Scheme 1, include α- or γ-lithiation of allenamines [umpolung equivalents: see the box],[5,6] additions,[7] 1,3-dipolar,[8] [2 + 2],[9,10] and hetero [4 + 2] cycloadditions.[10,11] Other examples [not shown here] would include cyclizations,[12] dimerizations,[13] and rearrangement.[14]

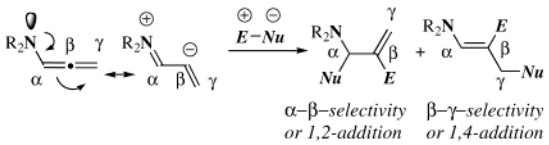
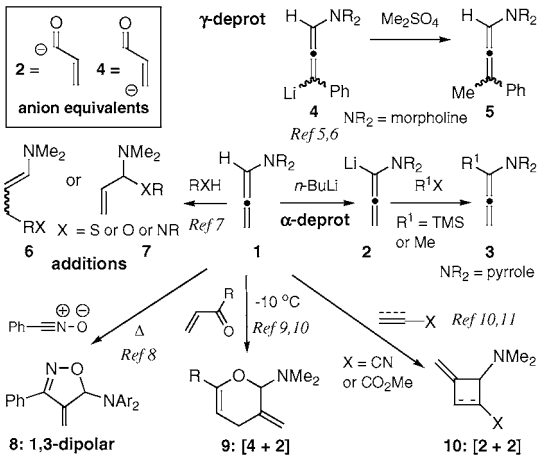
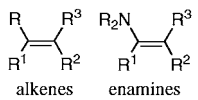


FIGURE 1. An overview.

Scheme 1. Precedents



However, allenamines are also known to be sensitive to hydrolysis, polymerization, and isomerization even at low temperatures, thereby creating serious difficulties in their preparation and handling.[1] Consequently, unlike enamines, which are corresponding subgroups of alkenes, the extent of synthetic applications of allenamines has remained limited for the last 30−40 years.[2−4]



1.2. Potential Significance of Allenamines. Transformations involving allenamines are not only regioselective and stereoselective, but also, more importantly, the resulting products all possess nitrogen functionalities [Scheme 1]. Nitrogen-containing structures are prevalent among medicinally interesting natural and unnatural products and, thus, are useful in developing new therapeutics. Therefore, efforts in developing the chemistry of allenamines and identifying an allenamine-equivalent that possesses the right balance between stability and reactivity can be significant and rewarding.

1.3. Introduction of Allenamides. Allenol ethers, with their oxygen atom being less able to donate the lone pair, are less reactive but represent a more stable allenic system. Thus, they have been more visible in synthesis

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Richard P. Hsung attended The University of Chicago and obtained his Ph.D. in Organic Chemistry in 1994. After postdoctoral stays at The University of Chicago and Columbia University, he moved to the University of Minnesota as an Assistant Professor in 1997 and was promoted to Associate Professor in 2002. His research interests involve developing cycloaddition approaches to total syntheses of natural products and stereoselective methods using allenamides and ynamides.

Lin-Li Wei obtained her B.S. and M.S. degrees from Peking University in 1992 and 1995, respectively. In 1999, she received her Ph.D. from the National University of Singapore. From 1998 to 2001, she was a postdoctoral associate in Professor Hsung's group, and she is currently a research scientist at Selectide.

Hui Xiong received his B.S. from Peking University in 1998 and his Ph.D. in 2003 from the University of Minnesota under the supervision of Professor Hsung. His Ph.D. work involves cycloadditions of chiral allenamides, and he is currently a postdoctoral fellow at Scripps Research Institute.

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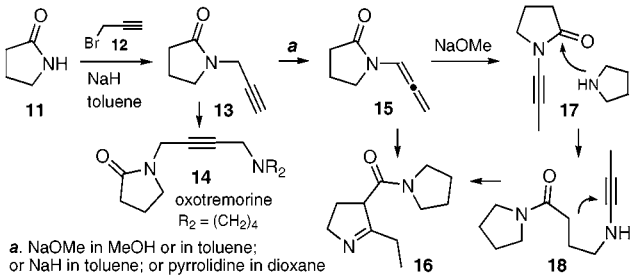
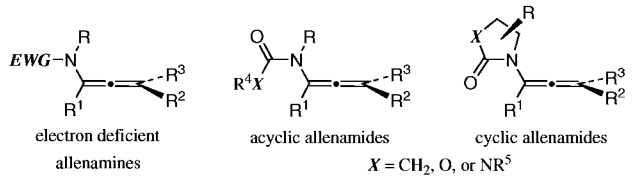
Scheme 2. Dickinson's First Synthesis



than allenamines.[1,15] By extrapolation, electron-deficient allenamines, such as allenamides, have the potential to function as an allenamine-equivalent. The electron-withdrawing group on the nitrogen atom should diminish its donating ability and lead to improved stability.



Allenamides had been studied rarely until recently.[1] After Dickinson's first preparation of 1,2-propadienyl-2-pyrrolidinone in 1967,[16] there were very few reports until 1989.[17−20] Since then, there has been an emerging interest in the chemistry of allenamides that ranges from medicinal studies,[21−23] to materials using living polymerization,[24] to synthetic methodologies.[25−44] These efforts support the notion that allenamides are becoming a proven allenamine-equivalent with the right balance of stability and reactivity.

We wish to highlight in this account recent development in the chemistry of allenamides with an emphasis on synthetic methods and with the intention of provoking further interest in the chemistry of allenamides.

2. Part I. Synthesis of Allenamides

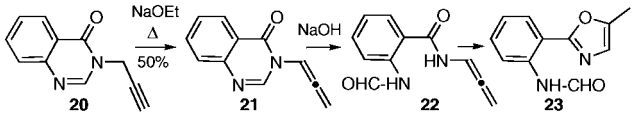
2.1. Historical Examples. To repeat an earlier preparation of propargyl amide **13** en route to oxotremorine **14**,[45] a potent muscarinic agent,[46] Dickinson[16] reported in 1967 the first preparation of allenamide **15** from lactam **11** and propargyl bromide **12** under basic conditions [Scheme 2]. Allenamide **15** could also be prepared from **13** using NaOMe or NaH. This based-induced isomerization protocol is one of the most efficient methods for allenamide synthesis.

Subsequently, allenamide **15** was found to give **16** in the presence of NaOMe and pyrrolidine with, interestingly, ynamide **17**[47,48] postulated as a key intermediate.

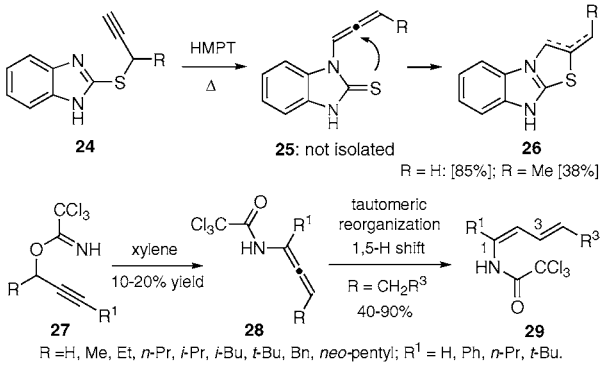
In 1969, Bogentoft[17] prepared allenamide **21** via isomerization in 50% yield. Oxazole **23** was also isolated, and likely derived from allenamide **22** after ring opening of the quinazolone [Scheme 3].

2.2. Sigmatropic Rearrangement. Claisen-type rearrangement of propargyl thiol benzimidazole **24** was found

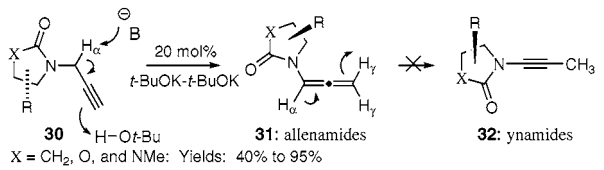
Scheme 3. Bogentoft's Isomerization



Scheme 4. Overman's Claisen Rearrangement



Scheme 5. First Chiral Allenamides



to give thiazole **26**, with allenamide **25** being postulated as a key intermediate [Scheme 4].[19]

In 1979, Overman[20] first demonstrated that Claisen rearrangement of propargyl trichloroacetyl imidates **27** could afford allenamides **28** in 10−20% isolated yields [Scheme 4]. Allenamides **28** could further isomerize to 1*Z*-3*E*-dienamides **29** in a highly stereoselective manner. This protocol represents an attractive method for the synthesis of highly substituted chiral allenamides.

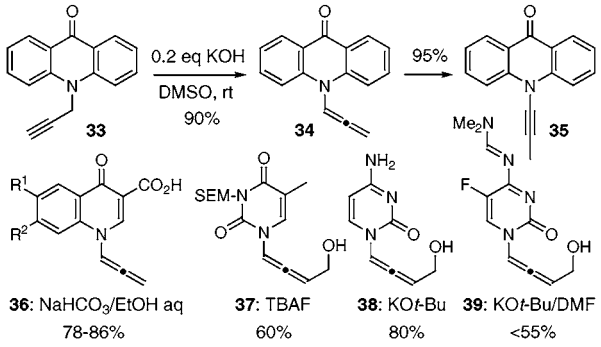
2.3. Base-Induced Isomerization. *2.3.1. Cyclic Propargyl Amides.* We became involved with allenamide chemistry because of our interest in ynamides.[47,48,49−52] We attempted to prepare ynamides **32** via the based-induced isomerization of propargyl amides **30** [Scheme 5]. However, ynamides **32** were not found. Instead, the isomerization gave achiral and chiral allenamides **31**.[41,53]

There are very few examples of isomerizations of propargyl amides to ynamides. The only case in which the ynamide has been isolated is the preparation of vinylogous ynamide **35**[54] [Scheme 6], although allenamide **34** is still found on occasions.[21−22,49,53−55]

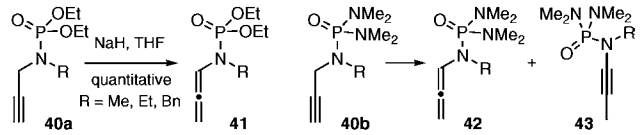
In most cases, isomerizations of propargyl amides provided only allenamides especially with propargyl amides in which the nitrogen atom is part of aromatic heterocycles [their isomerization would lead to the corresponding allenamides **36**−**39**].[21−23] This poses an interesting fundamental question as to why the thermodynamically more stable ynamide [based on our own experience with ynamides[47,50,53]] was not found if these isomerizations involved an equilibration mechanism.

2.3.2. Acyclic Propargyl Amides. Corbel in 1976[18] reported the first example of an acyclic allenamides **41** and

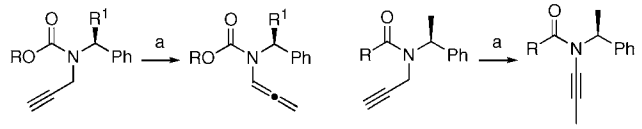
Scheme 6. Heteroaromatic Allenamides



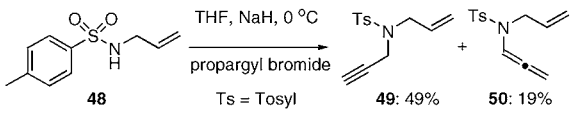
Scheme 7. Corbel's Isomerization



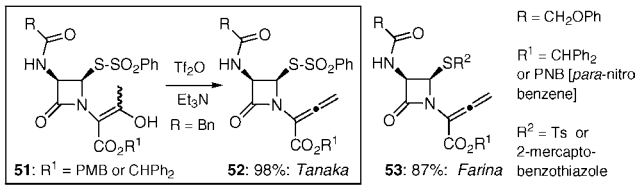
Scheme 8. First Chiral Acyclic Allenamides



Scheme 9. De Meijere's Isomerization



Scheme 10. Tanaka and Farina's Eliminations



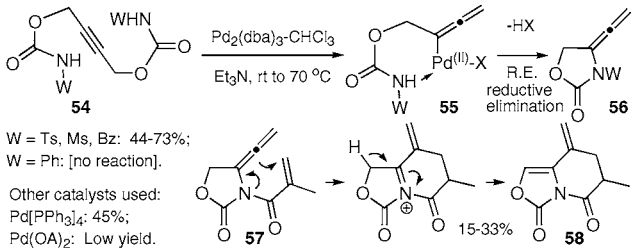
42 via the isomerization of *N*-propargyl phosphoramides **40a** and **40b**, respectively, with the latter providing also ynamide **43** in the mixture [Scheme 7].

Inspired by these results, we examined isomerizations of acyclic propargyl urethanes **44a**,**b** and found they again gave allenamides **45a**,**b** using 20 mol % KO*t*-Bu/*t*-BuOH [Scheme 8]. However, in contrast, propargyl amides **46a**,**b** did isomerize successfully to ynamides **47a**,**b** in 83% and 50% yield, respectively, for the first time.[50]

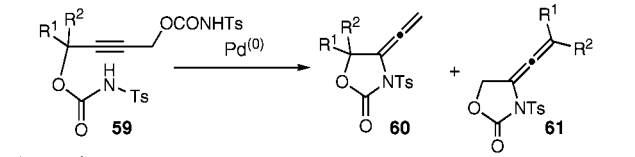
de Meijere[56] also reported an acyclic *N*-tosyl allenamide **50** as a byproduct when preparing propargyl amide **49** from the sulfonamide **48** [Scheme 9].

2.4. Elimination. Tanaka[29] and Farina[30] both communicated an elimination protocol for preparations of β-lactam-based α,α-disubstituted allenamides **52** and **53**, respectively, [Scheme 10] from enol triflates. These allenamides were specifically designed to access cepham analogues [see below].[29,30]

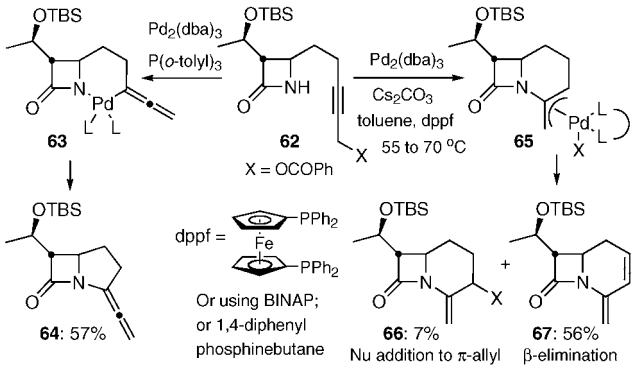
Scheme 11. Tamaru's Allenamides



Scheme 12. Tamaru's Allenamides



Scheme 13. Mori's Carbapenam Synthesis



2.5. Aminocyclization. Some interesting cyclic urethane substituted allenamides **56** via palladium catalyzed intramolecular cyclization of propargyl bis-urethanes **54** were reported recently by Tamaru [Scheme 11].[39,57] Allenamide **57** could further cyclize to give **58**.

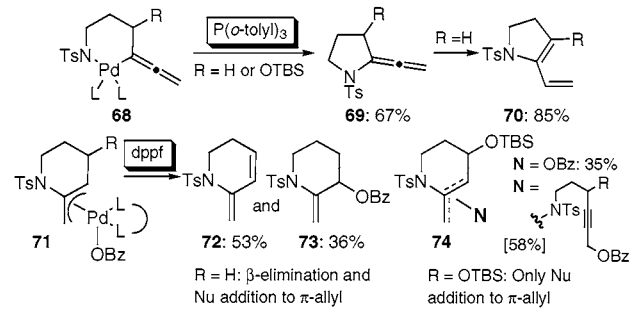
The direction of oxidative addition of $Pd^{(0)}$ en route to allenyl palladium intermediates **55** is not relevant if **54** is symmetrical. Asymmetric bis-urethanes **59** did give a mixture of **60** and **61** [Scheme 12]. The oxidative addition of $Pd^{(0)}$ was found to be in favor of the less hindered propargyl carbon, leading to **60** with the level of selectivity depending upon the size of R^1 and R^2.

Mori[58] recently showed a fascinating study in a similar palladium catalyzed aminocyclization of the propargyl carbamate **62** [Scheme 13].

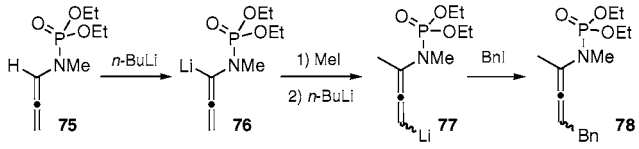
When the ligand was P(*o*-tolyl)$_3$ or other monodentate phosphines, allenamide **64** with a carbapenam skeleton was found in 57% yield via the allenyl palladium complex **63**. On the other hand, a mixture of **66** and **67** containing the carbacepham skeleton were found in 7% and 56% yields, respectively, when the bidentate ligand dppf was used.

Evidently, an amide coordinated allenyl palladium intermediate like **63** was not possible sterically when a bidentate ligand was used, presumably due to sterics. Instead, attack by the amide nitrogen at the central carbon

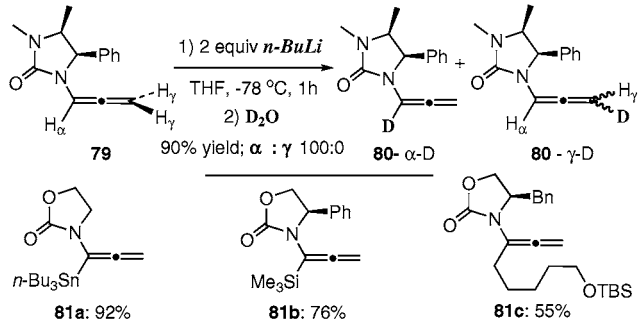
Scheme 14. Mori's Allenamides



Scheme 15. Corbel's Deprotonation



Scheme 16. α-Substituted Chiral Allenamides



of the allenyl palladium intermediate [i.e., uncoordinated **63**] would lead to π-allyl complex **65**. Subsequent nucleophilic addition would give **66** and β-elimination would give **67**.

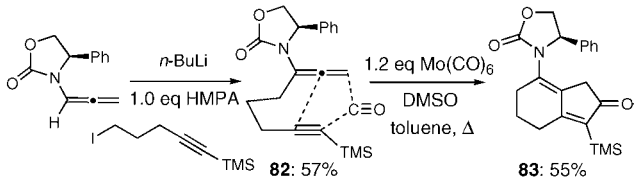
This trend was also found in a more general system where P(*o*-tolyl)$_3$ led to cyclic *N*-tosyl allenamide **69** in 67% yield that further isomerized to **70** if R = H [Scheme 14].[58] Using dppf provided **72** via β-elimination and **73** [R = H] and **74** [R = OTBS] via nucleophilic addition.

3. Part II. Reactions of Allenamides

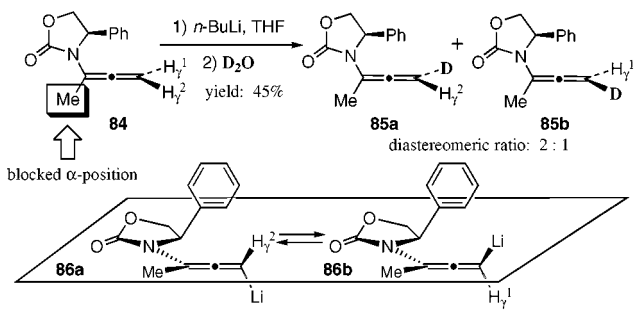
3.1. Deprotonations and Addition Reactions. *3.1.1.* α-*Deprotonation*. Corbel[18] provided the earliest example where allenamides **75** could be deprotonated at α- and γ-positions sequentially. The lithiated allenamides **76** and **77** were configurationally stable and could be trapped with electrophiles such as MeI and BnI [Scheme 15].

We embarked on developing this deprotonation method because of its potential as an efficient entry to more functionalized allenamides. After screening a variety of bases, *n*-BuLi was found to be the most suitable, leading to exclusively α-lithiation of **79**, as evident by deuterium quenching [Scheme 16].[25] This led to synthesis of a variety of new α,α-disubstituted chiral allenamides, including chiral allenyl stannanes and allenyl silanes useful for transition metal mediated reactions.[25]

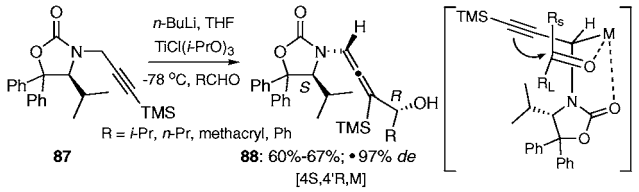
Scheme 17. Allenamide Pauson−Khand



Scheme 18. g-Deprotonation



Scheme 19. Seebach's 1,2-Additions



An application of these new allenamides in regioselective allenic Pauson−Khand cycloadditions[59] was carried out using allenamide **82** [Scheme 17].

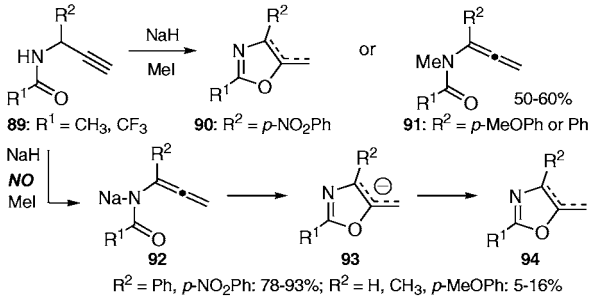
3.1.2. γ-*Deprotonation*. γ-Deprotonation of **84**, having the α-position blocked with a methyl group, led to diastereomeric allenamides **85a/b** [Scheme 18] in modest yield.[25] The ratio is only 2:1, implying that either there was very little diastereoselectivity during the deprotonation or the diastereomeric allenyllithium anions **86a** and **86b** equilibrated rapidly even at low temperature.

Seebach[26] recently elegantly demonstrated that lithiated chiral allenamides could be useful in stereoselective additions to aldehydes and ketones. The chiral propargyl amide substituted with Seebach's chiral auxiliary **87** was treated with *n*-BuLi at low temperatures, and upon addition of a variety of aldehydes, γ,γ-disubstituted allenamides were isolated in good yields and high diastereoselectivities [Scheme 19]. The stereochemical outcome was rationalized using the complex as shown in the bracket.

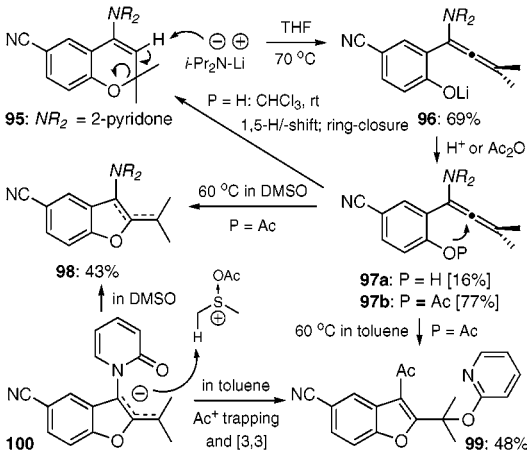
3.2. Cyclizations. *3.2.1. Non-Transition Metal Mediated.* Hackesell reported the first cyclization involving an allenamide.[27] Attempts to methylate propargyl amides **89** led to isolation of the oxazole **90** when R^2 = *p*-NO$_2$Ph, and the desired allenamides **91** were isolated when R^2 = *p*-MeOPh or Ph [Scheme 20]. This cyclization occurred for all substrates when MeI was not added, and presumably, **92** and **93** were key intermediates. Cyclization is actually faster than methylation when R^2 = *p*-NO$_2$Ph.

Gericke[28] showed an interesting cyclization involving 2-pyridone substituted allenamides **97a** and **97b** gener-

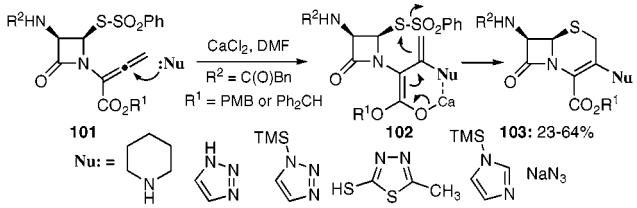
Scheme 20. Hackesell's Cyclization



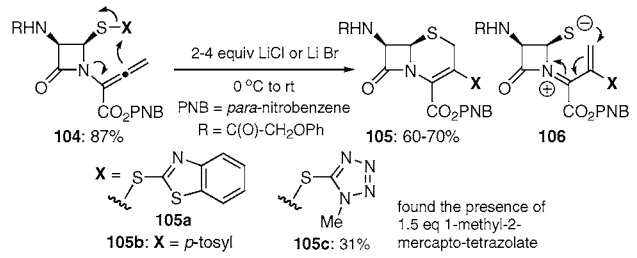
Scheme 21. Gericke's Cyclization



Scheme 22. Tanaka's Cephem Synthesis



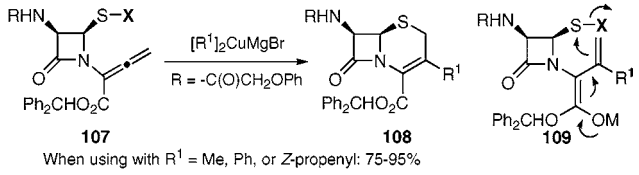
Scheme 23. Farina's Cephem Synthesis



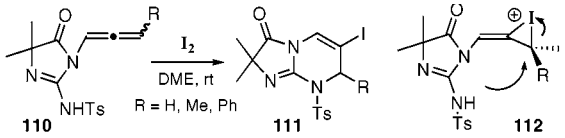
ated from chromene **95** via deprotonation using LDA [Scheme 21]. While **97a** reverted readily to **95** via a 1,5-H shift and pericyclic ring-closure, **97b** led to benzofuran **98** and **99** upon heating in DMSO and toluene, respectively. Both **98** and **99** were likely derived from the common intermediate **100** with [Ac^+] activated DMSO as a proton source leading to the former, and Ac^+ trapping and [3,3]-sigmatropic rearrangement leading to the latter.

Tanaka[29] and Farina[30a] both embarked on preparation of cephem analogues using β-lactam substituted allenamides **101** and **104** [Scheme 22 and Scheme 23, respectively]. In Tanaka's work, a 1,4-addition of an external

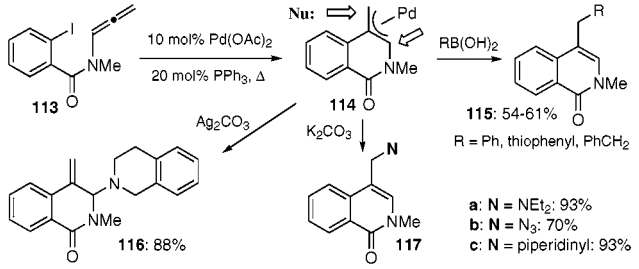
Scheme 24. Farina's Cepham



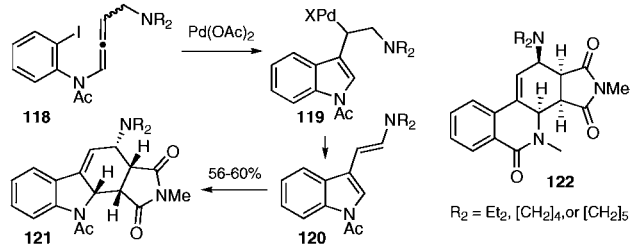
Scheme 25. Noguchi's Cyclization



Scheme 26. Grigg's Pd-Catalyzed Cyclization-Addition



Scheme 27. Grigg's Cyclization-Cycloaddition



nucleophilic amine to the central carbon of allenamide occurred with assistance of $CaCl_2$ followed by a vinylogous enolate addition to the disulfide in **102**.

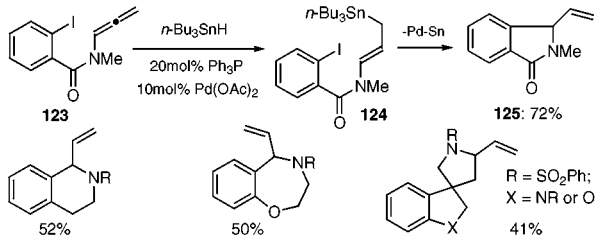
In Farina's work, an internal attack of the disulfide by the allenamide [functioning as an enamide] occurred, transferring the X group to the central carbon of allenamide followed by an intramolecular 1,4-addition of the resulting sulfide anion to *N*-acyl vinyl iminium **106**. Farina[30b] also reported cuprate additions to allenamide **107** via a mechanistic pathway [see **109**] similar to Tanaka's work en route to cepham **108** [Scheme 24].

Noguchi[31] demonstrated that iodine could promote cyclization of allenamide **110** leading to **111** via a 6-*endo*-trig pathway [Scheme 25]. It was postulated that the iodine activation took place at the terminal olefin [distal from the nitrogen atom] shown in **112**.

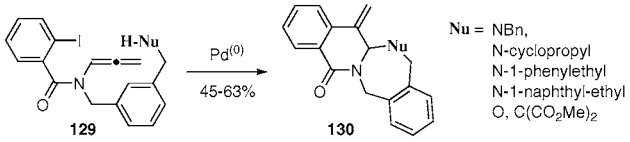
3.2.2. Palladium Catalyzed Cyclizations. Grigg[32−35] reported a series of highly creative designs in palladium-catalyzed cyclizations of allenamides [Schemes 26−29].

Reaction of allenamide **113** with $Pd(OAc)_2$ led to the π-allyl complex **114** that could be captured with various nucleophiles [Scheme 26]. Transmetalation of **114** with boronic acids gave isoquinolones **115** in a regioselective manner.[32b] Addition of amines to **114**, in the presence

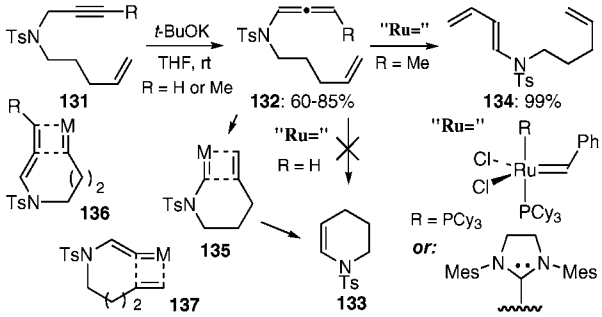
Scheme 28. Grigg's Hydrostannylation-Cyclization



Scheme 29. Grigg's Cyclization−Addition



Scheme 30. RCM



of $AgCO_3$, occurred at the endo position to give **116**, whereas the use of K_2CO_3 led to **117** resulting from exo additions.[32a,c]

By using allenamide **118**, amino diene **120** was obtained and trapped successfully using *N*-methyl maleimide to give **121** in a highly stereoselective manner [Scheme 27].[33] Tetracycle **122** could also be obtained in a similar manner.

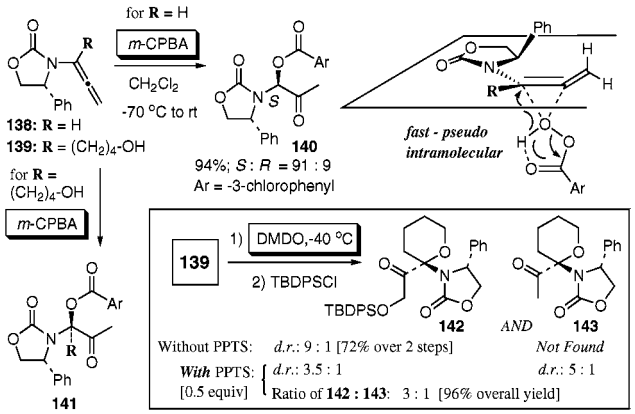
Hydrostannylation of allenamide **123** led to allyl stannane **124** that cyclized to give **125** and a series of other useful heterocycles [Scheme 28].[34] Such strategy could be realized in a tandem manner using allenamide **129** in which the π-allyl intermediate could be trapped intramolecularly [Scheme 29].[35]

This methodology demonstrates the potential of allenamides in transition metal mediated reactions for constructing complex structures.

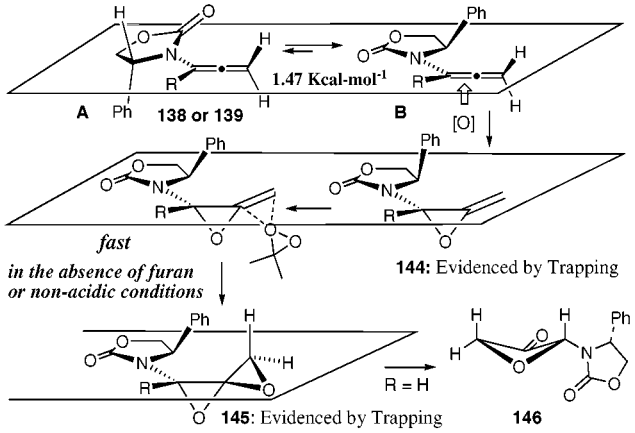
3.3. Ring-Closing Metathesis. Given the power of ring-closing metathesis [RCM],[60] Rutjes[36] attempted RCM using allenamides **132** [Scheme 30]. However, the desired RCM product **133** was not found using either Generation-I or II Ru catalyst. Instead, diene **134**, an isomerization product, was obtained quantitatively when R = Me, thereby implying that the Ru-alkylidene complex **135** was not formed. One wonders if instead the Ru complex **136** or **137** were formed, in what way they would proceed to give RCM-type products.

3.4. Cycloadditions. *3.4.1. [2 + 1].* The only known [2 + 1]-type cycloaddition involved epoxidation of allenamides that was done in our lab in pursuit of [4 + 3] oxyallyl cation cycloaddition.[37] To the best of our knowledge, epoxidation of heteroatom substituted allenes in general is not well precedented.[61−63]

Scheme 31. Epoxidation of Allenamides



Scheme 32. A Model



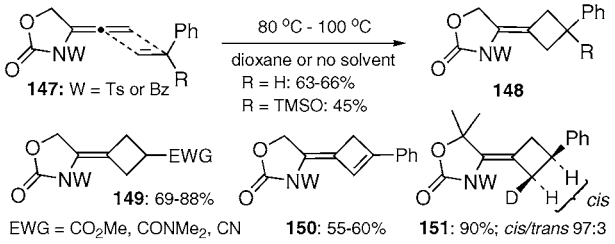
Epoxidation of allenamides **138** and **139** with *m*-CPBA led to aminals **140** and **141**, repectively, in a highly stereoselective manner via a pseudo intramolecular trapping of the allene oxide intermediate [Scheme 31]. The pseudo intramolecular trapping by *m*-chlorobenzoate anion was actually faster than trapping by the hydroxyl group in **139**.

DMDO [dimethyldioxirane] epoxidations of **139** in the absence of pyridinium *para*-toluenesulfonic acid [PPTS] provided only the pyran **142** [after silylating the primary hydroxyl group], suggesting the presence of the bis-epoxidized intermediate. In the presence of PPTS, both **142** and **143** were isolated, implying that epoxidation had led to the bis- and monoepoxides.

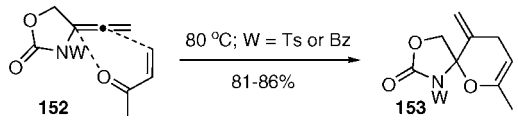
Our studies suggest that DMDO would likely approach from the bottom face of allenamide **138** or **139** in the more favored conformer **B** [Scheme 32]. The resulting monoepoxide **144** was observed by low temperature ^{1}H NMR spectroscopy and isolated by intramolecular trapping [see **143**]. The second epoxidation also occurred rapidly at low temperatures in nonacidic conditions leading to bis-spiroepoxide **145** that could be trapped [see **142**], or rearrange to 3-oxetanone **146**, when R = H, as observed in the low temperature ^{1}H NMR spectrum.

This study also indicated that the second epoxidation by DMDO was again slow in the presence of furan,

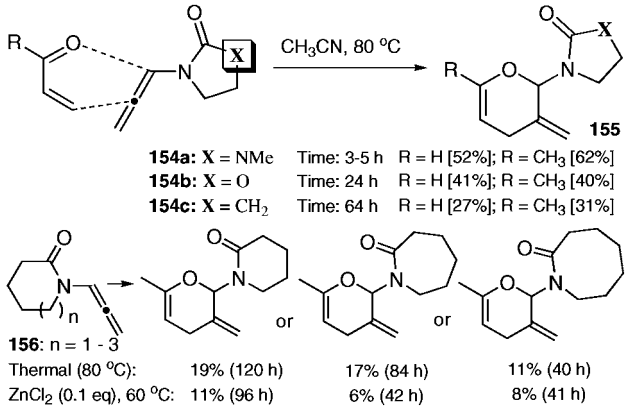
Scheme 33. [2 + 2] Cycloaddition



Scheme 34. Tamaru's Hetero-[4 + 2]



Scheme 35. Hetero-[4 + 2]



thereby allowing the subsequent [4 + 3] cycloaddition [see below].

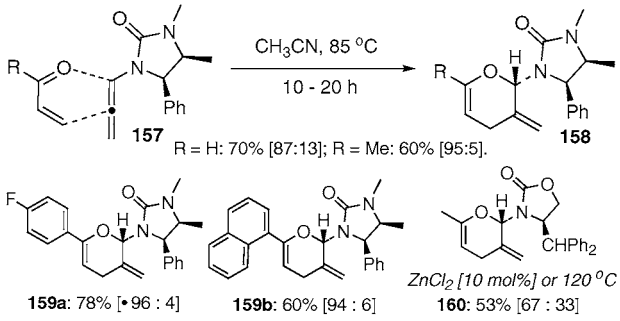
3.4.2. [2 + 2]. An excellent study describing the feasibility of [2 + 2] cycloaddition reactions of allenamides was reported recently by Tamaru.[3b] Allenamides **147** underwent [2 + 2] cycloadditions with alkenes to give cyclobutane **148**. Even electron deficient alkenes and alkynes reacted to give **149** and **150**, respectively. These reactions are also both highly regioselective and stereoselective, as shown in the cycloadduct **151** derived from reactions with *cis*-2-D-styrene.

3.4.3. [4 + 2]. Tamaru[39] carried out the first inverse electron-demand hetero [4 + 2] cycloaddition reaction, as shown in Scheme 34, in which the cycloaddition actually favored the internal olefin of allenamide **152**.[39]

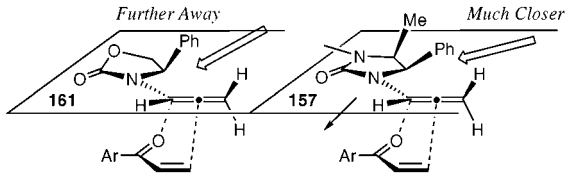
We have studied this hetero Diels–Alder reaction in detail.[41,42] It was found that cycloadditions using our allenamides **154** led to pyrans **155** with the same regiochemistry as reported by Tamura[39] [Scheme 35].

The substitutent pattern of these cyclic amides also impacts the reactivity of allenamides. Urea substituted allenamide **154a** was the most reactive in [4 + 2] cycloadditons with acrolein or methy vinyl ketone [MVK], and γ-lactam substituted allenamide **154c** [X = CH_2] was the least and required the longest reaction time. This is directly related to the extent of delocalization of the nitrogen lone pair into the amide carbonyl. The ring size of the lactam also has an effect on the reactivity.

Scheme 36. Stereoselective Hetero-[4 + 2]



Scheme 37. A Proposed Model



The [4 + 2] cycloaddition could be rendered highly stereoselective using chiral allenamide **157** that can lead to pyrans **158** and **159a**,**b** [Scheme 36], representing the first highly stereoselective inverse demand hetero [4 + 2] cycloaddition of a chiral enamide. Control experiments showed that the observed isomeric ratio was not a result of the thermodynamic distribution of final cycloadducts.

In contrast, oxazolidinone substituted allenamides afforded pyranyl heterocycles such as **160** in lower yields and moderate stereoselectivity. This contrast is likely attributed to the fact that oxazolidinone substituted allenamides [see **161** in the lowest-energy conformer: PM3-Spartan Model^{TN}] provide less facial differentiation with the phenyl ring being further away from the internal olefin of the allene [Scheme 37]. In the imidazolidinone-substituted allenamide **157**, the phenyl ring is much closer, thereby providing a greater facial bias that would favor the hetero diene approaching preferentially from the bottom face.

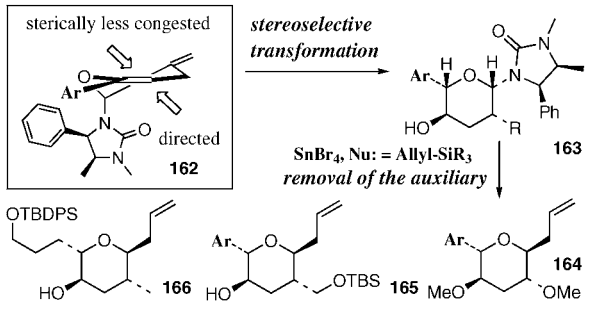
It is noteworthy that oxazolidinone-substituted allenamides are more robust than imidazolidinone-substituted allenamides because the former can tolerate Lewis acidic conditions as well as much higher temperatures [than 80 °C], whereas the latter would decompose under the same conditions.

Applications for these stereoselective cycloaddition products have been examined. The planarity of pyranyl heterocycle **162** [Scheme 38] allowed highly stereoselective transformation of both the sterically accessible *exo*-cyclic olefin and electron-rich *endo*-cyclic olefin leading to **163**. The selectivity could be rationalized as a result of electrophile or nucleophile preferring the less hindered face away from the chiral imidazolidinone group.

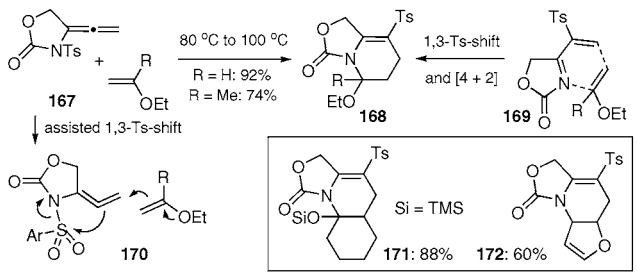
The imidazolidinone group in **163**, serving as an auxiliary, could be removed [and recovered] using a mild Lewis acid [$SnBr_4$] and replaced with allylsilanes.

These applications provide a new approach to *C*-glycosides[64,65] [**164**–**166**] with the pyranyl heterocycles serving as excellent chiral templates. A major advantage

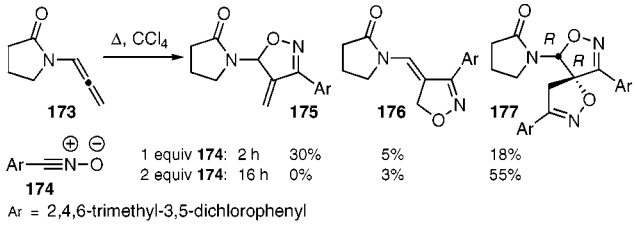
Scheme 38. Applications of Hetero-[4 + 2]



Scheme 39. Tamaru's Formal [4 + 2]



Scheme 40. Zecchi's [3 + 2]



of this approach is that protection and deprotection steps can be avoided.[66,67]

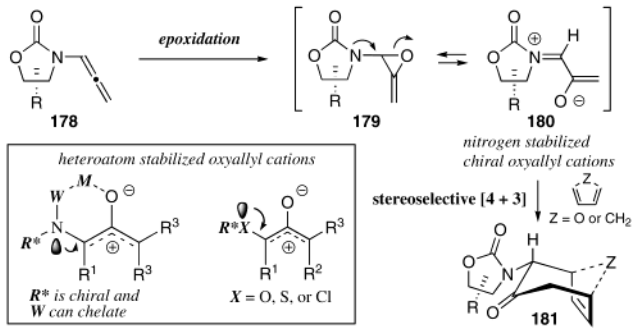
Tamura[40] communicated a formal [4 + 2] cycloaddition of allenamide **167** with enol ethers [Scheme 39], leading to **168** [also see **171**-**172**]. This reaction was also stereoselective. Mechanistically, it most likely involved a 1,3-Ts shift that either simply led to an aza-diene **169** that could be added to enol ethers in a [4 + 2] cycloaddition fashion, or was assisted by the enol ether [shown as **170**] followed by a cyclization.

3.4.4. [3 + 2]. Zecchi[43] showed the first example of a 1,3-dipolar cycloaddition utilizing allenamides. Allenamide **173** reacted with aryl nitrile oxide **174** efficiently under various conditions that led to [3 + 2] cycloadducts **175**, **176**, and **177** resulting from addition to internal, terminal olefin, and double addition, respectively [Scheme 40]. Yields and ratios varied with reaction times and equivalents of **174** used.

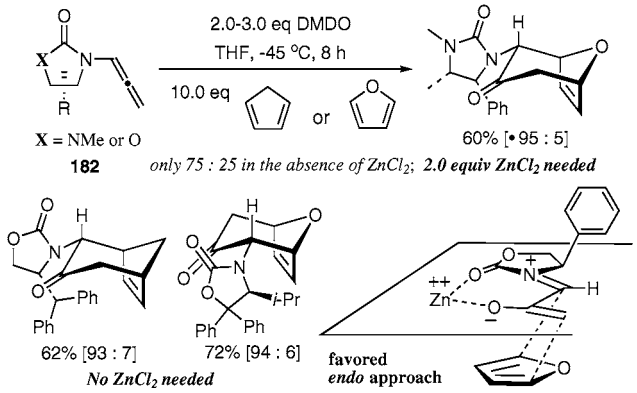
3.4.5. [4 + 3]. On the basis of our studies in epoxidation of allenamides shown earlier [Scheme 32], we were able to explore whether allene oxide **179** and/or nitrogen stabilized chiral oxyallyl cations **180** could be efficiently trapped by dienes in a highly stereoselective manner [Scheme 41]. Achieving highly stereoselective [4 + 3] cycloadditions remains a challenge in the area of oxyallyl cation cycloaddition.[68,69]

While heteroatom stabilized oxyallyl cations are known,[69] the nitrogen stabilized *chiral* oxyallyl cation has not been

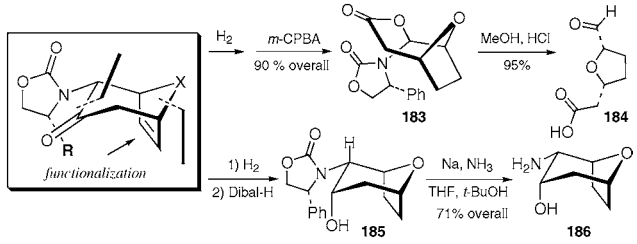
Scheme 41. An Overview of [4 + 3]



Scheme 42. Tandem Epoxidation/[4 + 3] Cycloaddition



Scheme 43. Synthetic Applications



reported.[70−72] The trivalent nature of the nitrogen atom allows simultaneous tethering of a chirality inducing unit and a coordination unit, leading to greater rigidity of the oxyallyl cation species, and thus, also better stereochemical outcome in the cycloaddition. This feature is an advantage over other heteroatom stabilized oxyallyl cations.[69] In addition, we believe that the readily accessible chiral allenamides could serve as excellent sources for nitrogen stabilized chiral oxyallyl cations.

DMDO epoxidation of allenamides **182** in the presence of various dienes led to corresponding [4 + 3] cycloadducts in a highly stereoselective manner [Scheme 42].[44] In some cases, 2.0 equiv of $ZnCl_2$ was needed to achieve high levels of selectivity. This was rationalized using a mechanistic model in which the Zn cation was coordinated to both oxygen atoms, providing greater conformational rigidity of the oxyallyl cation.

These cycloadducts can be excellent building blocks for constructing five-, six-, or seven-membered rings. This methodology has been specifically applied to synthesis of furan **184** and chiral amino alcohol **186** [Scheme 43].[44]

4. Conclusion

We have highlighted recent studies describing utility of allenamides in organic synthesis. Although chemistry involving other heteroatom-substituted allenes is of high impact and value, nitrogen substituted allenes offer some advantages. The trivalent nature of the nitrogen atom allows (1) tethering of a chirality-inducing unit to introduce new stereocenters, (2) inclusion of a coordination unit to provide conformational rigidity, and (3) a greater flexibility in designing intramolecular reactions. These features are attractive for developing stereoselective synthetic methods, and the future of allenamide chemistry should be promising. We hope this Account will provide further interest in the chemistry of allenamides.

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References

(1) For reviews, see: (a) Saalfrank, R. W.; Lurz, C. J. Heterosubstituierte Allene and Polyallene. In *Methoden Der Organischen Chemie (Houben-Weyl)*; Kropf, H., Schaumann, E., Eds.; Georg Thieme Verlag: Stuttgart, 1993; pp 3093−3102. (b) Schuster, H. E.; Coppola, G. M., *Allenes in Organic Synthesis*; John Wiley and Sons: New York, 1984. (c) For a review on chemistry of allenol ethers, see: Zimmer, R. Alkoxyallenes-Building Blocks in Organic Synthesis. *Synthesis* **1993**, 165.

(2) Hubert, A. J.; Viehe, H. G. Base-Catalyzed Prototropic Isomerisations. *J. Chem. Soc.* **1968**, 228−231.

(3) Brandsma, L.; Verkruijse, H. D., *Synthesis of Acetylenes, Allenes and Cumulenes*; Elsevier: Amsterdam, 1981.

(4) Maas, G.; Mayer, T. The Organocopper Route From [2-Propynylidene]morpholinium Triflates to Morpholino Allenes, 1-Morpholino-1,3-butadienes and 2-Morpholino-1-3-butadienes. *Synthesis* **1991**, 1209−1215.

(5) Examples of α-lithiated allenamines: (a) Tarasova, O. A.; Taherirastgar, F.; Verkruijsse, H. D.; Mal′kina, A. G.; Brandsma, L.; Trofimov, B. A., Metallation and Functionalization of 1-Allenylpyrrole. *Recl. Trav. Chim. Pays-Bas* **1996**, *115*, 147−145. (b) Pennanen, S. I. Lithiated 3-Trimethylsilyl-1-ethylaminopropynes. *Finn. Chem. Lett.* **1984**, 95−96.

(6) An example of γ-lithiated allenamines: Craig, J. C.; Ekwuribe, N. N., Synthesis of α,β-Unsaturated Aldehydes via 1-Aminopropa-1,2-dienes. Mechanistic Studies. *Tetrahedron Lett.* **1980**, *21*, 2587−2590.

(7) Klop, W.; Klusener, P. A. A.; Brandsma, L. Electrophilic Additions to Dimethylaminoallene. *Recl. J. Royal Neth. Chem. Soc.* **1984**, *103*, 27−29.

(8) For [3 + 2] cycloaddition, see: Broggini, G.; Zecchi, G., Site-Selective and Regioselective Cycloaddition of *N*-Propadienylanilines with Nitrile Oxides. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1843−1846.

(9) For [2 + 2] cycloadditions, see: (a) Niji, R.; Verkruijsse, H. D.; Harder, S.; van der Kerk, A. C. H. T. M.; Brandsma, L. A Peculiar Reaction of Aminoallenes with Aromatic and Heteroaromatic Aldehydes. *Synth. Commun.* **1991**, *21*, 653−656. (b) Klop, W.; Brandsma, L., An Unusual Ring-Enlargement in the Reactions of Acetylenic Esters and Ketones with *N, N*-Dimethylaminoallene. *J. Chem. Soc., Chem. Commun.* **1983**, 988−989.

(10) For [4 + 2] and [2 + 2] cycloadditions, see: Klop, W.; Klusener, P. A. A.; Brandsma, L., Cycloaddition of (Dimethylamino)allene to Some Electrophilic Alkenes and Its Application to the Synthesis of 3-Alkylidenecyclobutenes. *Recl. J. Royal Neth. Chem. Soc.* **1984**, *103*, 85−86.

(11) For [4 + 2] cycloadditions using allenammonium salts, see: Barlett, A. J.; Laird, T.; Ollis, W. D. Base Catalysed Intramolecular Cycloadditions of Allyl 3-Phenlprop-2-ynyl Ethers and 4-Methylpent-4-en-2-ynyl Prop-2-ynyl Ethers. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1315−1320.

(12) Mayer, T.; Maas, G., Thermal Isomerization of 1-Morphlino-3-phenyl-(or vinyl)-allenes. Synthesis of the [1,4]oxazino-[4,3-a]-azepine Framework. *Tetrahedron Lett.* **1992**, *33*, 205−208.

(13) Dimerization via radical: Garratt, P. J., Base Catalyzed Rearrangement of Bispropargyl Sulfides, Ethers, and Amines. *J. Am. Chem. Soc.* **1975**, *97*, 3255−3257.

(14) Rearrangements: N. Manisse, N.; Chuche, J., A New Valence Tautomerism. *J. Am. Chem. Soc.* **1977**, *99*, 1272−1273.

(15) (a) Breuil-Desvergnes, V.; Compain, P.; Vatéle, J.-M.; Goré, J. Reactions of the Lithio-Derivatives of Methoxy Allene with SAMP Hydrazones. Access to Enantiopure 3-Pyrrolines. *Tetrahedron Lett.* **1999**, *40*, 5009−5012. (b) Arnold, T.; Orschel, B.; Ressig, H.-U. Diacetoneglucose as Auxiliary Group for the Asymmetric Hetero-Diels-Alder Reactions with Nitrosoalkenes. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1033−1035.

(16) Dickinson, W. B.; Lang, P. C. The Synthesis and Rearrangement of an Allenamide. *Tetrahedron Lett.* **1967**, *8*, 3035−3040.

(17) Bogentoft, C.; Ericsson, Ö.; Stenberg, P.; Danielsson, B. Cyclization Reactions of an Allenic Oxoquinazoline. *Tetrahedron Lett.* **1969**, *10*, 4745−4748.

(18) Corbel, B.; Paugam, J.-P.; Dreux, M.; Savignac, P., *N*-Propargylphosphoramides-Nouveaux Reactifs de Synthese. *Tetrahedron Lett.* **1976**, *17*, 835−838.

(19) Balasubramanian, K. K.; Venugopalan, B. Studies in Claisen Rearrangement of 2-Propargylthiobenzimidazoles. *Tetrahedron Lett.* **1974**, *15*, 2643−2644.

(20) Overman, L. E.; Marlowe, C. K.; Clizbe, L. A. The Preparation of *N*-Trichloroacetamido-1,2-dienes. *Tetrahedron Lett.* **1979**, *20*, 599−600.

(21) For examples of quinolone based allenamides, see: (a) Rádl, S.; Kovárová, L. *Collect. Czech. Chem. Commun.* **1991**, *56*, 2413−2419. (b) Rádl, S.; Kovárová, L.; Holubeck, J. *Collect. Czech. Chem. Commun.* **1991**, *56*, 439−448.

(22) For examples of acridone based allenamides, see: (a) Rádl, S.; Kovárová, L.; Holubeck, J. Synthesis and Antibacterial Activity of Some 1-(2-Propynyl) and 1-Propadienyl Derivatives of 1,4-Dihydro-4-oxoquinoline-2-carboxylic Acids and Similar Heterocycles. *Collect. Czech. Chem. Commun.* **1991**, *56*, 439−448. (b) Reisch, J.; Salehi-Artimani, R. A. Acetylenchemie 12. *J. Heterocycl. Chem.* **1989**, *26*, 1803−1806. (c) Mahamoud, A.; Galy, J. P.; Vincent, E. J.; Barbe, J. Synthesis of (Allenic) *N*-Propadienyl- and (Acetylenic) *N*-(1-Propynyl)-acridones Using Phase-Transfer Catalysis. *Synthesis* **1981**, 917−918.

(23) Jones, B. C. N. M.; Silverton, J. V.; Simons, C.; Megati, S.; Nishimura, H.; Maeda, Y.; Mitsuya, H.; Zemlicka, J. Synthesis, Absolute Configuration, and Enantioselectivity of Antiretroviral Effect of (*R*)-(−)- and (*S*)-(+)-Cytallene. Lipase-Catalyzed Enantioselective Acylations N-Acylcytallenes. *J. Med. Chem.* **1995**, *38*, 1397−1405.

(24) Takagi, K.; Tomita, I.; Endo, T. Living Coordination Polymerization of *N*-Allenylamides by π-Allylnickel Catalyst. *Macromolecules* **1998**, *31*, 6741−6747.

(25) Xiong, H.; Hsung, R. P.; Wei, L.-L.; Berry, C. R.; Mulder, J. A.; Stockwell, B. The First Regioselective α-Deprotonation and Functionalization of Allenamides. *Org. Lett.* **2000**, *2*, 2869−2871.

(26) Gaul, C.; Seebach, D. Metallations and Reactions with Electrophiles of 4-Isopropyl-5,5-diphenyloxazolidin-2-one (DIOZ) with *N*-Allyl and *N*-Propargyl Substituents: Chiral Homo-enolate Reagents. *Helv. Chim. Acta* **2002**, *85*, 963−978.

(27) Nilsson, B. M.; Hacksell, U. Base-Catalyzed Cyclization of *N*-Propargylamides to Oxazoles. *J. Heterocycl. Chem.* **1989**, *26*, 269−275.

(28) Gericke, R.; Lues, I. The Transformation of a Chromene Derivative into Benzofurans via Allene Intermediates. *Tetrahedron Lett.* **1992**, *33*, 1871−1874.

(29) Tanaka, H.; Kameyama, Y.; Sumida, S.; Yamada, T.; Tokumaru, Y.; Shiroi, T.; Sasaoka, M.; Taniguchi, M.; Torri, S. A New Short Cut Route to 3-Norcephalosporins. *Synlett* **1991,** 888−890.

(30) (a) Farina, V.; Kant, J. A New Strategy for the Conversion of Penams into Cephems via Allene Chemistry. *Tetrahedron Lett.* **1992**, *33*, 3559−3562. (b) Kant, J.; Farina, V. A Stereocontrolled Synthesis of Cefprozil and Related Cephems *via* Allenylazetidiones. *Tetrahedron Lett.* **1992**, *33*, 3563−3566.

(31) Noguchi, M.; Okada, H.; Wantanabe, M.; Okuda, K.; Nakamura, O. Iodocyclization of 3-Alkynyl- and 3-Allenyl-2-(Substituted Amino)-1-imidazolin-4-ones. *Tetrahedron* **1996**, *52*, 6581−6590.

(32) (a) Grigg, R.; Sridharan, V.; Xu, L.-H. Palladium-Catalysed Cyclisation of Allenes. *J. Chem. Soc., Chem. Commun.* **1995**, 1903−1904. (b) Grigg, R.; Sansano, J. M.; Santhakumar, V.; Sridharan, V.; Thangavelanthum, R.; Thornton-Pett, M.; Wilson, D. Palladium Catalysed Tandem Cyclisation-Anion Capture Process. *Tetrahedron* **1997**, *53*, 11803−11826. (c) Gardiner, M.; Grigg, R.; Sridharan, V.; Vicker, N. Cascade and Sequential Palladium Catalysed Cyclisation-Azide Capture-1,3-Dipolar Cycloaddition Route to Complex Triazoles. *Tetrahedron Lett.* **1998**, *39*, 435−438.

(33) Grigg, R.; Loganathan, V.; Sridharan, V.; Stevenson, P.; Sukirthalingam, S.; Worakun, T. Palladium Catalysed Tandem Cyclisation-Anion Capture Processes. *Tetrahedron* **1996**, *52*, 11479−11502.

(34) Grigg, R.; Sansano, J. M. Sequential Hydrostannylation-Cyclisation of δ- and ω-Allenyl Aryl Halides. Cyclisation at the Proximal Carbon. *Tetrahedron* **1996**, *52*, 13441−13454.

(35) Grigg, R.; Köppen, I.; Rasparini, M.; Sridharan, V. Synthesis of Spiro- and Fused Heterocycles by Palladium Catalysed Carbo and Hetero-annulation Cascades of Allenes. *Chem. Commun.* **2001**, 964−965.
(36) Kinderman, S. S.; van Maarseveen, J. H.; Schoemaker, H. E.; Hiemstra, H.; Rutjes, F. P. T. Enamide-Olefin Ring-Closing Metathesis. *Org. Lett.* **2001**, *3*, 2045−2048.
(37) Rameshkumar, C.; Xiong, H.; Tracey, M. R.; Berry, C. R.; Yao, L. J.; Hsung, R. P. NMR Studies on Epoxidations of Allenamides. *J. Org. Chem.* **2002**, *67*, 1339−1345.
(38) Kimura, M.; Horino, Y.; Wakamiya, Y.; Okajima, T.; Tamaru, Y. Pronounced Chemo-, Regio-, and Stereoselective [2 + 2] Cycloaddition Reaction of Allenes Toward Alkenes and Alkynes. *J. Am. Chem. Soc.* **1997**, *119*, 10869−10870.
(39) Kimura, M.; Wakamiya, Y.; Horino, Y.; Tamaru, Y. Efficient Synthesis of 4-Ethenylidene-2-oxazolidiones via Palladium Catalyzed Amino Cyclization of 2-Butyn-1,4-diol Biscarbamates. *Tetrahedron Lett.* **1997**, *38*, 3963−3966.
(40) Horino, Y.; Kimura, M.; Wakamiya, Y.; Okajima, T.; Tamaru, Y. Efficient Entry to Tetrahydropyridines: Addition to Enol Ethers to Allenesulfonamides Involving a Novel 1,3-Sulfonyl Shift. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 121−123.
(41) Wei, L.-L.; Xiong, H.; Douglas, C. J.; Hsung, R. P. Inverse Demand [4 + 2] Cycloaddition Reactions of Allenamides. Reactivity Scopes of an Electron Deficient variant of Allenamines. *Tetrahedron Lett.* **1999**, *40*, 6903−6907.
(42) Wei, L.-L.; Hsung, R. P.; Xiong, H.; Mulder, J. A.; Nkansah, N. T. First Stereoselective Inverse Demand [4 + 2] Cycloaddition Reactions of Novel Chiral Allenamides with Heterodienes. *Org. Lett.* **1999**, *1*, 2145−2148.
(43) Broggini, G.; Bruché, L.; Zecchi, G. 1,3-Dipolar Cycloadditions to Nitrogen-Substituted Allenes. *J. Chem. Soc., Perkin Trans. 1* **1990**, 533−539.
(44) (a) Xiong, H.; Hsung. R. P.; Berry, C. R.; Rameshkumar, C. The First Epoxidation of 1-Amidoallenes. *J. Am. Chem. Soc.* **2001**, *123*, 7174−7175. (b) Xiong, H.; Hsung, R. P.; Shen, L.; Hahn, J. M. Chiral Enamide. Part 1. Epoxidations of Chiral Enamides. A Viable Approach to Chiral Nitrogenstablized Oxyallyl Cations in [4+3] Cycloadditions. *Tetrahedron Lett.* **2002**, *43*, 4449−4453.
(45) Cho, A. K.; Haslett, A. L.; Jenden, D. The Identification of An Active Metabolite of Tremorine. *Biochem. Biophys. Res. Commun.* **1961**, *5*, 276−279.
(46) Bebbington, A.; Shakeshaft, D. An Improved Synthesis of Oxotremorine. *J. Med. Chem.* **1965**, *8*, 274−275.
(47) For a recent review, see: Hsung, R. P.; Zificsak, C. A.; Mulder, J. A.; Rameshkumar, C.; Wei, L.-L. Recent Advances in the Chemistry of Ynamines and Ynamides. *Tetrahedron* **2001**, *57*, 7575−7606.
(48) For other reviews, see: (a) Himbert, G. 1-Hetero-1-alkine,-polyine bzw. 1,2-Dihetero-ethine. In *Methoden Der Organischen Chemie (Houben-Weyl)*; Kropf, H., Schaumann, E., Eds.; Georg Thieme Verlag: Stuttgart, 1993; Vol. E15, pp 3267−3443. (b) Ficini, J. Ynamines: A Versatile Tool in Organic Synthesis. *Tetrahedron* **1976**, *32*, 1448−1486.
(49) Hsung, R. P.; Zificsak, C.; Wei, L.-L.; Douglas, C. J.; Xiong, H.; Mulder, J. A. Lewis Acid Promoted Hetero [2 + 2] Cycloaddition Reactions of Aldehydes with 10-Propynyl-9(10*H*)-acridone. *Org. Lett.* **1999**, *1*, 1237−1240.
(50) Huang, J.; Xiong, H.; Hsung, R. P.; Rameshkumar. C.; Mulder, J. A.; Grebe, T. P. The First Successful Base-Promoted Isomerization of Propargyl Amides to Chiral Ynamides. *Org. Lett.* **2002**, *4*, 2417−2420.
(51) Mulder, J. A.; Hsung, R. P.; Frederick, M. O.; Tracey, M. R.; Zificsak, C. A. The First Highly Stereoselective Ficini-Claisen Rearrangement Using Chiral Ynamides. *Org. Lett.* **2002**, *4*, 1383−1386.
(52) Frederick, M. O.; Mulder, J. A.; Tracey, M.; Hsung, R.; Huang, J.; Kurtz, K. C. M.; Shen, L.; Douglas, C. J. A Copper Catalyzed C−N Bond Formation Involving *sp*-Hybridized Carbons. *J. Am. Chem. Soc.* **2003**, *125,* 2368−2369.
(53) Wei, L.-L.; Mulder, J. A.; Xiong, H.; Zificsak, C. A.; Douglas, C. J.; Hsung, R. P. Efficient Preparations of Novel Ynamides and Allenamides. *Tetrahedron* **2001**, *57*, 459−466.
(54) Zaugg, H. E.; Swett, L. R.; Stone, G. R. An Unusual Reaction of Propargyl Bromide. *J. Org. Chem.* **1958**, *23*, 1389−1390.
(55) (a) Katritzky, A. R.; Ramer, W. H. Heterocyclic Ynammonium Salts. *J. Org. Chem.* **1985**, *50*, 852−856. (b) Majumdar, K. C.; Ghosh, S. K. Phase-Transfer-Catalyzed Alkylative Eliminations. *Synth. Commun.* **1994**, *24*, 217−231.
(56) van Boxtel, L. J.; Korbe, S.; Noltemeyer, M.; de Meijere, A. Facile Synthesis of Bicyclic and Tricyclic Skeletons by Cycloisomerizations of Hept-1-en-6-ynes and 4,9-Diheteradodeca-1,11-dien-6-ynes. *Eur. J. Org. Chem.* **2001**, 2283−2292.
(57) Kimura, M.; Kure, S.; Yoshida, Z.; Tanaka, S.; Fugami, K.; Tamaru, Y. Convenient Synthesis of Densely Functionalized *N*-Substituted 4-Methylene-2-oxazolidinoe. *Tetrahedron Lett.* **1990**, *31*, 4887−4890.
(58) (a) Kozawa, Y.; Mori, M. Synthesis of Different Ring-Size Heterocycles from the Same Propargyl Alcohol Derivative by Ligand Effect on $Pd^{(0)}$. *Tetrahedron Lett.* **2002**, *43*, 1499−1502. (b) Kozawa, Y.; Mori, M. Construction of a Carbapenam Skeleton Using Palladium-Catalyzed Cyclization. *Tetrahedron Lett.* **2001**, *42*, 4869−4873.
(59) For an excellent review, see: Brummond, K. M.; Kent, J. L. Recent Advances in the Pauson-Khand Reaction and Related [2+2+1] Cycloadditions. *Tetrahedron* **2000**, *56,* 3263−3283.
(60) (a) Grubbs, R. H.; Miller, S. J.; Fu, G. C. Ring-Closing Metathesis and Related Processes in Organic Synthesis. *Acc. Chem. Res.* **1995**, *28*, 446−452. (b) Schrock, R. R. Olefin Metathesis by Molybdenum Imido Alkylidene Catalysts. *Tetrahedron* **1999**, *55*, 8141−8153.
(61) Chan, T. H.; Ong, B. S. Chemistry of Allene Oxides. *Tetrahedron* **1980**, *36*, 2269−2289.
(62) Crandall, J. K.; Rambo, E. Synthesis of Functionalized Lactones by the DMDO Oxidation of Allenic Acid. *Tetrahedron* **2002**, *58*, 7027−7036.
(63) Reich, H. J.; Kelly, M. J. Silylketone Chemistry. Synthesis and Reactions of Olefinic and Acetylenic Silyl Ketones. *J. Am. Chem. Soc.* **1982**, *104*, 1119−1120.
(64) Postema, M. H. D. *C-Glycoside Synthesis* CRC Press: Ann Arbor, **1995**.
(65) Parker, K. A. Novel Methods for the Synthesis of *C*-Aryl Glycoside Natural Products. *Pure Appl. Chem.* **1994**, *66*, 2135−2138.
(66) Berry, C. R.; Rameshkumar, C.; Tracey, M. R.; Wei, L.-L.; Hsung, R. P. A Lewis-Acid Mediated Stereoselective Removal of An Anomeric Urea Substituent. *Synlett* **2003**, 791−796.
(67) Rameshkumar, C.; Hsung, R. P. Pyranyl Heterocycles from Inverse Electron Demand Hetero [4 + 2] Cycloaddition Reactions of Chiral Allenamides. *Synlett* **2003**,1241−1246.
(68) For reviews, see: (a) Harmata, M.; Rashatasakhon, P. Cycloaddition Reactions of Vinyl Oxocarbenium Ions. *Tetrahedron* **2003**, *59*, 2371−2395. (b) Harmata, M., Exploration of Fundamental and Synthetic Aspects of the Intramolecular 4+3 Cycloaddition Reaction. *Acc. Chem. Res.* **2001**, *34*, 595−605.
(69) Also see: Harmata, M., Heteroatom-Stabilized Allylic Cation in 4+3 Cycloaddition Reactions. *Recent Res. Dev. Org. Chem.* **1997**, *1*, pp523−535.
(70) Katritzky, A. R.; Dennis, N. Cycloaddition Reactions of Heteroaromatic Six-Membered Rings. *Chem. Rev.* **1989**, *89*, 827−861.
(71) Walters, M. A.; Arcand, H. R. Cycloaddition Reactions of a Nitrogen-Substituted Oxyallyl Cation with Cyclopentadiene and Substituted Furans. *J. Org. Chem.* **1996**, *61*, 1478−1486.
(72) For other elegant studies on nitrogen-substituted oxyallyls, see: (a) Myers, A. G.; Barbay, J. K., On the Inherent Instability of α-Amino α′-Fluoro Ketones. Evidence for Their Transformation to Reactive Oxyvinyliminium Ion Intermediates. *Org. Lett.* **2001**, *3*, 425−428. (b) Harmata, M.; Ghosh, S. K.; Hong, X.; Wacharasindhu, S.; Kirchhoefer, P., Asymmetric Organocatalysis of 4 + 3 Cycloaddition Reactions. *J. Am. Chem. Soc.* **2003**, *125*, 2058−2059.

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