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Aziridinium Ylides: Underutilized Intermediates for Complex Amine Synthesis

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Abstract

Harnessing the chemistry of onium ylide intermediates generated from transition metal catalysis is a powerful strategy to convert simple precursors into complex scaffolds. While the chemistry of onium ylides has been studied for over three decades, transformations of aziridinium ylides have just recently emerged as a versatile way to exploit the strain of these reactive intermediates to furnish densely functionalized *N*-heterocycles in a highly stereocontrolled manner. Herein, we provide a short overview of the key concepts and recent developments in this area, with a focus on how mechanistic studies to delineate the factors controlling the reactivity of aziridinium ylides can stimulate fruitful future investigations.

Keywords

ylide; ring expansion; cheletropic extrusion; carbene transfer; aziridine

Transition metal-catalyzed generation of ammonium and related ylides

The generation of ammonium ylides *via* inter- and intramolecular reactions of tertiary amines with thermally or photochemically generated **carbenes** (see Glossary) is well-established in the literature [1–6]. However, the high reactivity of “free” carbenes typically results in low yields and competing side reactions. To address these issues, methods for the catalytic generation of ammonium ylides have been developed that involve the attack of an amine lone pair on an electrophilic metal carbene complex [7]. These strategies are attractive alternatives to traditional base-promoted procedures, as ylides are formed under mild conditions and display attenuated reactivity. The resultant carbene-generated ylides have been employed in diverse synthetic transformations, including [2,3]-sigmatropic rearrangements, **Stevens rearrangements**, and **1,3-dipolar cycloadditions** [8–14]. Creative ways to manipulate the reactivity of these unusual intermediates can lead to powerful methodologies to convert simple starting materials into stereochemically complex, densely functionalized heterocycles with high levels of diastereo- and enantiocontrol.

The structural features of ylides, particularly the nature of the onium group, play key roles in influencing reactivity [15–17]. Nitrogen ylides are the third most common type of onium ylide, behind phosphorus and sulfur [18–42]; however, the strongly Lewis basic nitrogen of

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tertiary amines presents a challenge, as it may inactivate the transition metals required to decompose diazoesters and other carbene precursors [43].

In contrast to the attention afforded to ammonium ylides, the **aziridinium ylide** subclass has been underexplored. The few published reports describing their reactivity highlight the potential for diverse pathways, including ring expansion *via* rearrangement or fragmentation by **cheletropic extrusion** [44–50]. If aziridinium ylides are to be viewed as truly versatile intermediates, the factors dictating their ultimate fate must be better understood and controlled.

Intramolecular Cu-catalyzed [2,3]-Stevens rearrangements of aziridinium ylides

In 2001, Clark explored the stereoselective synthesis of bicyclic amines through the ring expansion of ammonium ylides derived from various cyclic amines tethered to copper-supported carbenoids (Figure 1A) [44]. Cyclization precursor **1** was subjected to $Cu(acac)_2$ in benzene at reflux. The bicyclic amine **2** (obtained in 24% isolated yield) was hypothesized to arise from a stereoselective, intramolecular [2,3]-rearrangement of the aziridinium ylide **3**, where the ring strain imparted by the vinyl aziridine moiety facilitated productive ring expansion. Decomposition of indolizidine **2** was noted within one day of storage at −30°C, suggesting that product instability may have contributed to the modest yield.

In 2004, Rowlands disclosed a single example of an aziridine ring expansion proposed to proceed through an intramolecular [2,3]-Stevens rearrangement of an aziridinium ylide intermediate (Figure 1B) [45]. In this study, a vinyl aziridine containing an internal diazoacetate tether was prepared as a 3:4 mixture of nitrogen invertomers, favoring **4b**. The mixture was heated in the presence of catalytic $Cu(acac)_2$ to furnish the bicyclic amine **5** in 21% isolated yield. The low yield was attributed to the orientations of the substituents in nitrogen invertomers **4a** and **4b**. Productive [2,3]-Stevens rearrangement requires a *cis* orientation between the alkene and the lone pair of electrons on the nitrogen prior to formation of the aziridinium ylide **6**; thus, effective reaction occurs only from conformer **4a**. In conformer **4b**, the ineffective overlap between the anionic carbon and alkene pose steric and spatial constraints on the desired rearrangement. This leads to a [1,5]-hydrogen shift outcompeting nitrogen inversion in **4b** to furnish imine **7**, which degrades under the reaction conditions. This result highlights how productive ylide formation and subsequent rearrangement depend heavily on the presence of an accessible nitrogen lone pair and control over the stereochemistry at the newly pyramidalized ring nitrogen. The challenges encountered in this original study inspired recent investigations to expand the scope of chemistry involving aziridinium ylides by limiting nitrogen inversion through the use of tethers and electron-withdrawing groups within the aziridine scaffold.

Intermolecular Rh-catalyzed formal [3+1] ring expansion of bicyclic methyleneaziridines

The Schomaker group has extensively explored the chemistry of bicyclic methyleneaziridines (MAs), initially focusing on nucleophilic ring-opening and functionalization of the exocyclic alkene [51–58]. Methyleneaziridines have been readily transformed to other nitrogen-containing heterocycles, including aminated stereotriads, azetidin-3-ones, strained cyclooctynes, and aminated cycloheptenes. Interestingly, the constrained geometry and ring strain in MAs inhibits undesired nitrogen inversion and renders the nitrogen lone pair both sterically accessible and unusually nucleophilic, due to lack of conjugation with the carbamate tether. In 2017, the group exploited these features in a formal [3+1] ring expansion of MAs to methyleneazetidines with good scope, yields, and diastereoselectivities (Figure 2) [46]. The key aziridinium ylide intermediate was generated by nucleophilic addition of the ring nitrogen to a rhodium-bound carbene, where the bicyclic nature of the precursor and high *E:Z* ratios were key to successful ylide formation. A stereocontrolled [2,3]-Stevens rearrangement of the ylide ultimately delivered the azetidine products.

Experimental results showed that the electronics of the aryl substituents on the diazoester carbene precursors do not significantly affect the reaction outcome (Figure 2A). No larger *N*-heterocyclic ring expansion products were noted from ylides formed from vinyl-substituted diazoacetate **9h**, despite the potential for competing vinylogous reactivity [59–62]. MAs containing a substituent *cis* to the aziridine nitrogen did not react with sterically hindered carbene **9a**, as no formation of **10ba** was observed; however, switching to the less-hindered styrenyl diazoester **9h** delivered fully substituted methyleneazetidine **10bh**. Adjacent quaternary stereocenters were successfully set in methyleneazetidine **10ch**, which was obtained as a mixture of diastereomers with 89% yield and 3:1 *dr*; separation of the diastereomers gave the *syn*-Me/CO_2Me isomer of **10ch** in 54% yield and 15:1 *dr*.

Several possible pathways for the [3+1] ring expansion were studied both experimentally and computationally (Figure 2B). The functionalized methyleneazetidine product was initially proposed to result from a stepwise ring-opening, ring-closing sequence through **8.3** and **8.4** (Figure 2B i); this pathway would ablate any stereochemical information present in **8.1**. In contrast, a concerted [2,3]-Stevens rearrangement through **8.6** was identified as an alternative mechanism that would result in enantioretention in **8.5** (Figure 2B ii). Cheletropic extrusion of the ylide **8.2** to give allenic intermediate **8.8**, followed by a [2+2] cycloaddition, was also considered as a potential pathway (Figure 2B iii). However, the absence of **8.9**, which would result from a [2+2] cycloaddition involving the proximal allene bond, renders this pathway unlikely. Rh-catalyzed alkene cyclopropanation is well-known [63]; in this system, cyclopropanation of **8.1**, followed by rearrangement of the azaspiropentane intermediate **8.10**, would yield methyleneazetidine **8.5** (Figure 2B iv). However, amines react readily with electrophiles and Lewis acids, supporting ylide formation over competing alkene cyclopropanation [51]. The possibility of a radical pathway was investigated using TEMPO as an intermolecular radical trap; no change was noted. In addition, methyleneazetidine **10da** was successfully accessed without any ring opening of the

cyclopropane substituent (Figure 2A), suggesting ring expansion is unlikely to proceed through a radical pathway. Excluding the Rh catalyst gave no azetidine product, highlighting the importance of metal-mediated decomposition of the diazoester prior to metallocarbene and subsequent ylide formation. Experimentally, the efficient transfer of chirality from enantioenriched (*S*)-**8a** to methyleneazetidine (*S,S*)-**10aa** indicates the ring expansion does not proceed through any intermediates that ablate the stereochemical information present in the aziridine precursor (Figure 2C). Thus, the most likely mechanism involves the concerted [2,3]-Stevens rearrangement shown in Figure 2B ii.

Follow-up computational studies by density functional theory (DFT) provided further support for this pathway (Figure 2D). Formation of aziridinium ylide **INT1** from the nucleophilic addition of methyleneaziridine **8e** to Rh-bound carbene **9a** (*via* **TS1**, $\Delta G^{\ddagger}$ = 3.2 kcal/mol) outcompeted an alternative concerted cyclopropanation pathway proceeding through **TS1′** ($\Delta G^{\ddagger}$ = 11.3 kcal/mol). Rh dissociation from **INT1** to generate metal-free ylide **INT2**, followed by ring opening *via* **TS3** (9.2 kcal/mol from **INT1**) was favored over a ring opening of the allylic C–N bond through **TS2** (12.5 kcal/mol). Reports on the fates of rhodium and copper ylides employed in O–H insertion chemistry support this metal-free route, in spite of the energetically costly metal dissociation [64]. In the final step of the mechanism, a highly asynchronous, concerted [2,3]-Stevens rearrangement, which proceeds through **TS3**, yields the product methyleneazetidine **10aa**. Overall, this efficient **stereospecific** reaction takes advantage of the strained bicyclic MA framework and the unique reactivity of aziridinium ylides to forge a new C-C bond, a new C-N bond, and two adjacent stereocenters.

N-Heterocycles from bicyclic aziridines *via* aziridinium ylides

Encouraged by the success of the [3+1] ring expansion, the Schomaker group sought to further develop the reactivity of aziridinium ylides by investigating aziridines lacking the exocyclic alkene present in MAs [47]. While no conversion was observed with the *trans*-**11a** aziridine isomer, the *cis*-**11a** aziridine isomer yielded imine **12** through a proposed cheletropic extrusion of an aziridinium ylide (Figure 3A,B). Similar aziridinium ylide reactivity was reported by Watanabe in 1972 [48], where $Cu(acac)_2$-catalyzed addition of aziridine **13** to diazoester **14** furnished ethylene **15** and an α-imino ester **16** in quantitative yield, instead of the expected azetidine **18** (Figure 3C).

The fragmentation of aziridinium ylide **17** indicates that the reaction proceeds *via* cheletropic extrusion of the aziridinium ylide intermediate, in lieu of the desired [1,2]-Stevens rearrangement.

Calculations on the bicyclic aziridine system show imine **12** results from cheletropic extrusion of either the rhodium-supported ylide **INT1-b** (*via* **TS4-b**) or the free ylide **INT2-b** (*via* **TS5-b**), with both pathways having favorable activation barriers of 9.9 and 7.2 kcal/mol, respectively (Figure 3D). However, both activation energy barriers for the cheletropic extrusion of **INT1-b** are significantly higher than the barrier of the analogous ring expansion of ylide **INT2** (1.6 kcal/mol, *via* **TS3**) in the previously studied MA system (Figure 2B).

Features of aziridinium ylides arising from a methyleneaziridine (**INT2**, Figure 3E) and a bicyclic aziridine (**INT2-b**, Figure 3E) were compared. The differing bond strengths (0.82 and 0.75, respectively) of the vinylic and allylic C-N bonds in **INT2** favor ring expansion through the initial rupture of the allylic C-N bond. In contrast, the nearly equivalent bond strengths (0.78 and 0.79, respectively) for the C-N bonds of the unbiased aziridine-derived ylide **INT2-b** favor a concerted extrusion over ring expansion. Based on this computational analysis, the absence of the exocyclic alkene in **INT2-b** contributes to cheletropic extrusion in the unbiased aziridine system. The increased ring strain (~4.5 kcal/mol) imparted by the exocyclic alkene of MA substrate **8e** helps to differentiate the bond strengths of the two aziridine C-N bonds, thus biasing the allylic C-N bond in **INT2** to break first.

Dehydropiperidines from bicyclic aziridines *via* aziridinium ylides

Building on the ability to control the fate of aziridinium ylide intermediates, the Schomaker group reported a formal [3+3] ring expansion of bicyclic aziridines to highly substituted dehydropiperidines with good yields and diastereoselectivities [49]. The aziridinium ylide was proposed to arise from the reaction of the bicyclic aziridine with a vinyl diazoacetate-derived rhodium carbene. Delocalization of the negative charge through the vinyl group of the diazo precursor was exploited to preclude competitive cheletropic extrusion and promote the desired ring expansion pathway to furnish the dehydropiperidine.

Bicyclic aziridine precursors were prepared from the corresponding homoallylic carbamates *via* Ag-catalyzed nitrene transfer [65], then subjected to the optimized Rh-catalyzed carbene transfer conditions. Carbene transfer was successful employing *cis*-substituted bicyclic aziridines, but no reaction was observed with the *trans*-aziridine isomers, likely due to steric congestion at the nitrogen lone pair that hindered productive ylide formation. A variety of substituents were tolerated in the *cis*-aziridine precursors, including alkyl groups, halides, and ethers (Figure 4A). A series of aryl-substituted diazoesters with varying steric and electronic features were surveyed to probe the impact on reaction outcome. Diazoesters with electron-donating and neutral substituents gave dehydropiperidines **20aa–20ac** in similar yields, demonstrating that the electronics of the styrene in the carbene precursor do not heavily affect the reaction outcome. This was further confirmed with dehydropiperidine **20ad**, which was obtained in good yield, despite the presence of an electron-withdrawing trifluoromethyl substituent. Dehydropiperidines **20ae** and **20af** were furnished in good yield and excellent *dr* from alkyl-substituted diazoacetates, which highlighted the extension of the chemistry beyond aryl diazoacetates.

DFT calculations supported formation of the aziridinium ylide **INT1** from nucleophilic attack of the aziridine nitrogen on the Rh-supported carbene (Figure 4B); exergonic dissociation of the rhodium catalyst from **INT1** gives zwitterion **INT2**. According to the computations, **INT2** can undergo either a cheletropic extrusion pathway or ring expansion through a ring-opening/ring-closing cascade. In the former case, cheletropic extrusion from **INT2** proceeding *via* **TS2** would form azadiene **INT3**. A subsequent aza-Diels Alder cycloaddition through **TS3** would then furnish the dehydropiperidine **20ba**. However, this pathway was ruled out as the chirality of enantioenriched aziridine (*S*,*R*)-**11g** was transferred to (*R*,*R*,*R*)-**20ga** with excellent retention at **C1** (Figure 4C). For the ring

expansion pathway, direct formation of dehydropiperidine **20ba** from **INT2** was predicted. In this scenario, stereochemical information at **C1** in **11b** would be transferred with retention to **C1** of the dehydropiperidine **20ba**, a prediction that was confirmed experimentally. This latter pathway, considered to be a pseudo-[1,4]-sigmatropic rearrangement, represents the most energetically favorable pathway of the mechanisms that were studied computationally.

The retention of stereochemical information in the ring expansion further provided insight into the details of the rearrangement step. A proposed intramolecular S_N2 attack of the benzylic carbon was invalidated, as an inversion of stereochemistry at C1 was not supported by the retention of chirality experiment or the X-ray crystal structure of **20ac**. Computational insight into the observed experimental results suggests the rearrangement proceeds instead through a stereoretentive S_N1-like mechanism. **TS2** and **TS2'** both present as low-barrier, early transition states, but C-N bond breakage in the two configurations is biased. In the lower energy **TS2'**, C-N bond breakage occurs at the external C1-N bond, which elongates to 1.937 Å. In the energetically disfavored **TS2**, the internal C2-N bond elongates to 2.360 Å, while the C1-N bond elongates to 1.735 Å. As predicted by **TS2'** and confirmed by experimental results, the ring-opening of the C1-N aziridine bond and the subsequent C-C bond formation proceed with retention of stereochemistry at **C1**. This work represents the first examples of aziridinium ylides derived from unbiased aziridines that are able to bypass competitive cheletropic extrusion in favor of ring expansion.

Dehydropiperazines from bicyclic aziridines *via* aziridinium ylides

The Schomaker group explored other types of carbene precursors to further develop aziridinium ylide chemistry for the synthesis of complex *N*-heterocycles that are not easily prepared with current methods. Pyridotriazoles **21a** have been reported to form α-imino metal carbenes **23a** in the presence of a transition metal catalyst [66]. These metal-supported carbenes participate in transformations that include cyclopropanation, X-H insertion, and transannulations to form *N*-heterocycle derivatives [67–70]. However, in this case, reaction of bicyclic aziridine *cis*-**11a** with pyridotriazole **21a** furnished a ketimine product **24aa** through cheletropic extrusion of aziridinium ylide **26** (Figure 5A) [50]. DFT calculations were helpful in rationalizing the fate of the aziridinium ylide **INT2** formed from nucleophilic addition of the aziridine to the electrophilic center of the Rh carbene and subsequent metal dissociation (Figure 5B). Two proposed fates of the ylide **INT2** were investigated: cheletropic extrusion (*via* **TS2**) or ring expansion (*via* **TS2'**). The cheletropic pathway ultimately terminates at imine **INT3**, as a subsequent aza-Diels-Alder reaction to afford the desired tricyclic ring expansion product **25aa** is kinetically unfeasible, with a high barrier of >50 kcal/mol. This barrier is ascribed to the required loss of aromaticity of the pyridyl substituent prior to ring closure.

Altering the identity of the carbene precursor was proposed as a solution to access the desired dehydropiperazine scaffold through a ring expansion pathway (Figure 6A). *N*-Sulfonyl-1,2,3-triazoles were chosen, as their utility as precursors for accessing metal-supported imino carbenes have been demonstrated in reactions that include transannulations, ring expansions, ylide formation, and C–H functionalization reactions [71–76]. *N*-

Sulfonyl-1,2,3-triazoles **27a** are reported to tautomerize in solution upon heating to afford α-diazo imines **28a** in low concentrations, eliminating the need for slow addition of the carbene precursor to avoid dimerization [77]. Linear alkyl-substituted aziridines **11a–b** and branched aziridine **11c** gave the desired dehydropiperazines **31aa–ba** and **31ca** in good yield and excellent *dr* of >19:1. Heteroatom-containing substituents, including the alkyl chloride in **11d**, were well-tolerated to deliver **31da** in good yield as a single diastereomer. Dehydropiperazine **31ea** was obtained in good yield, showing that substitution on the aziridine was not necessary for productive reaction. Tosyl-protected aryl *N*-sulfonyl-1,2,3-triazoles **27c–f** were examined to evaluate the effect of altering the electronic and steric environment of the carbene precursor on reaction outcome (Figure 6B). *N*-sulfonyl-1,2,3-triazoles **27e–f**, bearing electron-donating substituents, furnished the respective dehydropiperazines **31ae–af** in good yields; however, strongly electron-withdrawing groups lowered the yield. As demonstrated with dehydropiperazine **31ag**, the use of alkyl-substituted triazoles failed to furnish any desired product. Calculations showed aryl carbenes have a smaller HOMO-LUMO gap (3.40 eV versus 3.71 eV), suggesting stabilized carbenes of this type are more reactive towards nucleophilic bicyclic aziridines as compared to alkyl carbenes (Figure 6C). DFT calculations support the nucleophilic addition of the bicyclic aziridine **11f** to the electrophilic center of the rhodium-supported carbene **29a**, followed by Rh dissociation to furnish the aziridinium ylide **INT2** (Figure 6D). A highly exergonic cheletropic extrusion of intermediate **INT2** is predicted to produce alkene intermediate **INT3** *via* **TS2**. **INT3** may then undergo an aza-Diels Alder cycloaddition through **TS3** to yield the corresponding dehydropiperazine **31fa**. In contrast, an alternative reaction pathway directly produces the dehydropiperazine **6aa′** from ylide **INT2** through a sigmatropic rearrangement in which breaking of the aziridine C-N bond and formation of a new C-N bond is concomitant, yet highly asynchronous. Calculations suggest the direct formation of dehydropiperazine **31fa** through **TS2′** is kinetically favored, though both reaction pathways are possible given the experimental reaction conditions.

Concluding Remarks

This review highlights recent strategies to exploit the unique features of aziridinium ylides as synthetic intermediates for the construction of densely substituted, stereochemically complex *N*-heterocycles. The key to expanding the utility of this chemistry hinges on obtaining a better mechanistic understanding of how to effectively form and control the subsequent reactivities of aziridinium ylide intermediates (see Outstanding Questions). A combination of experimental and computational studies has provided insight into some of the factors that contribute to the fate of diverse types of aziridinium ylides; continuing these investigations will enable the rational design of improved methods that furnish a broader range of complex nitrogen-containing heterocycles. Future work will aim to engage analogous onium ylides derived from smaller heterocycles as intermediates toward the synthesis of larger, highly functionalized heterocycles.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Glossary

Aziridinium ylide
a subclass of N(sp^3)-based ammonium ylides that contain a positively charged aziridinium nitrogen adjacent to an exocyclic nucleophilic carbanionic site; in this review, an ylide generated from the reaction between an aziridine and a metal-supported carbene

Carbene
a compound containing a divalent carbon atom with a pair of nonbonding electrons

Cheletropic extrusion
a pericyclic reaction in which two σ bonds terminating at the same atom are made or broken in a concerted fashion

1,3-Dipolar cycloaddition
a pericyclic chemical reaction between a 1,3-dipole and a dipolarophile leading to the formation of a five-membered ring

Stereospecificity
a condition of a reaction in which the production of a single stereoisomer is directly determined by the stereochemistry of the starting material

Stevens rearrangement
traditionally, a base-promoted transformation of a sulfonium or quaternary ammonium salt to a sulfide or tertiary amine, which is accompanied by the 1,2-mitrgration of an alkyl group from the central nitrogen or sulfur atom

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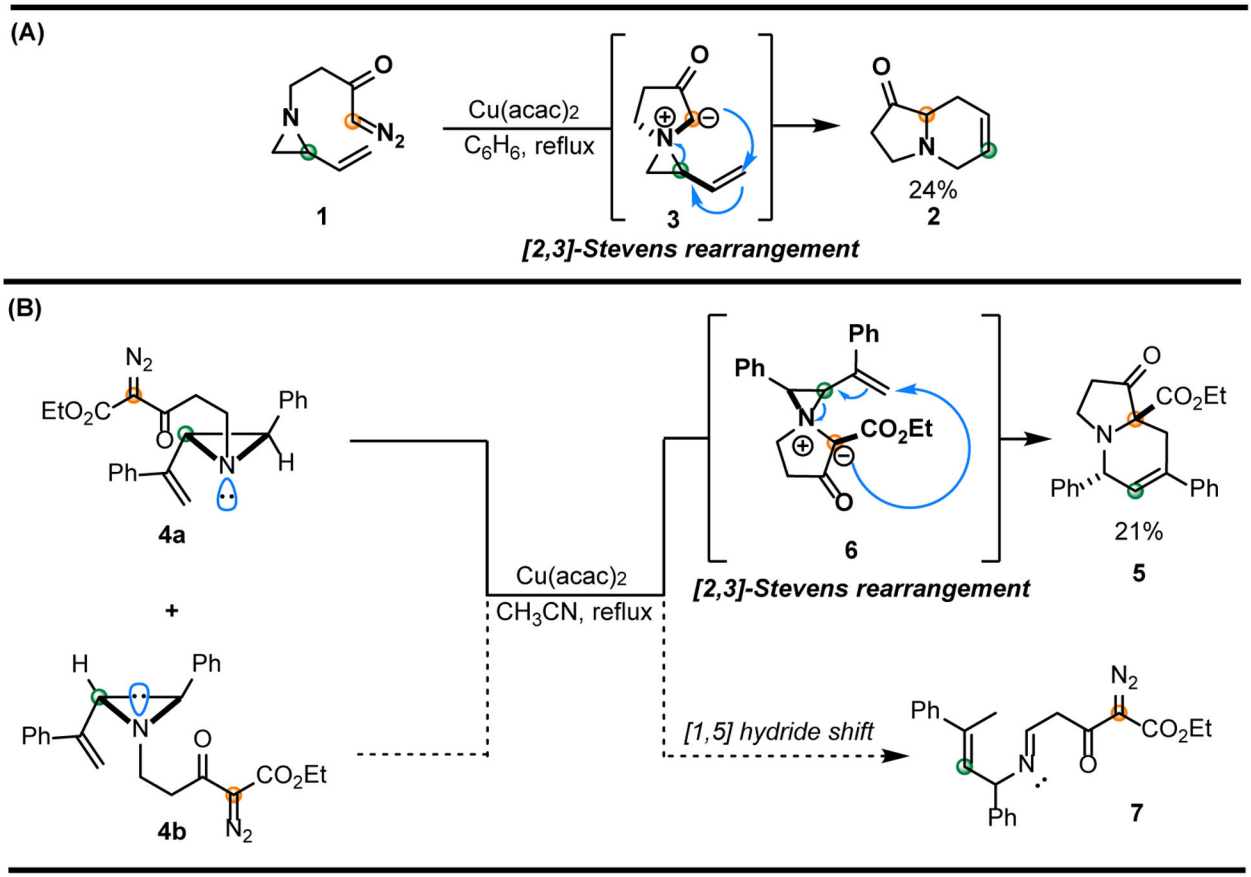

Figure 1.

Intramolecular [2,3]-Stevens rearrangements of aziridinium ylides. (A) Clark's attempted indolizidine synthesis from the [2,3]-rearrangement of spirocyclic ylide intermediate **3**. (B) Rowlands' Cu-catalyzed ring expansion attempt of aziridine invertomers **4a** and **4b**.

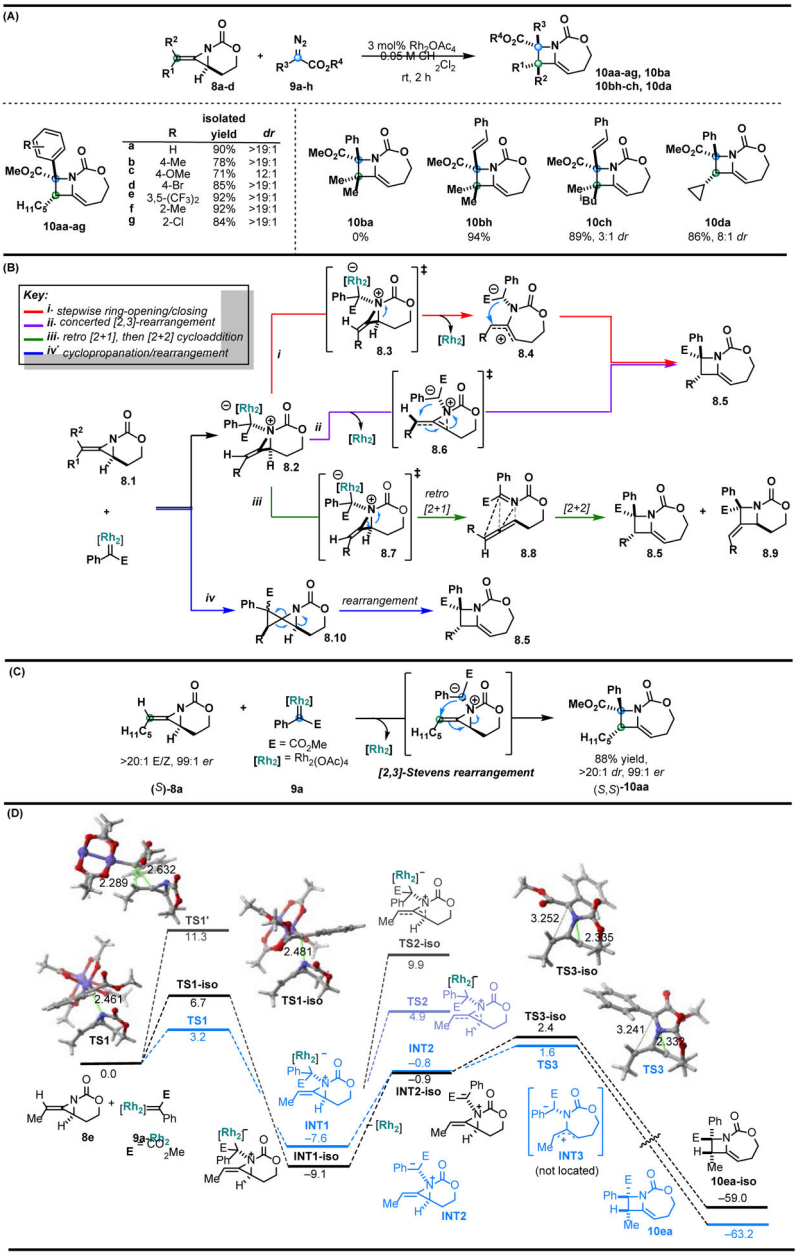

Figure 2.

Intermolecular Rh-catalyzed synthesis of methyleneazetidines. (A) Select substrates from the diazoester and aziridine scopes of the [3+1] ring expansion of bicyclic methyleneazetidines. (B) Chirality transfer experiment using enantiopure methyleneaziridine (*S*)-**8a**. (C) Potential mechanisms for the [3+1] ring expansion. (D) Computed reaction profile for the process involving methyl-substituted methyleneazeridine **8e** and dirhodium-bound carbene **9a**-Rh_2.

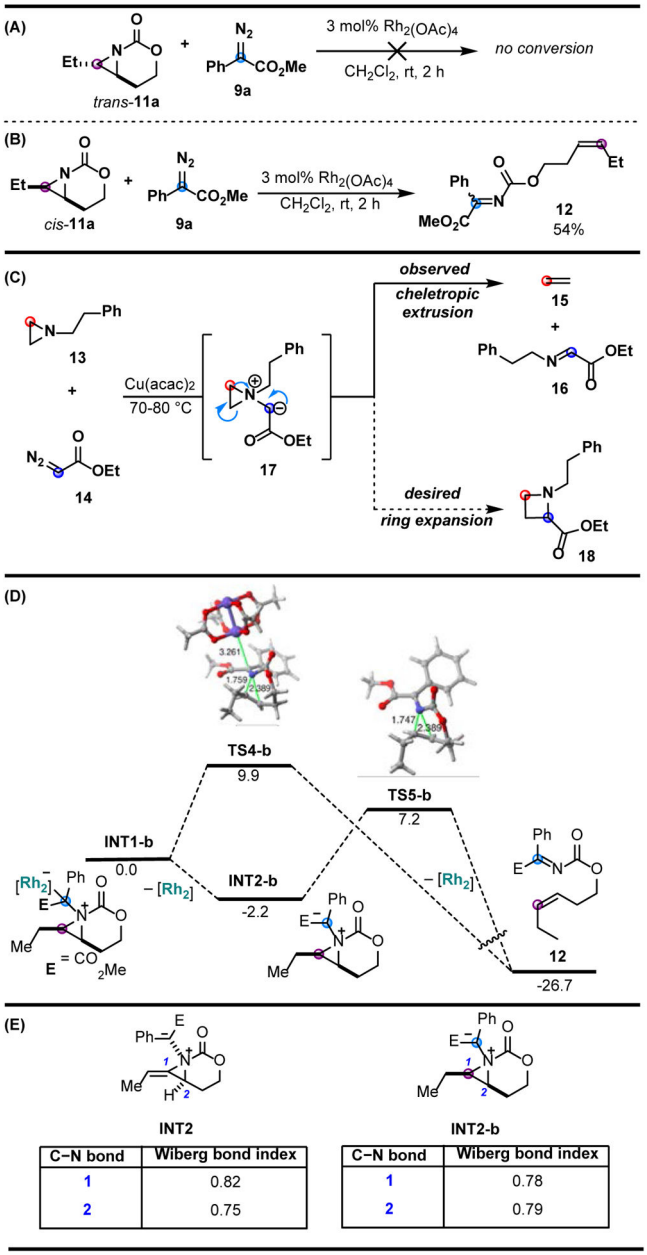

Figure 3.

Exploration of unbiased bicyclic aziridines. (A) Unsucessful Rh-mediated carbene transfer between *trans*-1**1a** and diazoacetate **9a**. (B) Cheletropic extrusion from the Rh-mediated carbene transfer between *cis*-**11a** and diazoacetate **9a**. (C) Cheletropic extrusion of an aziridinium ylide generated from a copper-mediated carbene transfer. (D) Computed reaction profile for the chelotropic extrusion of the aziridinium ylide formed in the reaction of **11a** and dirhodium-bound carbene **9a-Rh2**. (E) Computed Wiberg bond indices for the C-N bonds of **INT2** and **INT2-b**.

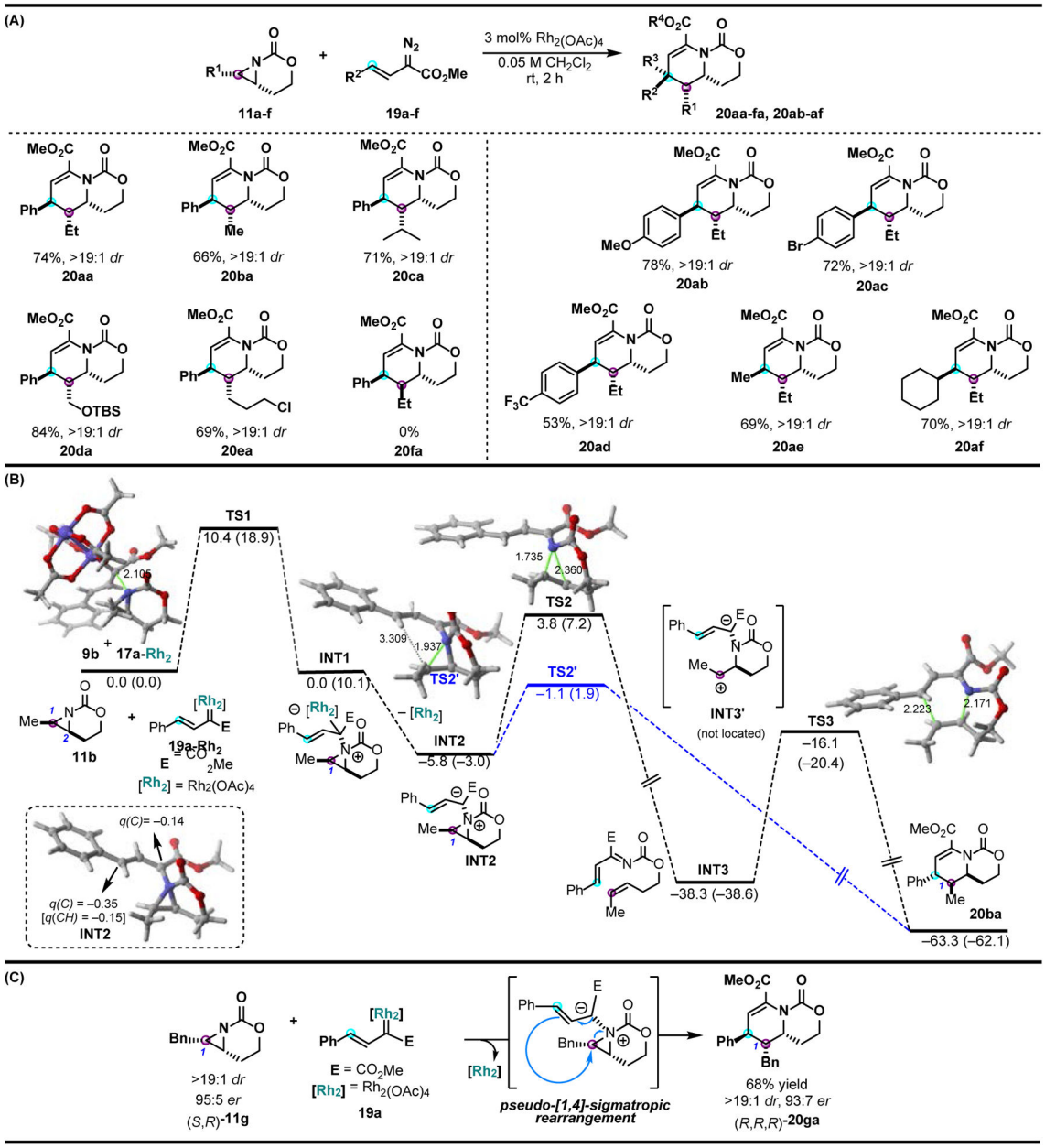

Figure 4.

Intermolecular Rh-catalyzed synthesis of dehydropiperidines. (A) Select substrates from the aziridine and diazoester scopes of the [3+3] ring expansion of bicyclic aziridines. (B) Computed reaction profile for the process involving aziridine **11b** and dirhodium-bound carbene **19a-Rh2**. (C) Chirality transfer experiment using enantiopure aziridine **(*S,R*)-11g**.

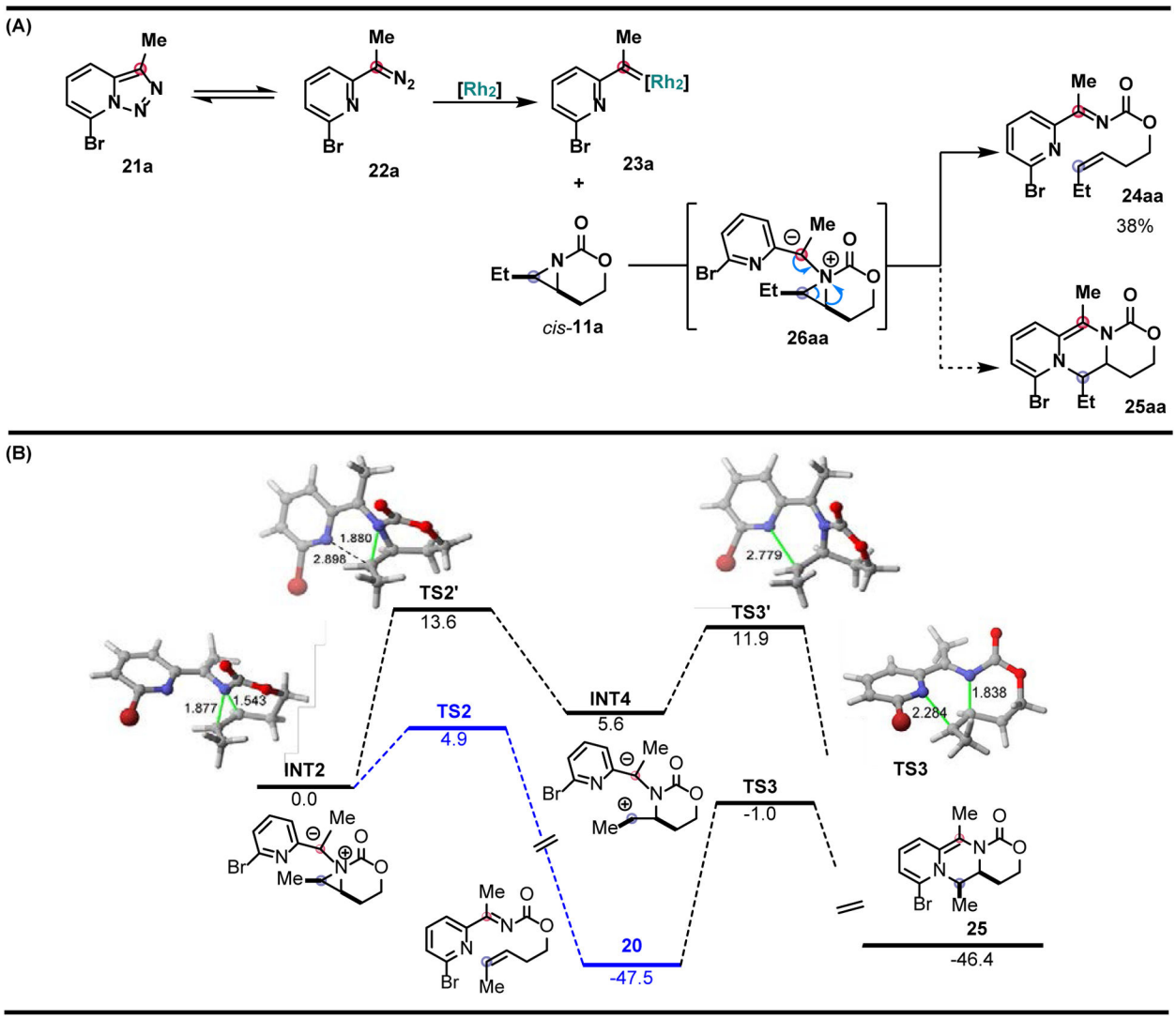

Figure 5.

Exploring pyridotriazoles as carbene precursors toward the synthesis of *N*-heterocycles. (A) Attempted carbene transfer to access fused piperazines from the reaction between aziridine **9a** and Rh-bound **23a-Rh2**. (B) Computed reaction profile for the process involving *cis*-aziridine **11a** and dirhodium-bound carbene **23a-Rh2**.

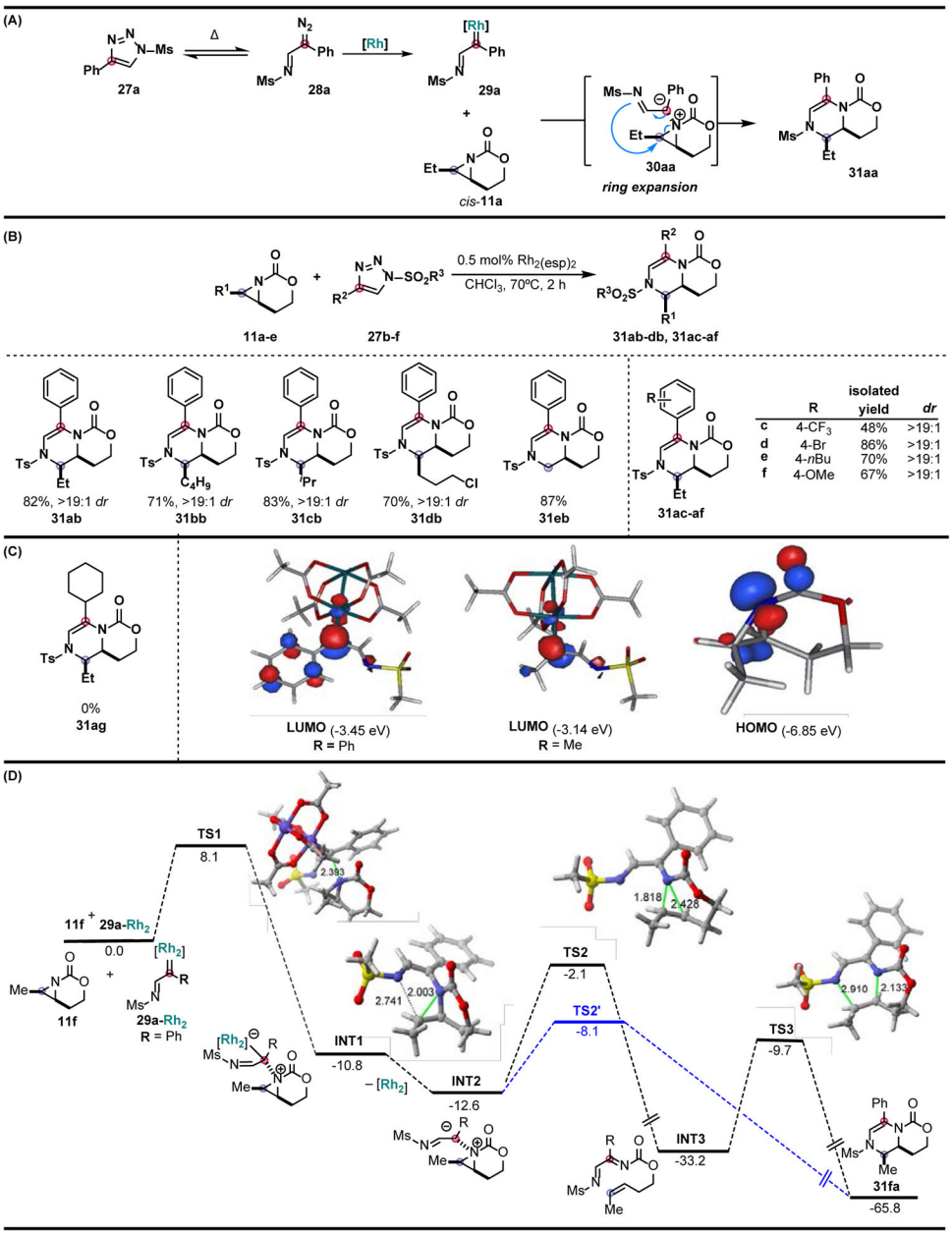

Figure 6.

Intermolecular Rh-catalyzed synthesis of dehydropiperazines. (A) Dehydropiperazine synthesis via the ring expansion of an aziridinium ylide generated from a Rh-mediated carbene transfer. (B) Select dehydropiperazine products from the aziridine and diazoester scopes. (C) Left: Example of an inaccessible alkyl substrate. Right: Computed HOMO and LUMO energies for the bicyclic aziridine, aryl carbene, and alkyl carbene. (D) Computed reaction profile for the ring expansion process involving aziridine **11f** and dirhodium-bound carbene **29a-Rh2**.