organics

MDPI

Review

Electrocyclizations of Conjugated Azapolyenes Produced in Reactions of Azaheterocycles with Metal Carbenes

Nikolai V. Rostovskii *, Mikhail S. Novikov and Alexander F. Khlebnikov

Institute of Chemistry, St. Petersburg State University, 7/9 Universitetskaya Nab., 199034 Saint Petersburg, Russia; m.s.novikov@spbu.ru (M.S.N.); a.khlebnikov@spbu.ru (A.F.K.)
* Correspondence: n.rostovskiy@spbu.ru

Abstract: Conjugated azapolyenes (azabuta-1,3-dienes, aza-/diaza-/oxaza-/oxadiazahexa-1,3,5-trienes) are highly reactive in electrocyclization reactions, which makes them convenient precursors for the synthesis of a wide range of four-, five-, and six-membered nitrogen heterocycles that are of relevance for medicinal chemistry. Ring opening reactions of 2*H*-azirines and azoles containing an N–N or N–O bond, initiated by a transition metal carbene, have become increasingly important in recent years, since they easily allow the generation of azapolyenes with different numbers of double bonds and heteroatoms in various positions. This review summarizes the literature, published mainly in the last decade, on the synthetic and mechanistic aspects of electrocyclizations of azapolyenes generated by the carbene method.

Keywords: electrocyclization; pericyclic reactions; azadienes; rhodium carbenes; isoxazoles; pyrazoles; 2*H*-azirines; 1,2,3-triazoles; diazo compounds; catalysis

Citation: Rostovskii, N.V.; Novikov, M.S.; Khlebnikov, A.F. Electrocyclizations of Conjugated Azapolyenes Produced in Reactions of Azaheterocycles with Metal Carbenes. *Organics* **2021**, *2*, 313–336. https://doi.org/10.3390/org2030017

Academic Editor: Stéphane P. Roche

Received: 10 August 2021
Accepted: 8 September 2021
Published: 14 September 2021

1. Introduction

Conjugated azapolyenes such as azabuta-1,3-dienes and aza-/diaza-/oxaza-/oxadiazahexa-1,3,5-trienes (Figure 1) are valuable building blocks in the synthesis of a variety of acyclic and heterocyclic nitrogen-containing compounds [1–5]. These highly unsaturated compounds are generally classified into three types: electron-rich, neutral, and electron-deficient azapolyenes. The compounds of the latter type, bearing one or more strong electron-withdrawing group in the polyene chain, exhibit especially diverse and sometimes unexpected reactivity. The most common reactions of electron-deficient azapolyenes are nucleophilic additions and pericyclic reactions including cycloadditions [6–8] and electrocyclizations [9–11]. Electrocyclizations of conjugated azapolyenes can occur via pericyclic or pseudopericyclic pathways [12] depending on the nature of the reaction centers in the reacting molecule. Electrocyclizations are of particular importance for the construction of thermally labile heterocycles since they do not require any additional reagents and usually proceed with high regio- and stereoselectivity under mild conditions. However, the use of electrocyclic reactions for the synthesis of heterocyclic compounds involves serious challenges due to the limited synthetic availability of azapolyenes of the required structure. Whereas 1-azabuta-1,3-dienes are readily available from a condensation of unsaturated carbonyl compounds with primary amines [13–15], the methods for the synthesis of their isomers, 2-azabuta-1,3-dienes, which include the Mannich olefination of alkylidene glycinates [16], the Wittig reaction of *N*-(diphenylmethylidene)oxamate [17], the coupling of imines with activated acetylenes [18], and the aza-Wittig reaction of *N*-vinylphosphazenes [19–23] are more complicated and allow the introduction of only a limited set of substituents.

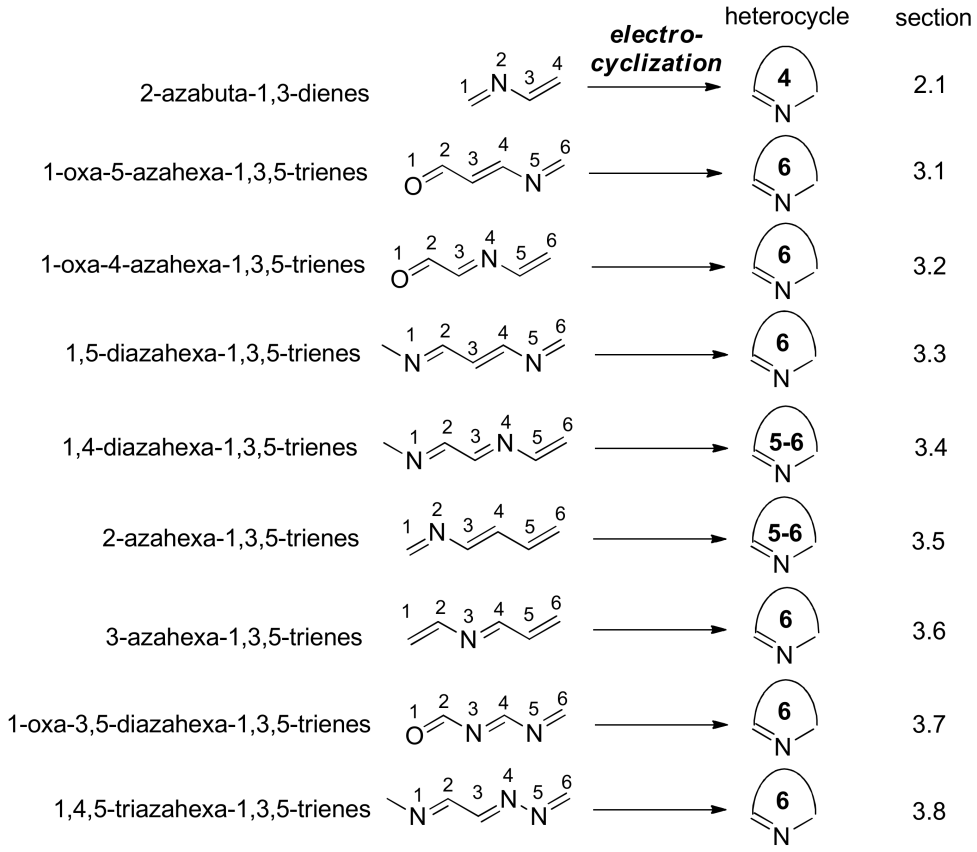
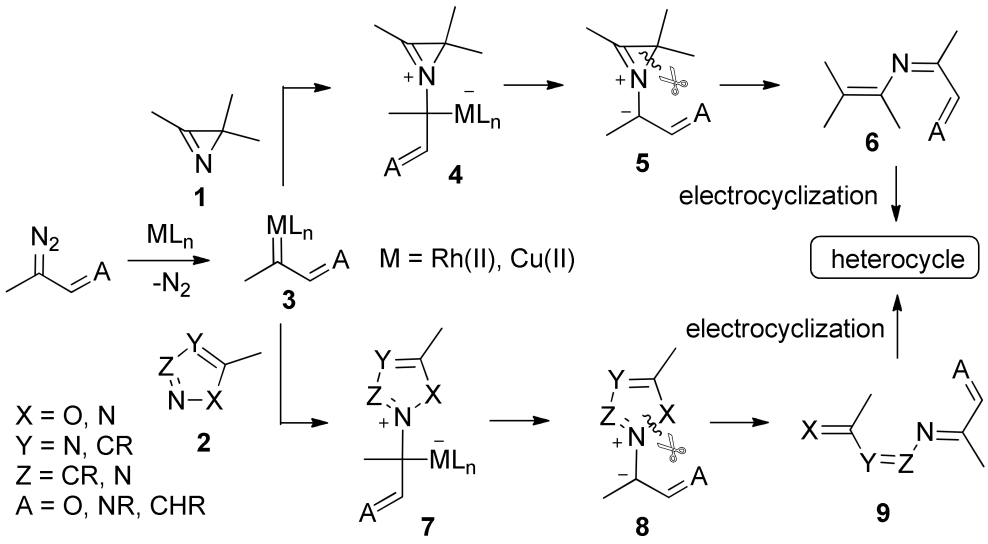


Figure 1. Conjugated azapolyenes in sections of the review.

In recent years, another convergent approach to azapolyenes **6** and **9** based on the ring opening of three- and five-membered heterocycles **1** and **2** under the action of transition metal carbenes **3** has been intensively developed (Scheme 1). The reactions are believed to proceed via the formation of metal-bound ylides **4** and **7** and metal-free ylides **5** and **8**. In this approach, metal carbenes **3** are generated from diazo compounds or their masked analogs, 1*H*-1,2,3-triazoles, in the presence of rhodium or copper catalysts, which are generally used for the initiation of the denitrogenative decomposition of diazo compounds [24]. This approach to azapolyenes is quite versatile since it allows one to synthesize conjugated N-, N,N-, and N,O-containing butadienes, hexatrienes, and even octatetraenes in one synthetic operation. The unique feature of the approach is the interchangeability of some three- and five-membered heterocycles in the reactions with transition metal carbenes. This allows flexibility of the starting material choice to obtain the azapolyene with the desired substitution pattern and configurations of double bonds.

In this short review, we summarize recent progress on electrocyclic reactions of azapolyenes generated by the transition metal catalyzed reaction of diazo compounds/1,2,3-triazoles with 2*H*-azirines [25] or azoles containing the weak N-N or N-O bond.

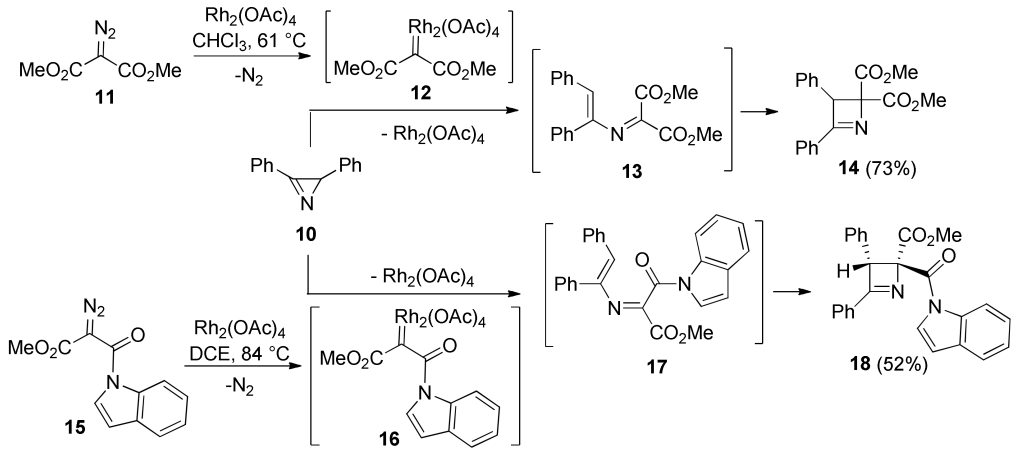


Scheme 1. Transition metal carbene reactions for the synthesis of azapolyenes and heterocycles.

2. 1,4-Electrocyclization of Azabutadienes

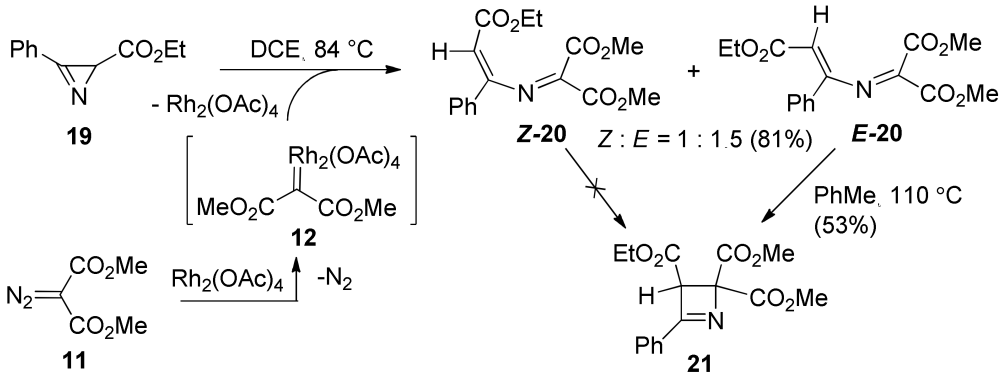
Electrocyclization of 2-Azabuta-1,3-dienes to 2,3-Dihydroazetes

Theoretically, a 2-azabuta-1,3-diene fragment can undergo conrotatory 1,4-electrocyclization, which is allowed by the rules of orbital symmetry. Since the four-membered ring of a 2,3-dihydroazete is significantly strained, such cyclization is possible only when at least one substituent is present at the C4 of 2-azadiene and more favorable 1,5- or 1,6-cyclizations are difficult or impossible. In particular, 1,4-cyclization of 3,4-diphenyl-substituted azadiene **13** derived from 2,3-diphenyl-2*H*-azirine **10** and rhodium carbene **12** gave dihydroazete **14** in good yield under mild conditions (Scheme 2) [26,27]. The analogous reaction of azirine **10** with diazoamidoester **15** in 1,2-dichloroethane (DCE) resulted in the formation of dihydroazete **18** and revealed the stereoselective nature of both the formation of the intermediate azadiene **17** and its cyclization [28]. It is notable that the cyclizations of azadienes **13** and **17** occurred irreversibly in both cases.



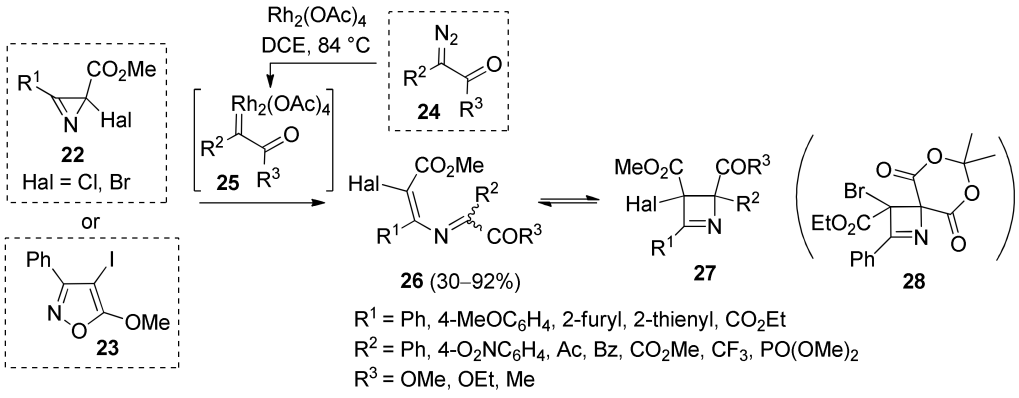
Scheme 2. Synthesis of dihydroazetes from azirine **1**.

It was found that azadienes bearing one substituent at C4 undergo cyclization more readily if the C=C double bond has the *E* configuration. For example, dihydroazete **21** was obtained only from azadiene ***E*-20**, while its *Z* isomer was found to be inactive in the cyclization (Scheme 3) [29].



Scheme 3. The effect of the C=C bond configuration of azadiene on 1,4-electrocyclization.

4,4-Disubstituted 2-azabuta-1,3-dienes can be generated by the reactions of azirines or isoxazoles with diazocarbonyl compounds under rhodium catalysis [30,31] (Scheme 4). It was found that a prerequisite for the 1,4-electrocyclization of the resulting 2-azabuta-1,3-dienes **26** is the presence of two electron-withdrawing groups at C1. In most cases, the cyclization reactions occur only at elevated temperatures in reversible fashion. 4-Halo-substituted azadienes **26** with the *E* configuration of the C=C bond were used to explore the influence of the substituents on the azadiene-dihydroazete equilibrium in C_6D_6 at 100 °C [31]. It was found that replacing iodine with chlorine led to a change in the azadiene/dihydroazete ratio from 2.6:1 to 1:1.3. The introduction of an electron-donating 4-MeO group to the phenyl ring located at the C3 of the 2-azadiene shifts the equilibrium from a 1:1 to 1:2.5 ratio in favor of dihydroazete **27**. A decrease in the electron-withdrawing ability of the substituent at the C1 of the azadiene (replacement of CO_2Me with CF_3) shifts the equilibrium toward the azadiene.

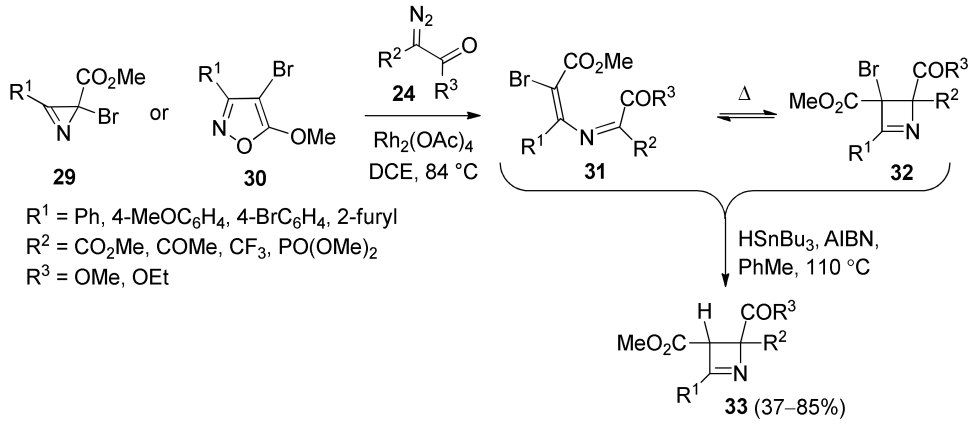


Scheme 4. Synthesis and 1,4-electrocyclization of 4,4-disubstituted 2-azabuta-1,3-dienes.

Since 3-halo-2,3-dihydroazetes **27** are rather stable at room temperature, their preparation in satisfactory yields turned out to be possible by using repeated heating of the azadiene to obtain an equilibrium azadiene–dihydroazete mixture and separation of the dihydroazete at each stage [31]. The 2-azadiene, prepared from the diazo Meldrum's acid, also underwent reversible 1,4-electrocyclization upon heating, leading to the spirocyclic derivative of 2,3-dihydroazete **28** [32]. Dihydroazete **28** turned out to be stable at room temperature, which made it possible to isolate it in pure form.

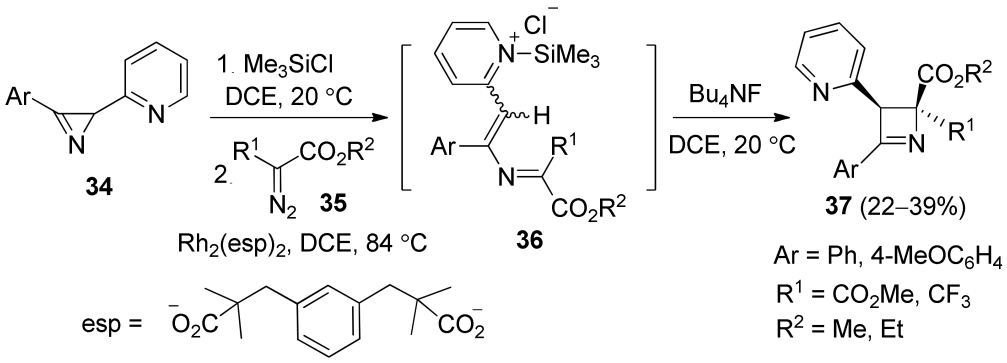
To obtain dihydroazetes with a hydrogen at the C3, an approach was developed based on the hydrodebromination of 3-bromo-2,3-dihydroazetes under the action of tributyltin hydride (Scheme 5) [29]. Using this method, 2,3-dihydroazetes **33** with various substitution patterns were obtained in good yields from both 2-bromoazirine-2-carboxylates **29** and 5-alkoxy-4-bromoisoxazoles **30**. It is noteworthy that the replacement of bromine with

hydrogen in 2,3-dihydroazetes led to a significant increase in their thermal stability: in contrast to dihydroazetes **32**, which undergo the ring opening to azadienes **31** at temperatures above 60 °C, dihydroazetes **33** are stable even at 150 °C. In addition, the cytotoxic activity of 2,3-dihydroazetes **32** and **33** on the THP-1 cell line (human monocytic leukemia cells) was studied in vitro. It was found that the maximum apoptotic potential, along with a high cytotoxic and minimal necrotic potential, can be displayed by a representative of 2,3-dihydroazetes **33**—trimethyl-4-phenyl-2,3-dihydroazete-2,3,3-tricarboxylate.



Scheme 5. Synthesis of stable 2,3-dihydroazetes via 1,4-electrocyclization–hydrodebromination.

For the synthesis of 2,3-dihydroazetes **37** bearing a 2-pyridyl substituent at C3, it was necessary to protect the pyridine nitrogen in the starting 2-(pyridin-2-yl)-2*H*-azirines **34** in order to avoid deactivation of the rhodium catalyst due to complexation (Scheme 6) [33]. For this purpose, one-pot protection/deprotection with a trimethylsilyl group was successfully used.



Scheme 6. Synthesis of 3-(2-pyridyl)-2,3-dihydroazetes.

The reaction of rhodium carbenes with azirines and isoxazoles is still the only way to synthesize 2,3-dihydroazetes having a carbon substituent at C4. Despite the low thermal stability of many representatives of these compounds, they can be easily detected in reaction mixtures due to the characteristic chemical shift of C4 in the ^{13}C NMR spectra, which is about 190 ppm.

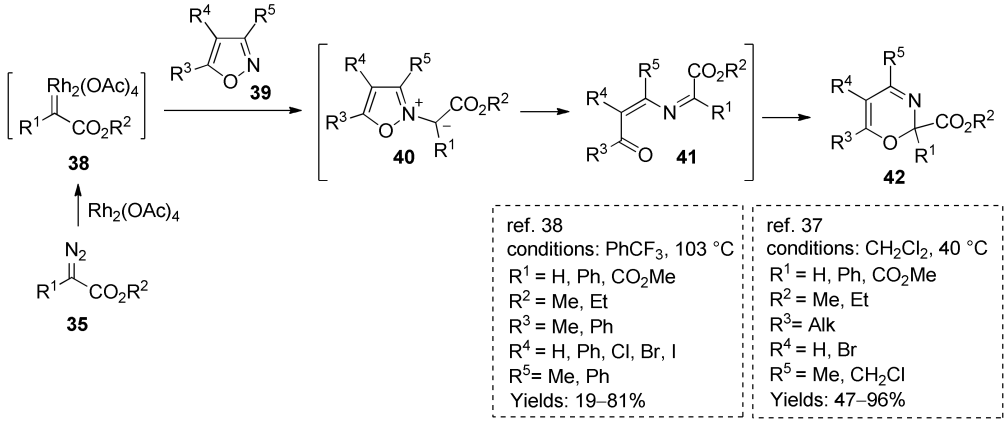
3. 1,6- and 1,5-Electrocyclizations of Aza-, Oxaza-, Diaza-, and Oxadiazahexatrienes

The most common type of electrocyclic reactions of azapolyenes is 1,6-electrocyclization, the products of which are aza and oxaza analogs of cyclohexa-1,3-diene. There are a limited number of reliable methods for the preparation of oxaza analogs of cyclohexa-1,3-diene that makes the 1,6-electrocyclization of azapolyenes a promising synthetic alternative [34–36].

An attractive feature of these compounds is the feasibility of a reverse reaction, ring opening, which determines their use as thermo- and photochromic materials as well as starting compounds for the synthesis of other heterocycles. In addition, under certain conditions, aromatization of the dihydro derivatives can take place to give azines. If a heteroatom is located at the end of the triene system, 1,6-cyclization occurs as a pseudopericyclic process [12]. Such reactions are characterized by a flattened structure of the cyclization transition state; therefore, they proceed through a lower activation barrier than classical 1,6-electrocyclizations, in which carbon atoms are at the ends of the triene system.

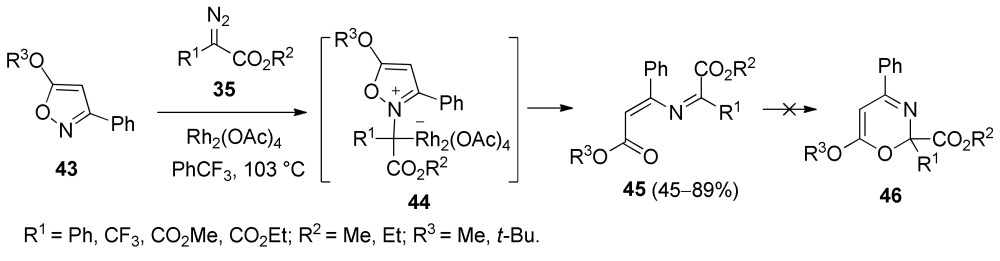
3.1. 1,6-Electrocyclization of 1-Oxa-5-azahexa-1,3,5-trienes to 2H-1,3-Oxazines

Manning and Davies reported the rhodium catalyzed synthesis of 2*H*-1,3-oxazines **42** from diazocarbonyl compounds **35** and isoxazoles **39** (Scheme 7) [37]. The authors proposed the mechanism for the formation of oxazine **42** involving the generation of isoxazolium ylide **40**, the ring opening to 1-oxa-5-azatriene **41**, followed by 1,6-electrocyclization. The scope of the reaction was further expanded by the work in [38].



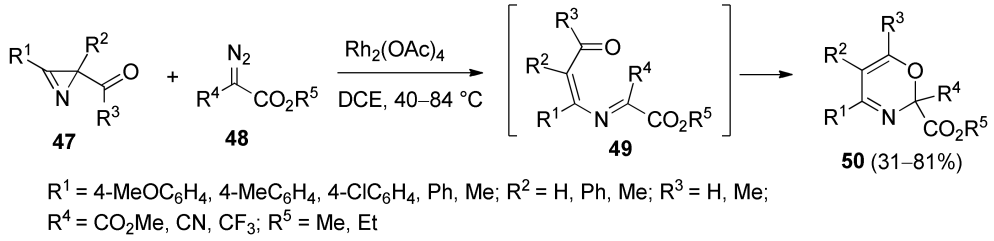
Scheme 7. Synthesis of 2*H*-1,3-oxazines from isoxazoles.

The authors of [38] confirmed the intermediate formation of 1-oxa-5-azatrienes in the reactions of rhodium metal carbenes with isoxazoles by experimental and computational methods. The density functional theory (DFT) calculations revealed that the metal-free isoxazolium ylides **40** are extremely unstable species, which undergo ring opening practically without an energy barrier, and their formation in these reactions therefore seems rather unlikely. The isoxazolium ring undergoes opening, most likely, at the stage of metal-bound ylides **44** (Scheme 8). The latter undergo simultaneous cleavage of the N–C and Rh–C bonds to give oxazatrienes **45** with the *Z* configuration of the C=C double bond. It is notable that the analogous reaction of 5-alkoxyisoxazoles **43** stops at the stage of oxazatrienes **45**, which is one more piece of evidence for the reaction to proceed through the oxazatriene intermediate [38]. The quantum chemical calculations confirmed that oxazatrienes **45** are thermodynamically more stable than their 1,3-oxazine isomers **46** by 16 kcal/mol, and 1,6-electrocyclization in this case is thermodynamically unfavorable.



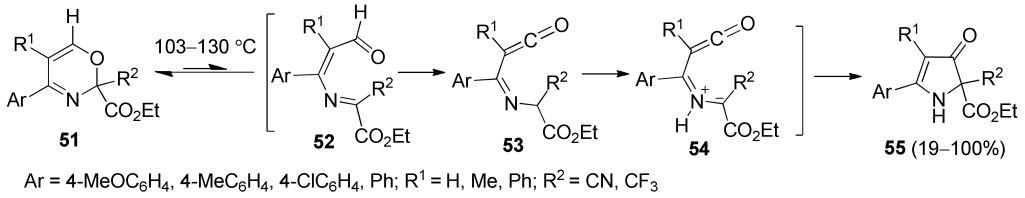
Scheme 8. Synthesis of 2-alkoxy-1-oxa-5-azahexa-1,3,5-trienes stable to 1,6-electrocyclization.

It was also shown that 2-acyl- and 2-formyl-substituted azirines **47** react similarly and can serve as sources of oxazatrienes **49**, which are capable of undergoing 1,6-electrocyclization (Scheme 9). Thus, dimethyl diazomalonate, ethyl 2-cyano-2-diazoacetate, and ethyl 2-diazo-3,3,3-trifluoropropanoate react with azirines **47** under rhodium catalysis to afford 2*H*-1,3-oxazines **50** in good yields [39,40].



Scheme 9. Synthesis of 2*H*-1,3-oxazines from 2*H*-azirines.

It turned out that the obtained 1,3-oxazines are capable of reversible ring opening to 1-oxa-5-azahexatrienes at elevated temperatures (Scheme 10) [40]. 1,3-Oxazine **51** bearing a hydrogen atom at C6 produces oxazatriene **52** upon heating, which undergoes a cascade of transformations, leading to the formation of pyrrolinones **55**. This isomerization occurs most easily for the 1,3-oxazines containing a cyano group at C2. The synthesis of pyrrolones **55** can also be carried out starting from azirines and diazo compounds, without isolation of the intermediate 1,3-oxazines.

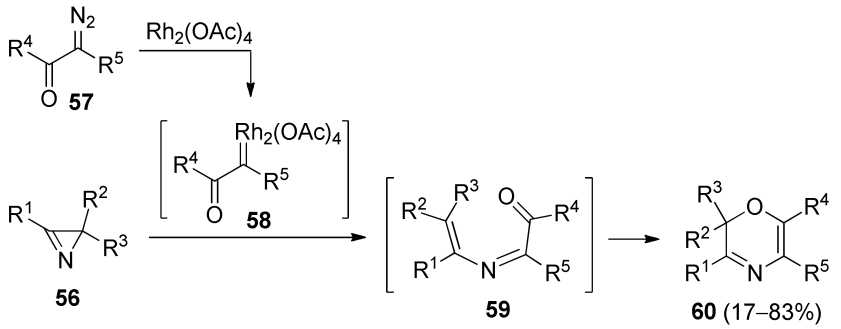


Scheme 10. Synthesis of pyrrolinones via electrocyclic ring opening of 2*H*-1,3-oxazines.

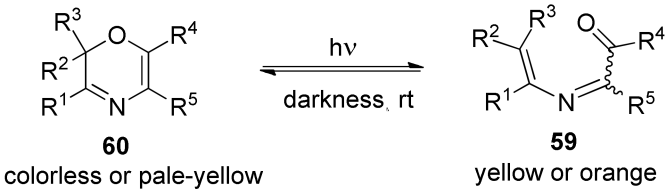
3.2. 1,6-Electrocyclization of 1-Oxa-4-azahexa-1,3,5-trienes to 2H-1,4-Oxazines

When an acyl group is introduced into the C1 position of 2-azadiene (1-oxa-5-azahexa-1,3,5-triene), 1,6-electrocyclization to form 2*H*-1,4-oxazines takes place. It was found that the cyclization of 1-oxa-4-azahexa-1,3,5-trienes **59**, derived from azirines **56** and diazo compounds **57** in most cases occurred readily and irreversibly to afford 2*H*-1,4-oxazines **60** with a wide range of substituents in good yields (Scheme 11) [41–43]. The presence of an electron-withdrawing substituent (ester group) at C6 and an alkyl substituent (methyl) at C5 of the oxazahexatriene impede the cyclization. It should be noted that no cyclization involving the ester group (R^4 = OAlk) was observed; the impossibility of such cyclization for both kinetic and thermodynamic reasons was confirmed by the results of quantum chemical calculations.

An interesting feature of the obtained monocyclic 2*H*-1,4-oxazines **60** is their photo- and thermochromic activity, which is attractive for their practical applications. When irradiated with UV light of a mercury lamp, colorless oxazines (λ_{max} 315–360 nm) convert to oxazatrienes **59**, colored from yellow to red (λ_{max} 380–455 nm) [42] (Scheme 12). After the termination of irradiation, the cyclization occurs again. For a series of oxazines, the half-life times of the open-chain form were determined; these were in a range of 0.5–29 h, and these times were highly dependent on the substitution pattern. Thermochromism was most pronounced for spirooxazines containing a fluorene fragment at C2 [42].



Scheme 11. Synthesis of 2*H*-1,4-oxazines via 1,6-electrocyclization of 1-oxa-4-azahexa-1,3,5-trienes.



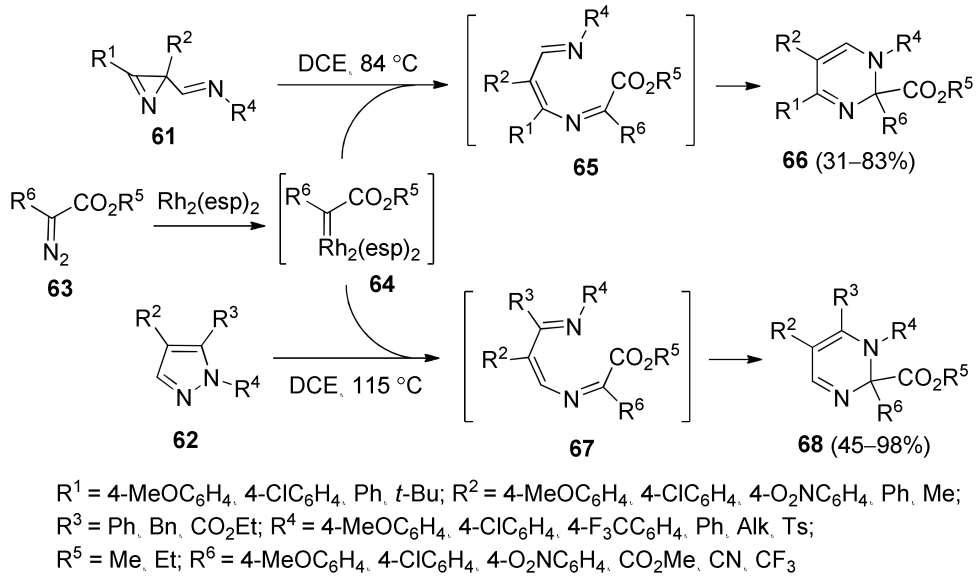
Scheme 12. Photochromism of monocyclic 2*H*-1,4-oxazines.

3.3. 1,6-Electrocyclization of 1,5-Diazahexa-1,3,5-trienes to 1,2-Dihydropyrimidines

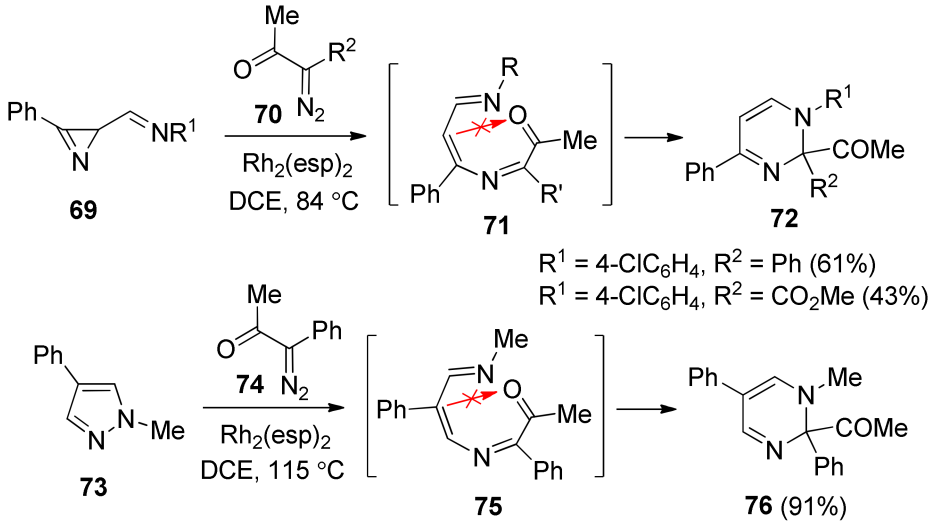
1,6-Electrocyclization of 1,5-diazahexa-1,3,5-trienes occurs with the formation of 1,2-dihydropyrimidine derivatives. Two complementary approaches have been developed for the generation of 1,5-diazatrienes **65**,**67**, precursors of 1,2-dihydropyrimidines **66**,**68**, based on the reactions of diazocarbonyl compounds **63** with either azirine-2-carbaldimines **61** or pyrazoles **62** (Scheme 13). The use of azirine-2-carbaldimines as the starting material makes it possible to obtain 1,2,2,4,5-pentasubstituted dihydropyrimidines [44]. Due to the peculiarities of the reactivity of pyrazoles (completely substituted pyrazoles do not react with rhodium carbenes), the reactions of pyrazoles are more suitable for obtaining 1,2,2,5,6-pentasubstituted dihydropyrimidines [45].

1,5-Diazahexatrienes **71**,**75** generated by the reactions of diazo ketones **70**,**74** have an additional keto group, therefore, they theoretically can undergo two types of 1,6-electrocyclizations: into 1,2-dihydropyrimidines or 2*H*-1,4-oxazines (Scheme 14). It was found that the 1,6-cyclization of such 1-oxa-4,8-diazaocta-1,3,5,7-tetraenes occurs exclusively onto the C=N bond to give dihydropyrimidine derivatives [44,45].

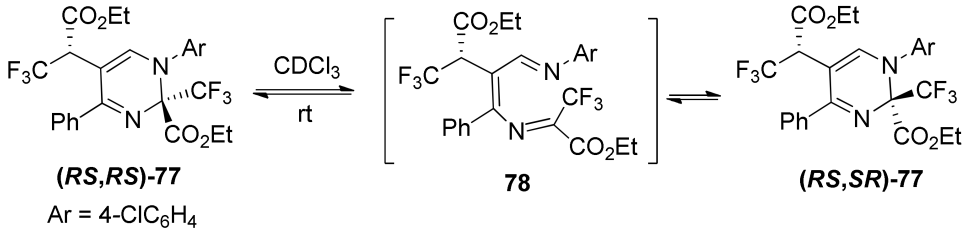
It is interesting that the synthesized 1,2-dihydropyrimidines exist in an equilibrium with 1,5-diazatrienes in solution at room temperature [44]. An indirect evidence of this fact, which was also confirmed by the results of quantum chemical calculations, is the rapid epimerization of a dihydropyrimidine, which contains two chiral centers. Thus, dihydropyrimidine **(*RS*,*RS*)-77**, which is stable in a solid state, rapidly transforms into a 1:1 mixture of two diastereomers in $CDCl_3$ solution via the ring opening–cyclization sequence (Scheme 15).



Scheme 13. Synthesis of 1,2-dihydropyrimidines via 1,6-electrocyclization of 1,5-diazahexa-1,3,5-trienes.



Scheme 14. 1,6-Electrocyclization of 1-oxa-4,8-diazaocta-1,3,5,7-tetraenes.

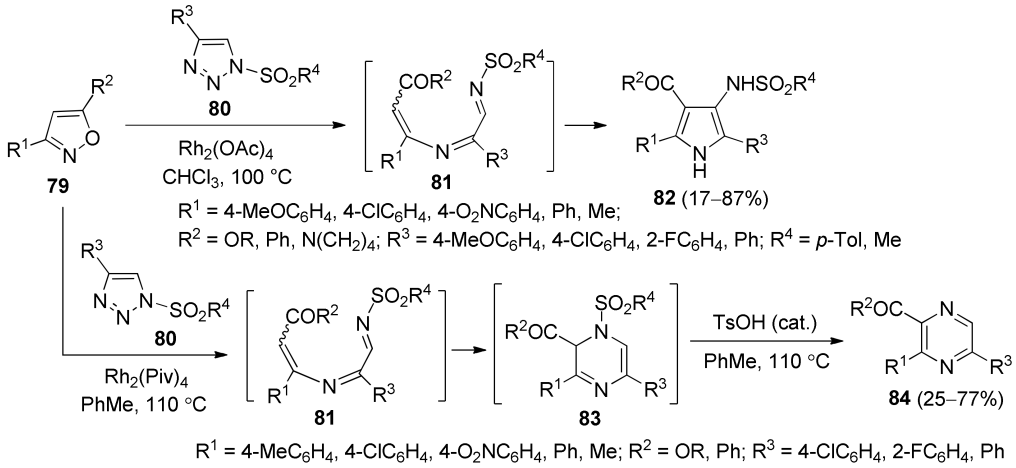


Scheme 15. Epimerization of 1,2-dihydropyrimidines via reversible electrocyclic ring opening.

3.4. 1,6- and 1,5-Electrocyclizations of 1,4-Diazahexa-1,3,5-trienes

Several approaches to the preparation of 1,4-diazahexa-1,3,5-trienes have been studied to date, the 1,6-electrocyclization of which provides access to 1,2-dihydropyrazine derivatives.

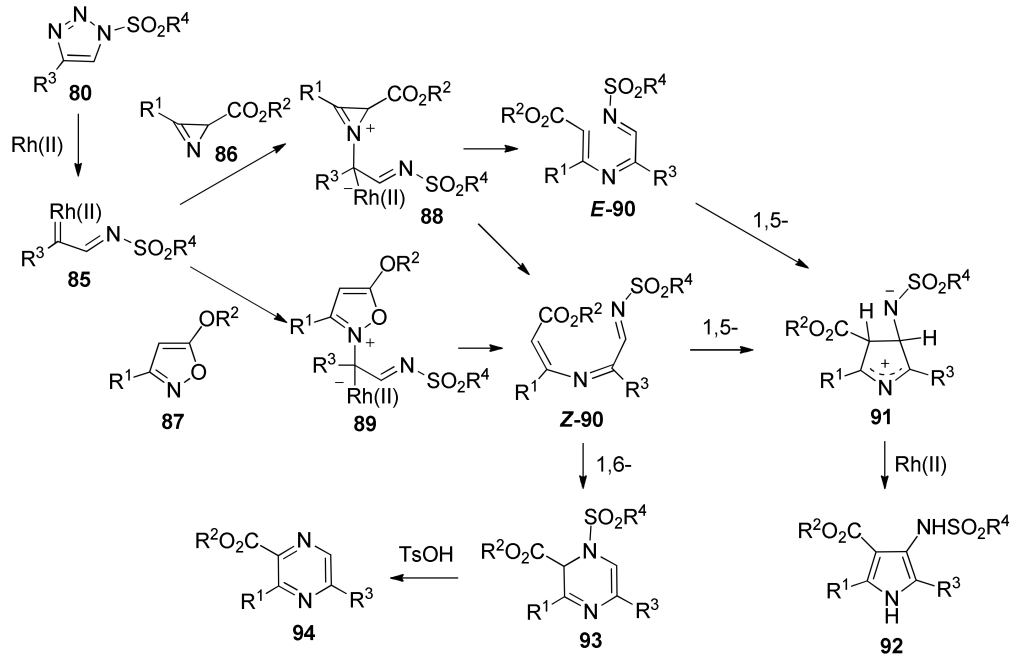
The reaction of isoxazoles **79** with rhodium azavinyl carbenes, generated from 1-sulfonyl-1,2,3-triazoles **80** under rhodium(II) catalysis, allows for the generation of 1,4-diazahexa-1,3,5-trienes **81** with a sulfonyl substituent at N1 [46]. In these reactions, two products were formed: 3-aminopyrrole **82** and 1,2-dihydropyrazine **83** (Scheme 16). The result of the reaction turned out to be extremely sensitive to reaction conditions (catalyst, solvent, temperature, etc.). The reaction, carried out in chloroform at 100 °C in the presence of $Rh_2(OAc)_4$ as a catalyst, is most suitable for the synthesis of 4-aminopyrrole-3-carboxylates **82**. The use of dirhodium tetrapivaloate ($Rh_2(Piv)_4$) in boiling toluene led to the formation of 1,2-dihydropyrazine-2-carboxylates **83** as the major products. The dihydropyrazines **83** were not very stable and gradually underwent dehydrosulfonylation; for this reason, they were converted without isolation to aromatic pyrazines **84** in the presence of TsOH.



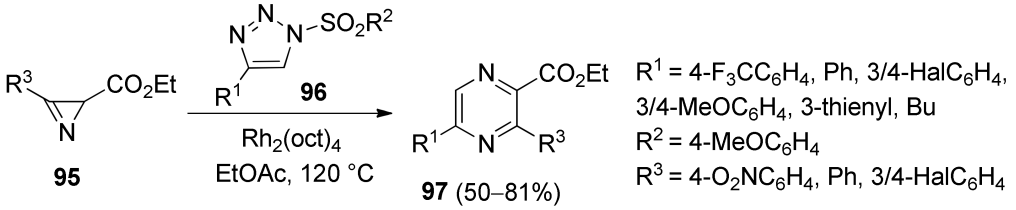
Scheme 16. Synthesis of 3-aminopyrroles and 1,2-dihydropyrazines from isoxazoles.

The NMR spectroscopy data and quantum chemical calculations showed that both products, pyrrole **92** and dihydropyrazine **93**, formed from (5*Z*)-1,4-diazahexa-1,3,5-triene intermediate ***Z*-90** (Scheme 17) [46]. The formation of pyrrole **92** proceeds via 5-*exo*-*trig*-cyclization of diazahexatriene ***Z*-90** to betaine **91**. The effect of the catalyst on the reaction direction can be explained by the stabilization of the betaine through coordination of the catalyst with the betaine anionic nitrogen.

Analogous 1,4-diazatrienes with a sulfonyl substituent at the nitrogen can also be generated from 2*H*-azirines **86** (Scheme 17) [46,47]. In this case, 3-aminopyrroles **92** are predominantly formed. The reason for this is associated with the selective ring opening of azirinium ylides **88** to (5*E*)-1,4-diazahexa-1,3,5-trienes ***E*-90**, which, as follows from quantum chemical calculations, undergo 5-*exo*-*trig*-cyclization through a lower energy barrier than the corresponding *Z*-isomers ***Z*-90** [46]. Isoxazolium ylide complexes **89**, due to geometrical reasons, can provide only diazahexatrienes ***Z*-90** with the C=C bond in the *Z* configuration, which is of crucial importance for the formation of pyrazines **93**. On the other hand, it turned out that the introduction of a strong electron-withdrawing substituent at the C5 of 1,4-diazatriene makes the 5-*exo*-*trig* cyclization to betaine **91** unfavorable, probably due to a decrease in the nucleophilicity of the C6 of the diazatriene [46]. As a result, in this case, 1,6-electrocyclization to dihydropyrazine **93** predominantly occurs. Furthermore, it is most likely that this fact helped the authors of [48] to synthesize the aromatic pyrazines **97** in good yields (Scheme 18).



Scheme 17. Mechanisms for the formation of 3-aminopyrroles and 1,2-dihydropyrazines.

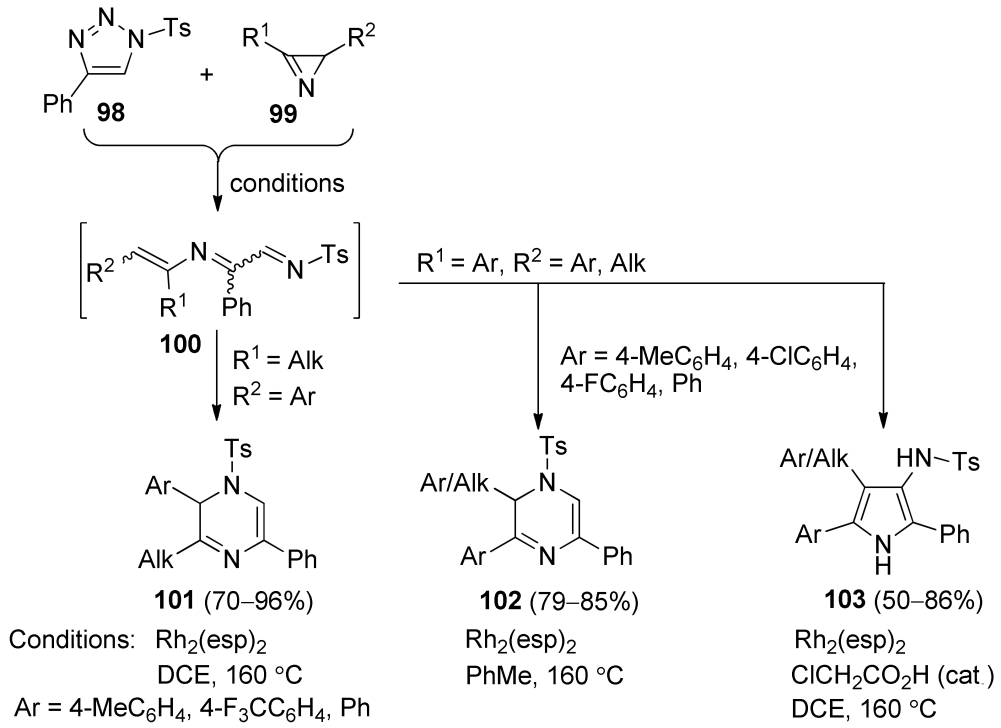


Scheme 18. Synthesis of pyrazines from ethyl azirine-2-carboxylates and 1,2,3-triazoles.

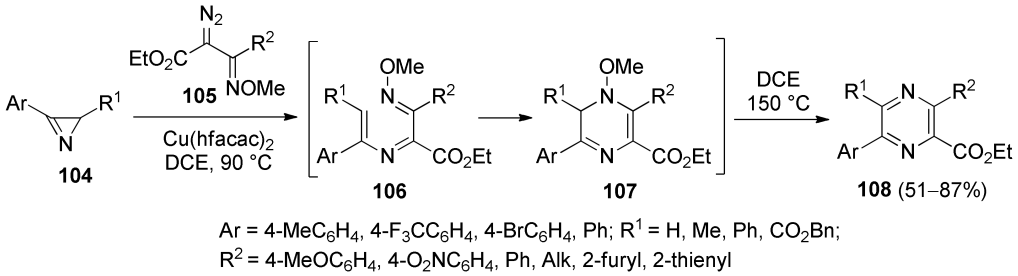
1,4-Diazahexatrienes **100** containing an aryl or alkyl substituent at the C6 and an aryl substituent at the C5 can be converted to dihydropyrazines **102** or 3-aminopyrroles **103** depending on the reaction conditions (Scheme 19) [49]. Tang and coworkers reported the conditions that provided good yields of both cyclic products. In contrast, 1,4-diazahexatrienes **100** containing an aryl substituent at C6 and an alkyl substituent at the C5 position exclusively underwent 1,6-electrocyclization to give dihydropyrazines **101**.

Park and coworkers showed that azirines **104** can react with diazo oxime ethers **105** under catalysis with copper(II) hexafluoroacetylacetonate (Scheme 20) [50]. In this case, 1,4-diazahexatrienes **106** are formed as intermediates, which are capable of undergoing 1,6-electrocyclization to dihydropyrazines **107**. Upon further heating of the dihydropyrazines at high temperature, the elimination of methanol takes place, leading to the formation of completely substituted pyrazine-2-carboxylates **108** in good yields.

The reactions of diazoindolinimines **110** with various 2*H*-azirines **109** give *ortho*-fused pyrazines **113** resulting from the 1,6-electrocyclization of intermediate 1,4-diazatrienes **111**. These reactions have been studied in detail in the works of three research groups (Scheme 21) [51–53]. In all these studies, the formation of the intermediate 1,2-dihydropyrazines **112** was observed. It was found that the aromatization of the 1,2-dihydropyrazines **112** can occur without any additives (when R^2 = CO_2Me), but at rather high temperature. To carry out this process under milder conditions, it was necessary to add a base (Et_3N, *t*-BuOK) or TsOH. Under these conditions, 5*H*-pyrazino[2,3-*b*]indoles **113** were obtained in good yields.



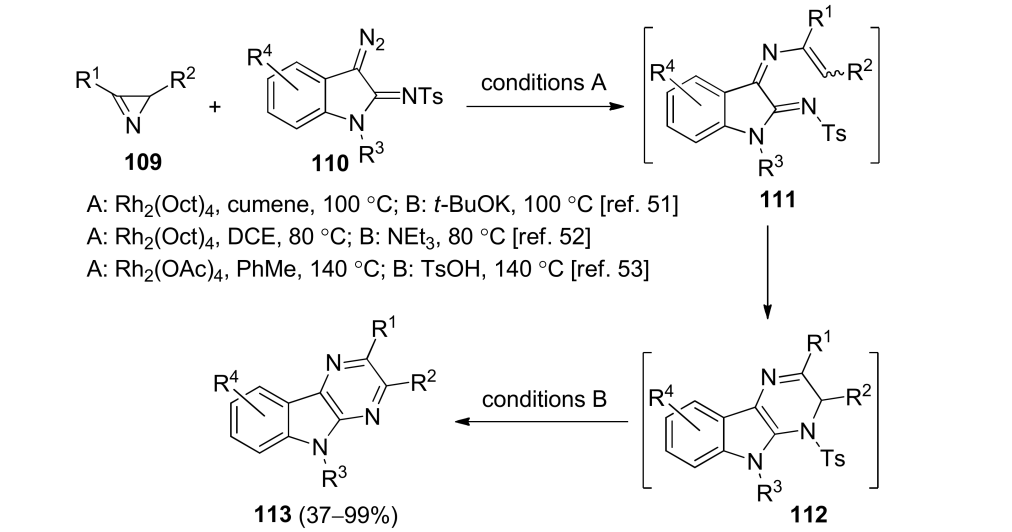
Scheme 19. Synthesis of 3-aminopyrroles and 1,2-dihydropyrazines from alkyl/aryl-2*H*-azirines.



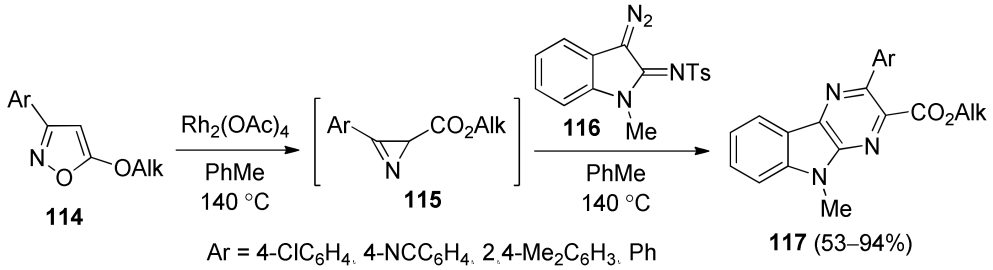
Scheme 20. Synthesis of pyrazines from 2*H*-azirines and diazo oxime ethers.

To obtain 5*H*-pyrazino[2,3-*b*]indoles **117** containing an ester substituent, according to the results of previous studies, it would be more convenient to use 5-alkoxyisoxazoles **114** rather than azirines **115** (Scheme 22). Unfortunately, however, isoxazoles **114** proved to be inactive toward diazoindolinimines in the presence of rhodium carboxylates. The authors of the work [53] took advantage of the isomerization of 5-alkoxyisoxazoles **114** to azirine-2-carboxylates **115** found in a previous study. It was found that the isomerization is catalyzed by the same rhodium carboxylate as the subsequent reaction with the diazo compound. Using this procedure, a number of pyrazinoindoles **117** bearing an ester substituent were obtained in good yields.

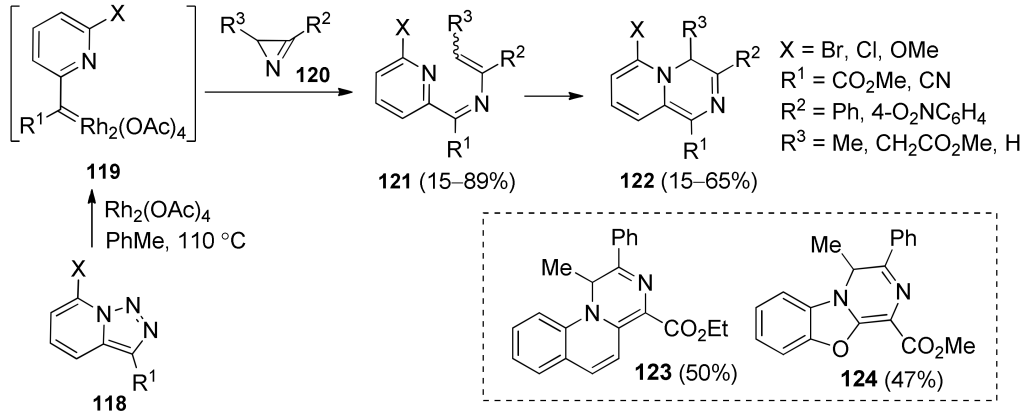
The rhodium-catalyzed reactions of azirines **120** with *ortho*-fused triazoles, [1–3]triazolo[1,5-*a*]pyridines **118**, have been studied in [54] (Scheme 23). The final products of the reaction were previously unknown 4*H*-pyrido[1,2-*a*]pyrazine derivatives **122**, which resulted from 1,6-electrocyclization of 1-(pyridin-2-yl)-2-azabuta-1,3-dienes **121** (1,4-diazahexa-1,3,5-trienes with the terminal C=N bond as part of the pyridine system). This process is quite remarkable because it belongs to a rare type of electrocyclization accompanied by the dearomatization of a pyridine ring.



Scheme 21. Synthesis of 5*H*-pyrazino[2,3-*b*]indoles from 2*H*-azirines.



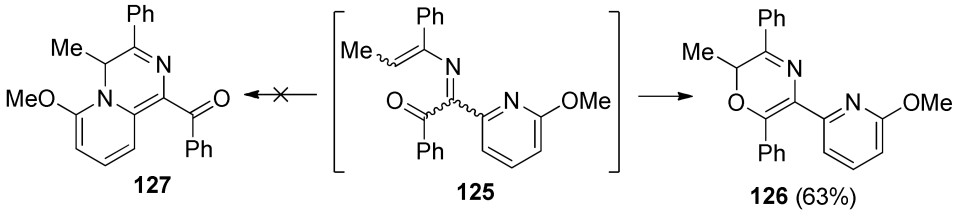
Scheme 22. Synthesis of 5*H*-pyrazino[2,3-*b*]indoles from isoxazoles.



Scheme 23. Synthesis of 4*H*-pyrido[1,2-*a*]pyrazines via 1,6-electrocyclization of 1-(2-pyridyl)-2-azabuta-1,3-dienes.

It was found that such 1,6-electrocyclization has limitations with respect to the substituents at the 2-azabutadiene [54]. The cyclization occurs for azadienes **121** bearing an electron-withdrawing substituent at C1 and a hydrogen atom, an alkyl, or aryl group at C4. The 4-alkyl-substituted pyridopyrazines **122** were found to be stable at room temperature and were isolated in moderate yields. Pyridopyrazines **122** with an aryl group at C4 exist in equilibrium with the corresponding 1,4-diazahexa-1,3,5-trienes **121**, even

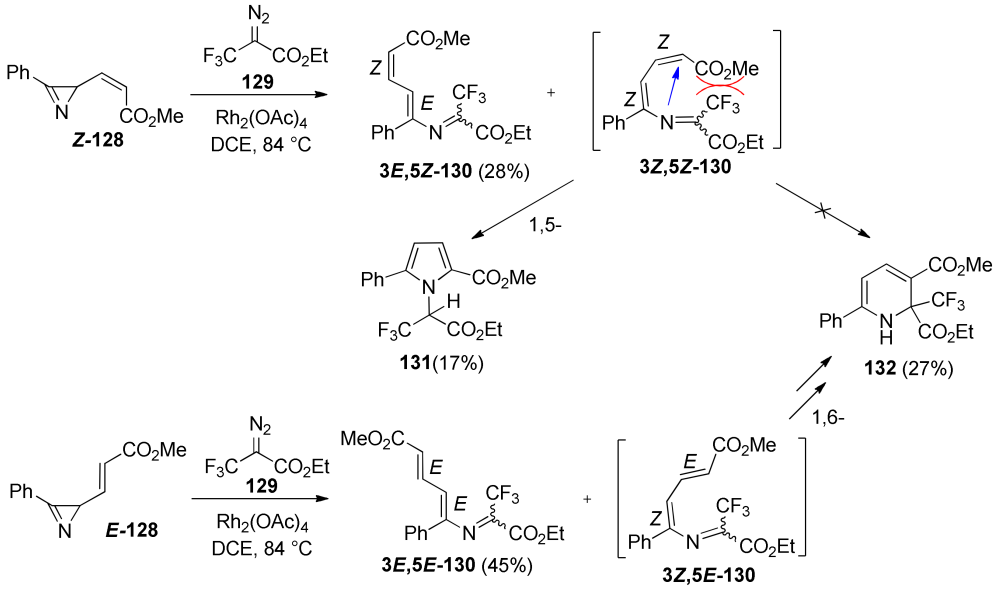
at room temperature. 1,6-Electrocyclization is also possible with the participation of the C=N bond of a quinoline and a benzoxazole (compounds **123** and **124**). According to the results of quantum chemical calculations, the 1,6-electrocyclization under consideration is a pseudopericyclic reaction proceeding through a significantly flattened transition state. It is noteworthy that 3-benzoyl-substituted 1,4-diazahexa-1,3,5-triene **125**, formed from the corresponding pyridotriazole, undergoes cyclization to 2*H*-1,4-oxazine **126**, rather than to 4*H*-pyrido[1,2-*a*]pyrazine **127** (Scheme 24).



Scheme 24. 1,6-Electrocyclization of 1-benzoyl-1-(2-pyridyl)-2-azabuta-1,3-diene.

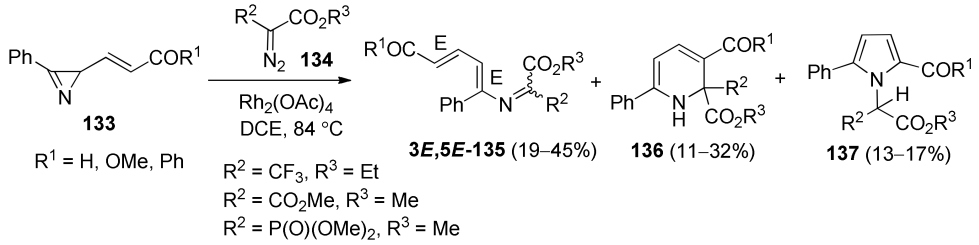
3.5. 1,6- and 1,5-Electrocyclizations of 2-Azahexa-1,3,5-trienes

The introduction of an alkenyl substituent at C4 of the 2-azabuta-1,3-diene system led to 2-azahexa-1,3,5-trienes, which can undergo 1,6-electrocyclization to dihydropyridines. Indeed, the reaction of alkenyl-substituted azirine ***E*-128** with diazo compound **129** in the presence of $Rh_2(OAc)_4$ led to azahexatriene **3*E*,5*E*-130** and dihydropyridine **132**. A similar reaction of the isomeric azirine ***Z*-128** gave azahexatriene **3*E*,5*Z*-130** and pyrrole **131** (Scheme 25) [55,56]. Dihydropyridine **132** is the result of 1,6-electrocyclization of the unstable azatriene **3*Z*,5*E*-130** and subsequent prototropic shift, while pyrrole **131** is the product of 1,5-electrocyclization of the unstable azatriene **3*Z*,5*Z*-130**. Thus, the configuration of the terminal C=C bond in (3*Z*)-2-azahexa-1,3,5-trienes **130** completely controls the direction of their cyclization. Following from the quantum chemical calculations, in the transition states of the 1,6-electrocyclizations of azatrienes with the *Z* configuration of the terminal C=C bond, in contrast to the *E* isomer, there were noticeable steric repulsive interactions created by the CO_2Me group at the C6 and a substituent at the C1. As a result, the barrier of the 1,6-electrocyclization increases, and the pseudopericyclic 1,5-electrocyclization becomes more preferable.



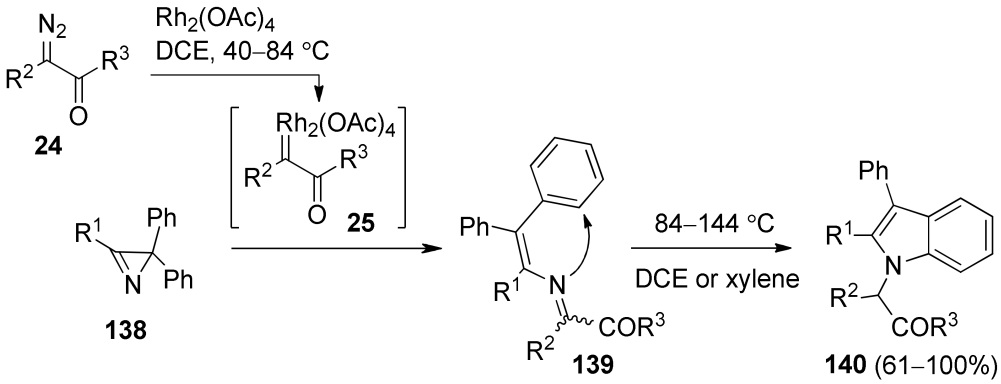
Scheme 25. 1,6- and 1,5-electrocyclizations of 2-azahexa-1,3,5-trienes.

The pathways of the azirine ring expansion in the $Rh_2(OAc)_4$-catalyzed reactions of various 2-carbonylvinyl-substituted azirines **133** with diazo esters **134** were also studied (Scheme 26) [56]. In all cases, the formation of dihydropyridines **136** and pyrroles **137**, along with the formation of stable azahexatrienes ***3E,5E*-135**, was observed, with the proportion of the pyrrole increasing with an increase in volume of a substituent at the C1 (phosphonate, $R^2 = P(O)(OMe)_2$) or C6 (benzoyl group, R^1 = Ph) of the azahexatriene.



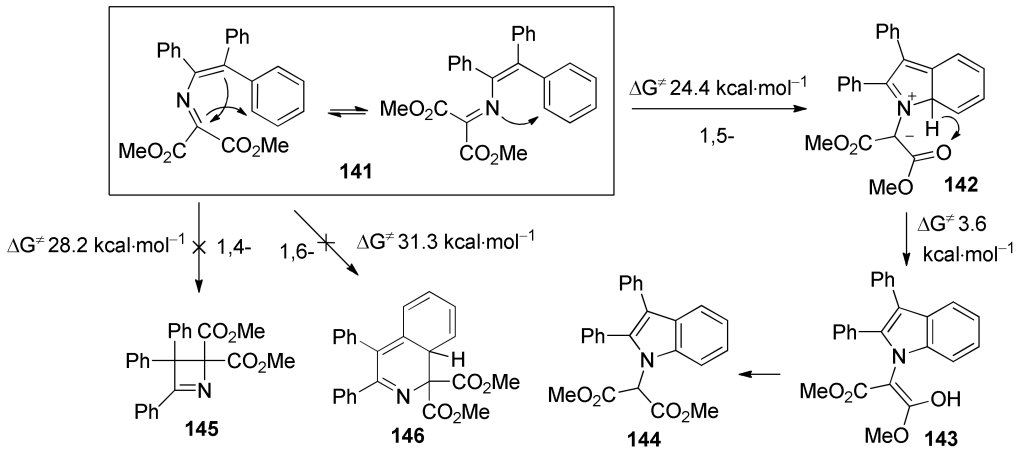
Scheme 26. Synthesis of pyrroles and dihydropyridines via electrocyclizations of 2-azahexa-1,3,5-trienes.

2-Azadienes **139** (2-azahexa-1,3,5-trienes with the terminal C=C bond as a part of the benzene system) containing two phenyl substituents at the C4 and two electron-withdrawing groups at the C1 undergo unusual 1,5-electrocyclization involving the C=C bond of the aromatic ring to give indole derivatives **140** (Scheme 27). On the basis of this reaction, an efficient method for the synthesis of *N*-substituted indoles **140** from 2,2-diphenyl-2*H*-azirines **138** and diazocarbonyl compounds **24** without isolation of the intermediate azahexatrienes **139** was developed [28]. It was found that an increase in the electron-withdrawing ability of substituents at the C1 of 2-azabutadienes facilitates the indole formation. Particularly, the azahexatriene containing an alkoxycarbonyl and cyano group at C1 isomerized smoothly to the corresponding indole, even at room temperature.



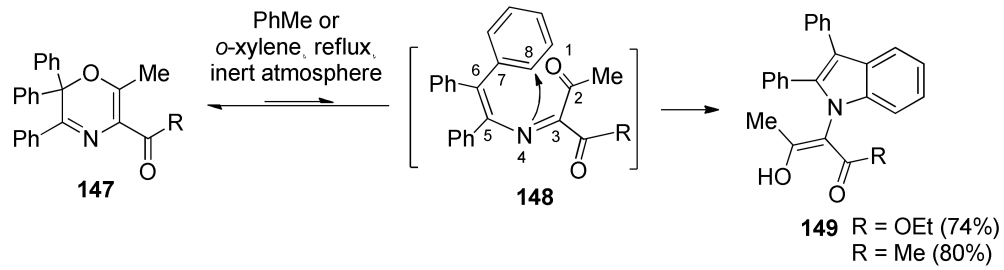
Scheme 27. Synthesis of indoles via 1,5-electrocyclization of 4-phenyl-2-azabuta-1,3-dienes.

According to the results of the DFT calculations, the activation barrier of 1,5-electrocyclization of azadiene **141** to indolium ylide **142** turned out to be lower than those of 1,4-electrocyclization to dihydroazete **145** and 1,6-electrocyclization to dihydroisoquinoline **146** (Scheme 28) [28]. Further intramolecular prototropic shift in indolium ylide **142** has an extremely low barrier. In contrast to the 1,4- and 1,6-cyclization, the formation of indolium ylide **142** is a pseudopericyclic cyclization, the structure of the transition state of which is significantly flattened. This, together with the effective stabilization of the emerging anionic center by electron-withdrawing substituents, determines the preference of the 1,5-electrocyclization.



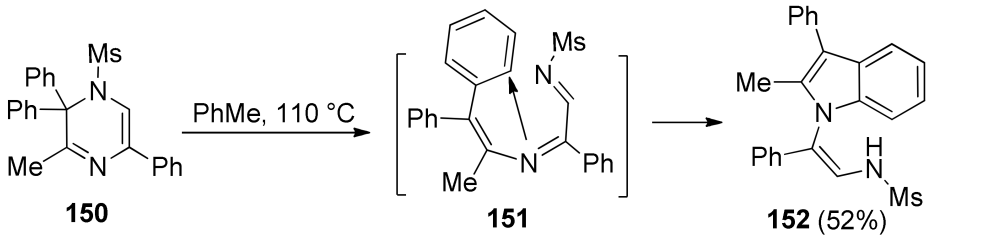
Scheme 28. Calculation data for the electrocyclizations of 4-phenyl-2-azabuta-1,3-dienes.

It was found that at elevated temperature, 2,2-diphenyl-substituted 2*H*-1,4-oxazines **147** obtained in the rhodium-catalyzed reaction of 2,2,3-triphenyl-2*H*-azirine with diazo keto esters or diazo diketones exist in equilibrium with the corresponding 1-oxa-4-azaocta-1,3,5,7-tetraenes **148** (Scheme 29) [28]. In turn, this intermediate, which is formed in small amounts, undergoes irreversible 1,5-electrocyclization to an indole derivative, thereby shifting the oxazine–oxazatetraene equilibrium until the complete conversion of the oxazine is achieved. In particular, the thermolysis of 2,2-diphenyl-2*H*-1,4-oxazines **147** led to *N*-substituted indoles **149** in good yields.



Scheme 29. Synthesis of indoles via electrocyclic ring opening of 2*H*-1,4-oxazines.

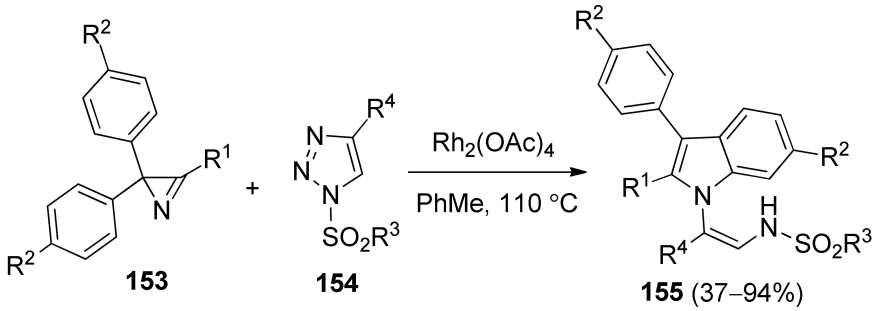
The reaction of 2,2-disubstituted 1,2-dihydropyrazines, obtained from 1-sulfonyl-1,2,3-triazoles and 2,2-diaryl-substituted 2*H*-azirines, proceeded in a similar manner [57]. In particular, dihydropyrazine **150** was found to be a stable compound at room temperature, however, upon heating, it underwent reversible ring opening to 1,4-diazaocta-1,3,5,7-tetraene **151** (Scheme 30). Eventually, prolonged heating of dihydropyrazine **150** led to the formation of aminovinylindole **152** in moderate yield.



Scheme 30. Synthesis of indole derivatives from 1,2-dihydropyrazines.

The synthesis of (2-aminovinyl)indoles **155** was succeeded to be carried out in a one-pot mode, starting from azirines **153** and sulfonyltriazoles **154** by prolonged heating of

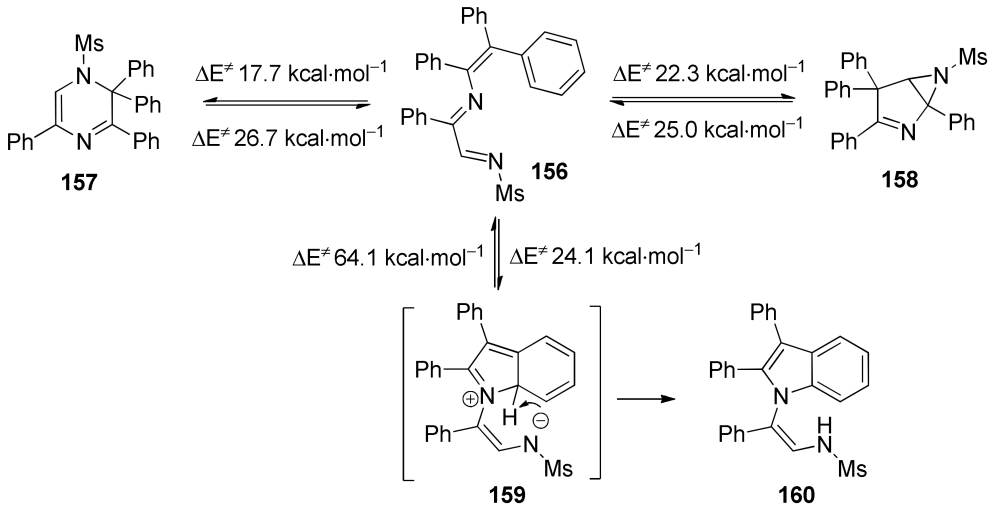
the reaction mixture containing the initially formed dihydropyrazine (Scheme 31) [57]. A number of aminovinylindoles have been obtained by this procedure in good yields. All indoles were obtained as a single stereoisomer with the *Z* configuration of the C=C double bond.



R^1 = Me, Ph; R^2 = H, Me; R^3 = 4-$O_2NC_6H_4$, *p*-Tol, Me; R^4 = 4-ClC_6H_4, 4-$O_2NC_6H_4$, Ph

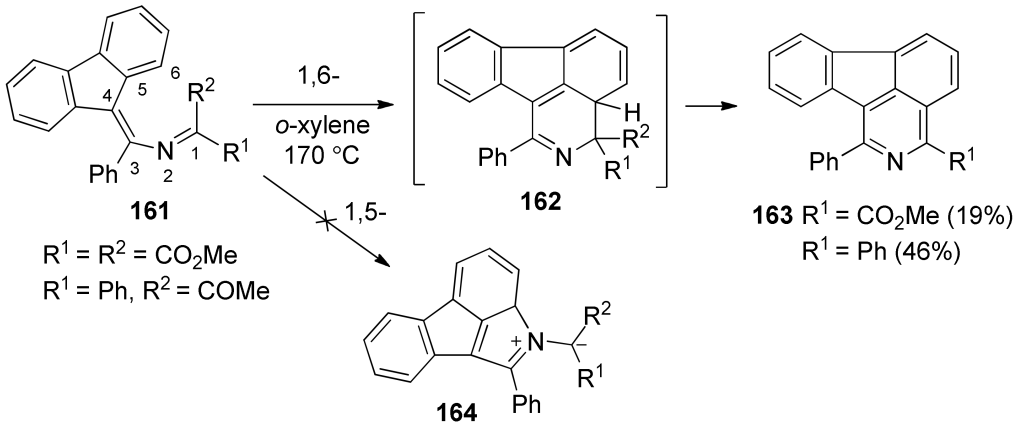
Scheme 31. Synthesis of (2-aminovinyl)indoles from 2*H*-azirines and 1,2,3-triazoles.

The data of DFT calculations showed that the most low-barrier cyclization of 6,6-diphenyl-1,4-diazahexa-1,3,5-trienes **156** is the 1,6-electrocyclization to dihydropyrazines **157** (Scheme 32) [57]. The ring opening of dihydropyrazine **157** has a relatively low barrier, and it can be overcome upon moderate heating. The reversible cyclization of azapolyene **156** to diazabicyclohexene **158** has a larger activation barrier. Thus, before irreversible cyclization of diazaoctatetraene **156** to indole occurs, it exists in an equilibrium with dihydropyrazine **157** and diazabicyclohexene **158**. Indolium ylide **159** is an extremely unstable compound, which transforms to indole **160** through the barrierless prototropic shift.



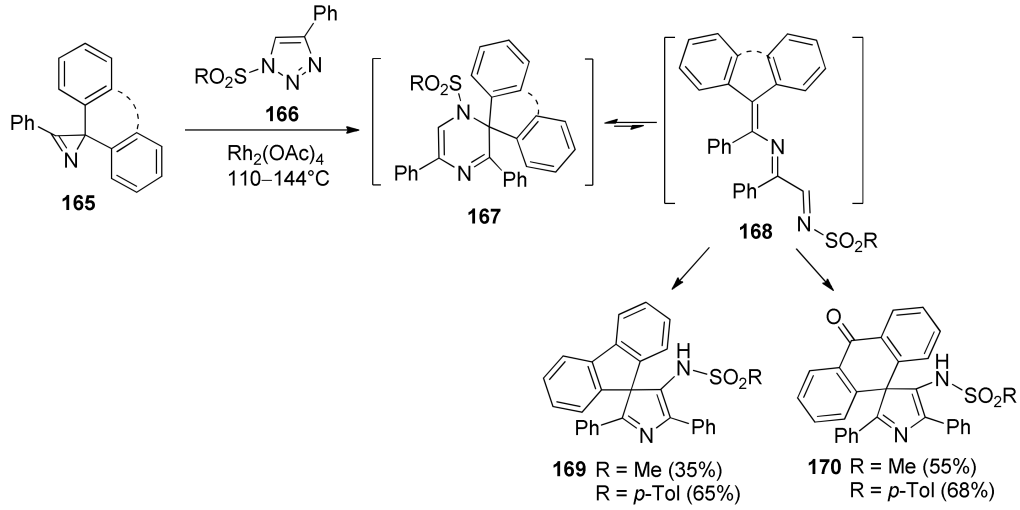
Scheme 32. Calculation data for the electrocyclizations of 6-phenyl-1,4-diazahexa-1,3,5-trienes.

The presence of a fluorene system at C4 of 2-azabutadiene moiety (2-azahexa-1,3,5-trienes with the terminal C=C bond as a part of the fluorene system) led to a change in the reaction course from 1,5-cyclization to 1,6-cyclization, giving rise to azafluoranthene derivatives [28]. In particular, azahexa-1,3,5-trienes **161** was converted by heating at 170 °C in *o*-xylene to 2-azafluoranthenes **163** in moderate yields (Scheme 33). The change in the cyclization mode on going from the *gem*-diphenyl to the fluorene system can be explained by a decrease in stability of the transition state, leading to a strained indeno[1,2,3-*cd*]indolium ylide **164**.



Scheme 33. Synthesis of 2-azafluoranthenes via 1,6-electrocyclization of 2-azahexa-1,3,5-trienes.

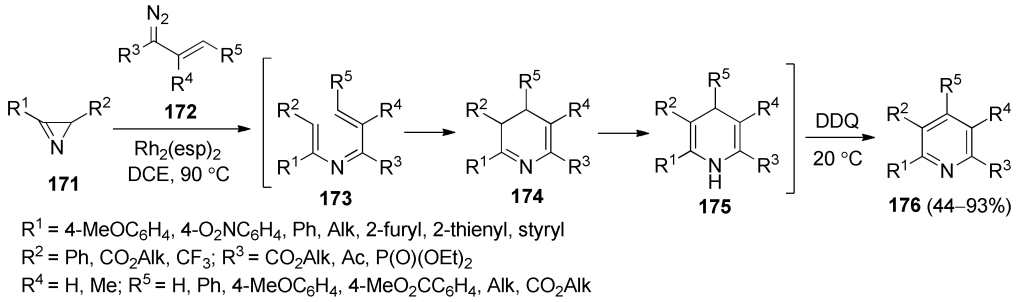
Analogously, the formation of indoles did not occur in the case of fluorene and anthrone derivatives of 1,4-diazahexa-1,3,5-triene (Scheme 34) [58]. As in previous cases, the rhodium-catalyzed reaction of azirines **165** with 1,2,3-triazoles **166** resulted in the initial formation of dihydropyrazines **167**, which upon further heating afforded spirocyclic 3*H*-pyrroles **169**, **170** via the 5-*exo*-*trig*-cyclizaion of azapolyene **168**, rather than indoles resulting from its 1,5-electrocyclization.



Scheme 34. Synthesis of 3*H*-pyrroles via electrocyclic ring opening of 1,2-dihydropyrazines.

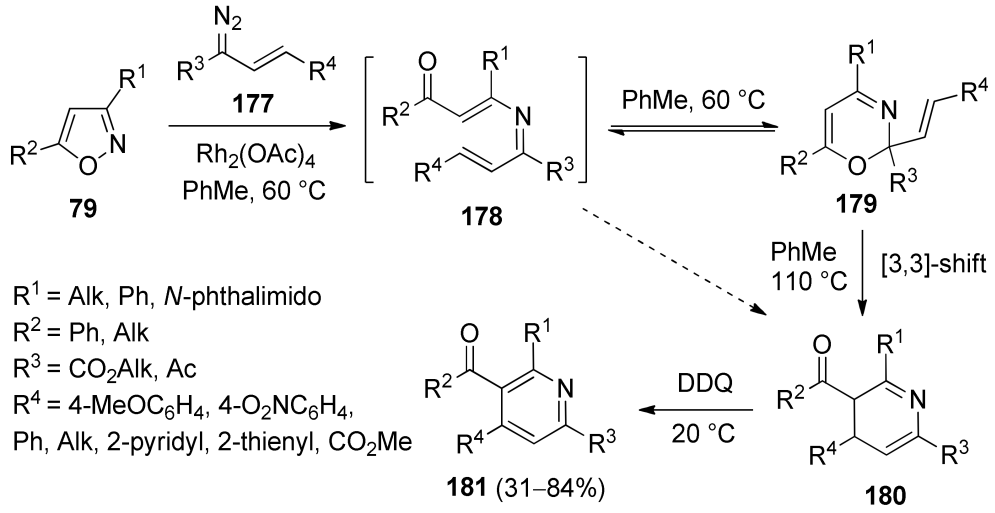
3.6. 1,6-Electrocyclization of 3-Azahexa-1,3,5-trienes to Dihydropyridines

A rhodium(II)-catalyzed reaction of diazo compounds **172**, containing an alkenyl substituent, with 2,3-disubstituted 2*H*-azirines **171** was used to generate 3-azahexa-1,3,5-trienes **173** (Scheme 35) [59,60]. These intermediates readily underwent 1,6-electrocyclization to 3,4-dihydropyridines **174**, which tautomerized to 1,4-dihydropyridines **175**. The oxidation of the latter in a one-pot mode by using 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) allowed the preparation of pyridines **176** bearing a wide range of substituents in moderate to high yields. In one case, the authors were able to isolate a 3-azahexatriene intermediate, which was transformed to a pyridine derivative at elevated temperature.



Scheme 35. Synthesis of pyridines from 2*H*-azirines.

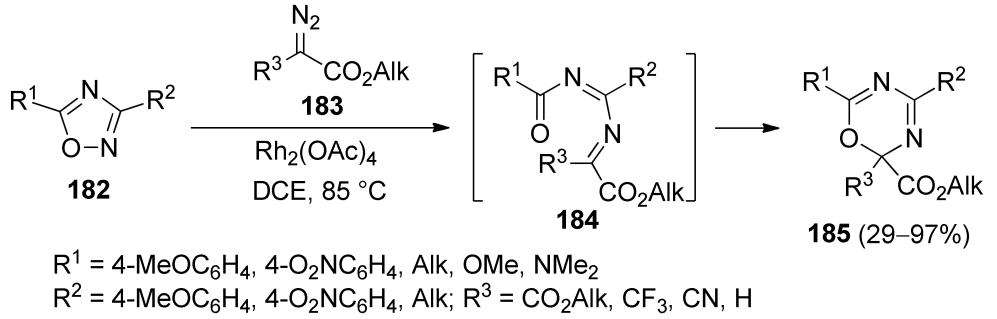
In a similar manner, isoxazoles can be successfully used in rhodium-catalyzed reactions with diazo compounds bearing an alkenyl substituent for the preparation of substituted pyridines. Manning and Davies reported the reaction of isoxazoles **79** with diazo compounds **177** catalyzed with $Rh_2(OAc)_4$ at 60 °C, which afforded 1,3-oxazines **179** (Scheme 36) [61]. When refluxed in toluene, the latter were converted to 3,4-dihydropyridines **180**. This transformation can be assumed to proceed either through the Cope rearrangement or through the ring opening to 1-oxa-5-azaoctatetraenes **178**, followed by 1,6-electrocyclization. Further oxidation of the dihydropyridines with DDQ led to the formation of pyridines **181** with a carbonyl substituent at C3.



Scheme 36. Synthesis of pyridines from isoxazoles.

3.7. 1,6-Electrocyclization of 1-Oxa-3,5-diazahexa-1,3,5-trienes to 2H-1,3,5-Oxadiazines

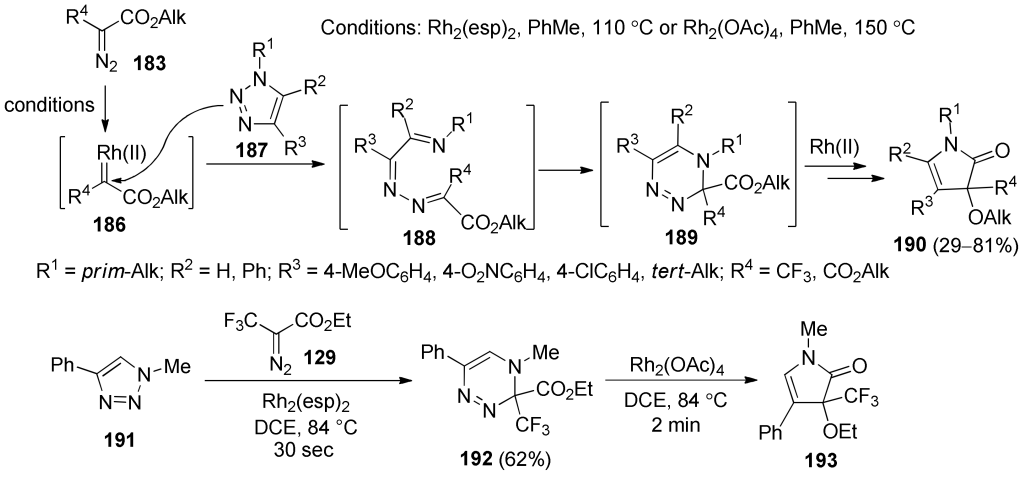
In the reaction of 1,2,4-oxadiazoles **182** with rhodium carbenes generated from α-diazoesters **183**, 1-oxa-3,5-diazahexa-1,3,5-trienes **184** were generated as reactive intermediates (Scheme 37) [62]. Despite the possibility of several directions of electrocyclization, heteropolyenes **184** underwent 1,6-electrocyclization involving the carbonyl group (both ketone and ester one) located at the nitrogen atom. As a result, a wide variety of 2*H*-1,3,5-oxadiazines **185** were obtained in good yields. Interestingly, the reaction can be efficiently catalyzed not only by rhodium compounds, but also by cheaper copper compounds. The involvement of an ester group in the electrocyclization process is rather unexpected, since no electrocyclization products with the participation of such groups were observed in previous studies. According to the data of the DFT calculations, in this case, the cyclization onto the ester group is favorable for both kinetic and thermodynamic reasons.



Scheme 37. Synthesis of 2*H*-1,3,5-oxadiazines via 1,6-electrocyclization of 1-oxa-3,5-diazahexa-1,3,5-trienes.

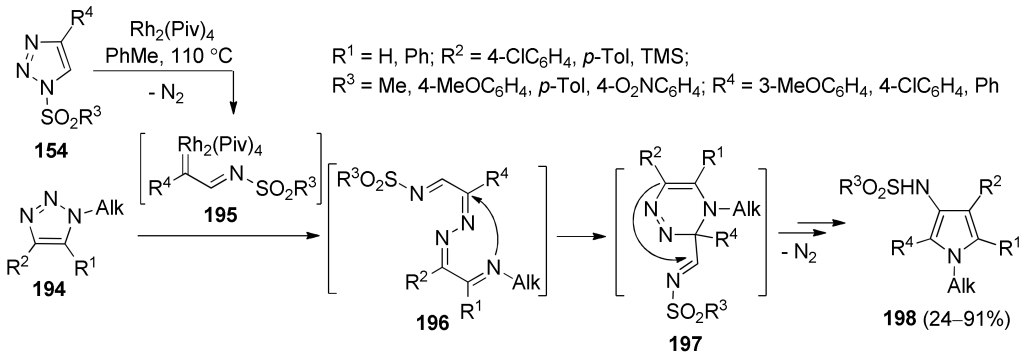
3.8. 1,6-Electrocyclization of 1,4,5-Triazahexa-1,3,5-trienes to 3,4-Dihydro-1,2,4-triazines

1,4,5-Triaza-1,3,5-hexatrienes **188**, generated by the reaction of 1-alkyl-1*H*-1,2,3-triazoles **187** with rhodium α-carbonyl carbenes **186**,derived from diazocarbonyl compounds **183**, underwent 1,6-electrocyclization to 3,4-dihydro-1,2,4-triazines **189** (Scheme 38) [63]. Under the reaction conditions, the latter rapidly rearranged to pyrrolin-2-ones **190**, which was accompanied by a nitrogen evolution, ring contraction, and 1,2-migration of the alkoxy substituent. To prove the intermediate formation of the 3,4-dihydro-1,2,4-triazines, the reaction of triazole **191** with 2-diazo-3,3,3-trifluoropropanoate **129** was carried out under milder reaction conditions. In this case, it was possible to isolate and characterize 3,4-dihydro-1,2,4-triazine **192**, which turned out to be quite stable in pure form. Heating its solution in DCE in the presence of catalytic amounts of $Rh_2(OAc)_4$ led to a triazine ring contraction to give pyrrolinone **193**.



Scheme 38. Synthesis of 4-pyrrolin-2-ones via electrocyclic formation of 3,4-dihydro-1,2,4-triazines.

The reaction of 1-alkyl-1,2,3-triazoles **194** with rhodium azavinyl carbenes **195**, derived from 1-sulfonyl-1,2,3-triazoles **154**, begins in a similar manner via the 1,6-electrocyclization of azapolyenes **196** to unstable 1,3,4-triazines **197,** which undergo, under the reaction conditions, denitrogenative ring contraction to give 3-sulfonamidopyrroles **198** (Scheme 39) [64]. According to the DFT calculations, the formation of pyrroles **198** from triazines **197** proceeds via a concerted rearrangement with a simultaneous nitrogen evolution followed by a 1,2-prototropic shift.



Scheme 39. Synthesis of 3-aminopyrroles via electrocyclic formation of 3,4-dihydro-1,2,4-triazines.

4. Conclusions

Reactions of transition metal carbenes with 2*H*-azirines and azoles containing an N-N or N-O bond is becoming an active field of research, as justified by the growing number of papers covered in this review. This approach is a novel versatile tool for the design of new reactive azapolyene intermediates suitable for the synthesis of various heterocycles via an electrocyclization (i.e., under atom-economical conditions). In contrast to other known methods, the present one features a wide diversity of accessible azapolyenes and, therefore, is able to provide a powerful impetus for the further development of the electrocyclization strategy in heterocyclic synthesis. The method has been exploited for the synthesis of unique 2,3-dihydroazetes, 2*H*-1,3-oxazines, 2*H*-1,4-oxazines, 1,2-dihydropyrimidines, various pyrazine and pyridine derivatives, etc. Moreover, the method provided azapolyenes, which are capable of undergoing an unprecedented 1,5-electocyclization to pyrrole and indole derivatives.

Although a great number of studies has been conducted, the described approach is just at the beginning stage. We believe that the use in the reactions of azirines and azoles containing polyene and heteropolyene substituents seems to be promising for further unlocking the potential of the method. Furthermore, the reactions of transition metal carbenes with azoles *ortho*-fused with aromatic and heteroatomatic rings remain practically unexplored. At the same time, these reactions should result in the formation of azapolyenes, which are most promising for the development of new photochromic materials. Another fruitful area of upcoming research, in our opinion, is switchable electrocyclizations of azapolyenes upon treatment by a specific catalyst, providing selective access to several heterocyclic systems from the same starting materials. In this context, it seems prospective to intensify the search for cheaper catalytic systems for azapolyene generation and pay attention to the reactions of azoles and their derivatives with copper carbenes. It also seems promising to study the transformation of non-aromatic diaza- and oxaza-derivatives of a cyclohexa-1,3-diene to stable aromatic heterocycles.

Funding: We gratefully acknowledge the financial support of the Russian Science Foundation (20-13-00044).

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Vinogradov, M.G.; Turova, O.V.; Zlotin, S.G. Catalytic Asymmetric Aza-Diels−Alder Reaction: Pivotal Milestones and Recent Applications to Synthesis of Nitrogen-Containing Heterocycles. *Adv. Synth. Catal.* **2021**, *363*, 1466–1526. [CrossRef]
2. Sarmah, M.M.; Prajapati, D. Aza-Diels–Alder Reaction: An Efficient Approach for Construction of Heterocycles. *Curr. Org. Chem.* **2014**, *18*, 1586–1620. [CrossRef]
3. Masson, G.; Lalli, C.; Benohoud, M.; Dagousset, G. Catalytic Enantioselective [4 + 2]-Cycloaddition: A Strategy to Access Aza-Hexacycles. *Chem. Soc. Rev.* **2013**, *42*, 902–923. [CrossRef] [PubMed]
4. Monbaliu, J.-C.M.; Masschelein, K.G.R.; Stevens, C.V. Electron-Deficient 1- and 2-Azabuta-1,3-dienes: A Comprehensive Survey of Their Synthesis and Reactivity. *Chem. Soc. Rev.* **2011**, *40*, 4708–4739. [CrossRef]

5. Jayakumar, S.; Ishar, M.P.S.; Mahajan, M.P. Recent Advances in Synthetic Applications of Azadienes. *Tetrahedron* **2002**, *58*, 379–471. [CrossRef]
6. Jiang, B.; Du, W.; Chen, Y.-C. Modified Cinchona Alkaloid-Catalysed Enantioselective [4 + 4] Annulations of Cyclobutenones and 1-Azadienes. *Chem. Commun.* **2020**, *56*, 7257–7260. [CrossRef] [PubMed]
7. He, L.; Laurent, G.; Retailleau, P.; Folléas, B.; Brayer, J.-L.; Masson, G. Highly Enantioselective Aza-Diels–Alder Reaction of 1-Azadienes with Enecarbamates Catalyzed by Chiral Phosphoric Acids. *Angew. Chem. Int. Ed.* **2013**, *125*, 11294–11297. [CrossRef]
8. Wang, C.-S.; Li, T.-Z.; Cheng, Y.-C.; Zhou, J.; Mei, G.-J.; Shi, F. Catalytic Asymmetric [4 + 1] Cyclization of Benzofuran-Derived Azadienes with 3-Chlorooxindoles. *J. Org. Chem.* **2019**, *84*, 3214–3222. [CrossRef]
9. Wan, Y.; Zheng, X.; Ma, C. Conjugated Dienyne-Imides as Robust Precursors of 1-Azatrienes for 6π Electrocyclizations to Furo[2,3-*b*]dihydropyridine Cores. *Angew. Chem. Int. Ed.* **2018**, *57*, 5482–5486. [CrossRef]
10. Kwon, S.H.; Seo, H.-A.; Cheon, C.-H. Total Synthesis of Luotonin A and Rutaecarpine from an Aldimine via the Designed Cyclization. *Org. Lett.* **2016**, *18*, 5280–5283. [CrossRef] [PubMed]
11. Sun, Y.-X.; Wang, X.-G.; Shen, G.-D.; Yang, T.; Yang, Y.-H.; Li, J.; Yang, M.-Y.; Sun, H.-M.; Wei, J.-F. A 6π Azaelectrocyclization Strategy towards the 1,5,9-Triazacoronenes. *Adv. Synth. Catal.* **2020**, *362*, 1651–1656. [CrossRef]
12. Ross, J.A.; Seiders, R.P.; Lemal, D.M. An extraordinarily facile sulfoxide automerization. *J. Am. Chem. Soc.* **1976**, *98*, 4325–4327. [CrossRef]
13. Zhao, Z.; Wei, H.; Xiao, K.; Cheng, B.; Zhai, H.; Li, Y. Facile Synthesis of Pyridines from Propargyl Amines: Concise Total Synthesis of Suaveoline Alkaloids. *Angew. Chem. Int. Ed.* **2019**, *58*, 1148–1152. [CrossRef] [PubMed]
14. Vargas, D.F.; Larghi, E.L.; Kaufman, T.S. Synthesis of Polysubstituted 3-Methylisoquinolines through the 6π-Electron Cyclization/Elimination of 1-Azatrienes derived from 1,1-Dimethylhydrazine. *Eur. J. Org. Chem.* **2018**, *2018*, 5605–5614. [CrossRef]
15. Lee, J.; Kim, H.Y.; Oh, K. Tandem Reaction Approaches to Isoquinolones from 2-Vinylbenzaldehydes and Anilines via Imine Formation–6π-Electrocyclization–Aerobic Oxidation Sequence. *Org. Lett.* **2020**, *22*, 474–478. [CrossRef]
16. Tarzia, G.; Balsamini, C.; Spadoni, G.; Duranti, E. Alkyl 2-(diphenylmethyleneamino)acrylates in the synthesis of α-amino acids. *Synthesis* **1988**, *1988*, 514–517. [CrossRef]
17. O'Donnell, M.J.; Arasappan, A.; Homback, W.J.; Huffman, J.C. Preparation and Wittig reactions of an α-keto amino acid derivative. *Tetrahedron Lett.* **1990**, *31*, 157–160. [CrossRef]
18. Barluenga, J.; Tomas, M.; Ballesteros, A.; Gotor, V. An easy synthesis of electron-withdrawing substituted 2-aza-1,3-dienes and their 1,4-cycloaddition with enamines. *J. Chem. Soc. Chem. Commun.* **1987**, 1195–1196. [CrossRef]
19. Barluenga, J.; Ferrero, M.; Palacios, F. An efficient and mild conditions synthesis of 2-aza-1,3-dienes from phospha-λ^5-azenes. *Tetrahedron Lett.* **1988**, *29*, 4863–4864. [CrossRef]
20. Barluenga, J.; Ferrero, M.; Palacios, F. Reactivity and selectivity of N-vinylic λ5-phosphazenes towards electrophiles. Synthesis of 2-aza-1,3-dienes. *J. Chem. Soc., Perkin Trans.* **1990**, *1*, 2193–2197. [CrossRef]
21. Barluenga, J.; Ferrero, M.; Palacios, F. A simple and efficient «One pot» synthesis of 2-aza-1,3-butadienes from *N*-vinylic λ^5-phosphazenes. *Tetrahedron Lett.* **1990**, *31*, 3497–3500. [CrossRef]
22. Polychronidou, V.; Krupp, A.; Strohmann, C.; Antonchick, A.P. Cascade aza-Wittig/6π-Electrocyclization in the Synthesis of 1,6-Dihydropyridines. *Org. Lett.* **2021**, *23*, 6024–6029. [CrossRef]
23. Wei, H.; Li, Y.; Xiao, K.; Cheng, B.; Wang, H.; Hu, L.; Zhai, H. Synthesis of Polysubstituted Pyridines via a One-Pot Metal-Free Strategy. *Org. Lett.* **2015**, *17*, 5974–5977. [CrossRef] [PubMed]
24. Ford, A.; Miel, H.; Ring, A.; Slattery, C.N.; Maguire, A.R.; McKervey, M.A. Modern Organic Synthesis with α-Diazocarbonyl Compounds. *Chem. Rev.* **2015**, *115*, 9981–10080. [CrossRef]
25. Khlebnikov, A.F.; Novikov, M.S.; Rostovskii, N.V. Advances in 2*H*-azirine chemistry: A seven-year update. *Tetrahedron* **2019**, *75*, 2555–2624. [CrossRef]
26. Khlebnikov, A.F.; Novikov, M.S.; Amer, A.A. Reactions of 2*H*-azirines with carbenoids from diazo esters: Transformations of novel azirinium ylides. *Tetrahedron Lett.* **2004**, *45*, 6003–6006. [CrossRef]
27. Khlebnikov, A.F.; Novikov, M.S.; Amer, A.A.; Kostikov, R.R.; Magull, J.; Vidovic, D. Azirinium ylides from alkoxycarbonylcarbenoids and 2*H*-azirines: Generation and transformations. *Russ. J. Org. Chem.* **2006**, *42*, 515–526. [CrossRef]
28. Novikov, M.S.; Khlebnikov, A.F.; Rostovskii, N.V.; Tcyrulnikov, S.; Suhanova, A.A.; Zavyalov, K.V.; Yufit, D.S. Pseudopericyclic 1,5- versus pericyclic 1,4- and 1,6-electrocyclization in electron-poor 4-Aryl-2-azabuta-1,3-dienes: Indole synthesis from 2H-azirines and diazo compounds. *J. Org. Chem.* **2015**, *80*, 18–29. [CrossRef]
29. Smetanin, I.A.; Novikov, M.S.; Agafonova, A.V.; Rostovskii, N.V.; Khlebnikov, A.F.; Kudryavtsev, I.V.; Terpilowski, M.A.; Serebriakova, M.K.; Trulioff, A.S.; Goncharov, N.V. A novel strategy for the synthesis of thermally stable and apoptosis-inducing 2,3-dihydroazetes. *Org. Biomol. Chem.* **2016**, *14*, 4479–4487. [CrossRef] [PubMed]
30. Novikov, M.S.; Smetanin, I.A.; Khlebnikov, A.F.; Rostovskii, N.V.; Yufit, D.S. Synthesis of electron-poor 4-halo-2-azabuta-1,3-dienes by Rh(II)-catalyzed diazo ester-azirine coupling. 2-Azabuta-1,3-diene-2,3-dihydroazete valence isomerism. *Tetrahedron Lett.* **2012**, *53*, 5777–5780. [CrossRef]
31. Smetanin, I.A.; Novikov, M.S.; Rostovskii, N.V.; Khlebnikov, A.F.; Starova, G.L.; Yufit, D.S. 4-Halo-2-azabuta-1,3-dienes as intermediates in the rhodium carbenoid-initiated transformation of 2-halo-2*H*-azirines into 2,3-dihydroazetes and 2,5-dihydrooxazoles. *Tetrahedron* **2015**, *71*, 4616–4628. [CrossRef]

32. Golubev, A.A.; Smetanin, I.A.; Agafonova, A.V.; Rostovskii, N.V.; Khlebnikov, A.F.; Starova, G.L.; Novikov, M.S. [2 + 1 + 1] Assembly of spiro β-lactams by Rh(II)-catalyzed reaction of diazocarbonyl compounds with azirines/isoxazoles. *Org. Biomol. Chem.* **2019**, *17*, 6821–6830. [CrossRef]
33. Koronatov, A.N.; Rostovskii, N.V.; Khlebnikov, A.F.; Novikov, M.S. One-pot synthesis of 3-(pyridin-2-yl)-2,3-dihydroazetes via Rh(II)-catalyzed reaction of diazoesters with trimethylsilyl-protected 2-(pyridin-2-yl)-2*H*-azirines. *Chem. Heterocycl. Compd.* **2019**, *55*, 1185–1189. [CrossRef]
34. Maeda, S. *Organic Photochromic and Thermochromic Compounds*; Plenum Press: New York, NY, USA, 1999; Volume 1, Chapter 2; pp. 85–109.
35. Minkin, V.I. Photo-, Thermo-, Solvato-, and Electrochromic Spiroheterocyclic Compounds. *Chem. Rev.* **2004**, *104*, 2751–2776. [CrossRef]
36. Barkauskas, M.; Martynaitis, V.; Šačkus, A.; Rotomskis, R.; Sirutkaitis, V.; Vengris, M. Ultrafast Dynamics of Photochromic Compound Based on Oxazine Ring Opening. *Lith. J. Phys.* **2008**, *48*, 231–242. [CrossRef]
37. Manning, J.R.; Davies, H.M.L. Efficient route to 2*H*-1,3-oxazines through ring expansion of isoxazoles by rhodium carbenoids. *Tetrahedron* **2008**, *64*, 6901–6908. [CrossRef] [PubMed]
38. Khlebnikov, A.F.; Novikov, M.S.; Gorbunova, Y.G.; Galenko, E.E.; Mikhailov, K.I.; Pakalnis, V.V.; Avdontceva, M.S. Isoxazolium N-ylides and 1-oxa-5-azahexa-1,3,5-trienes on the way from isoxazoles to 2*H*-1,3-oxazines. *Beilstein J. Org. Chem.* **2014**, *10*, 1896–1905. [CrossRef] [PubMed]
39. Zavyalov, K.V.; Novikov, M.S.; Khlebnikov, A.F.; Yufit, D.S. $Rh_2(OAc)_4$-Catalyzed Reaction of α-Diazocarbonyl Compounds with 2-Carbonyl-Substituted 2*H*-Azirines. *Tetrahedron* **2013**, *69*, 4546–4551. [CrossRef]
40. Zavyalov, K.V.; Novikov, M.S.; Khlebnikov, A.F.; Pakalnis, V.V. Selective Syntheses of 2*H*-1,3-Oxazines and 1*H*-Pyrrol-3(2*H*)-ones via Temperature-Dependent Rh(II)-Carbenoid-Mediated 2*H*-Azirine Ring Expansion. *Tetrahedron* **2014**, *70*, 3377–3384. [CrossRef]
41. Khlebnikov, V.A.; Novikov, M.S.; Khlebnikov, A.F.; Rostovskii, N.V. Rh(II)-Catalyzed reactions of 2*H*-azirines with ethyl 2-acyl-2-diazoacetates. Synthesis of novel photochromic oxazines. *Tetrahedron Lett.* **2009**, *50*, 6509–6511. [CrossRef]
42. Rostovskii, N.V.; Novikov, M.S.; Khlebnikov, A.F.; Khlebnikov, V.A.; Korneev, S.M. Rh(II)-carbenoid mediated 2*H*-azirine ring-expansion as a convenient route to non-fused photo- and thermochromic 2*H*-1,4-oxazines. *Tetrahedron* **2013**, *69*, 4292–4301. [CrossRef]
43. Rostovskii, N.V.; Novikov, M.S.; Khlebnikov, A.F.; Starova, G.L.; Avdontseva, M.S. Azirinium ylides from α-diazoketones and 2*H*-azirines on the route to 2*H*-1,4-oxazines: Three-membered ring opening vs 1,5-cyclization. *Beilstein J. Org. Chem.* **2015**, *11*, 302–312. [CrossRef]
44. Novikov, M.S.; Rostovskii, N.V.; Koronatov, A.N.; Zavyalov, K.V.; Zubakin, G.V.; Khlebnikov, A.F.; Starova, G.L. Synthesis of 1,2-Dihydropyrimidine-2-carboxylates via Regioselective Addition of Rhodium(II) Carbenoids to 2*H*-Azirine-2-carbaldimines. *J. Org. Chem.* **2017**, *82*, 13396–13404. [CrossRef]
45. Koronatov, A.N.; Rostovskii, N.V.; Khlebnikov, A.F.; Novikov, M.S. Rh(II)-Catalyzed Ring Expansion of Pyrazoles with Diazocarbonyl Compounds as a Method for the Preparation of 1,2-Dihydropyrimidines. *J. Org. Chem.* **2018**, *83*, 9210–9219. [CrossRef]
46. Rostovskii, N.V.; Ruvinskaya, J.O.; Novikov, M.S.; Khlebnikov, A.F.; Smetanin, I.A.; Agafonova, A.V. Switchable Synthesis of Pyrroles and Pyrazines via Rh(II)-Catalyzed Reaction of 1,2,3-Triazoles with Isoxazoles: Experimental and DFT Evidence for the 1,4-Diazahexatriene Intermediate. *J. Org. Chem.* **2017**, *82*, 256–268. [CrossRef]
47. Zhao, Y.-Z.; Yang, H.-B.; Tang, X.-Y.; Shi, M. Rh^{II}-Catalyzed [3+2] Cycloaddition of 2*H*-Azirines with *N*-Sulfonyl-1,2,3-Triazoles. *Chem. Eur. J.* **2015**, *21*, 3562–3566. [CrossRef] [PubMed]
48. Ryu, T.; Baek, Y.; Lee, P.H. Synthesis of Pyrazines from Rhodium-Catalyzed Reaction of 2*H*-Azirines with *N*-Sulfonyl 1,2,3-Triazoles. *J. Org. Chem.* **2015**, *80*, 2376–2383. [CrossRef] [PubMed]
49. Wang, Y.; Lei, X.; Tang, Y. Rh(II)-Catalyzed Cycloadditions of 1-Tosyl-1,2,3-triazoles with 2*H*-Azirines: Switchable Reactivity of Rh-Azavinylcarbene as [2C]- or Aza-[3C]-Synthon. *Chem. Commun.* **2015**, *51*, 4507–4510. [CrossRef]
50. Loy, N.S.Y.; Kim, S.; Park, C.-M. Synthesis of Unsymmetrical Pyrazines Based on α Diazo Oxime Ethers. *Org. Lett.* **2015**, *17*, 395–397. [CrossRef] [PubMed]
51. Ding, H.; Wang, Z.; Bai, S.; Lu, P.; Wang, Y. Rh-Catalyzed Conversion of 3-Diazoindolin-2-imines to 5*H*-Pyrazino[2,3-*b*]indoles with Photoluminescent Properties. *Org. Lett.* **2017**, *19*, 6514–6517. [CrossRef] [PubMed]
52. Baek, Y.; Maeng, C.; Kim, H.; Lee, P.H. Regioselective Synthesis of Indolopyrazines through a Sequential Rhodium-Catalyzed Formal [3+3] Cycloaddition and Aromatization Reaction of Diazoindolinimines with Azirines. *J. Org. Chem.* **2018**, *83*, 2349–2360. [CrossRef]
53. Ruvinskaya, J.O.; Rostovskii, N.V.; Filippov, I.P.; Khlebnikov, A.F.; Novikov, M.S. A Novel Approach to 5*H*-Pyrazino[2,3-*b*]indoles via Annulation of 3-Diazoindolin-2-imines with 2*H*-Azirines or 5-Alkoxyisoxazoles under Rh(II) Catalysis. *Org. Biomol. Chem.* **2018**, *16*, 38–42. [CrossRef]
54. Filippov, I.P.; Novikov, M.S.; Khlebnikov, A.F.; Rostovskii, N.V. Pseudopericyclic Dearomative 1,6-Cyclization of 1-(2-Pyridyl)-2-azabuta-1,3-dienes: Synthesis and Ring–Chain Valence Equilibria of 4*H*-Pyrido[1,2-*a*]pyrazines. *Eur. J. Org. Chem.* **2020**, *2020*, 3688–3698. [CrossRef]
55. Zavyalov, K.V.; Novikov, M.S.; Khlebnikov, A.F.; Rostovskii, N.V.; Starova, G.L. $Rh_2(OAc)_4$-catalyzed Reaction of 2-(2-Carbonylvinyl)-3-phenyl-2*H*-azirines with Diazo Esters. *Russ. J. Org. Chem.* **2017**, *53*, 1214–1221. [CrossRef]

56. Zavyalov, K.V.; Novikov, M.S.; Khlebnikov, A.F.; Rostovskii, N.V. (3*Z*)-2-Azahexa-1,3,5-trienes: Generation and Regioselectivity of 1,5- and 1,6-Cyclizations. *Russ. J. Org. Chem.* **2016**, *52*, 1851–1853. [CrossRef]
57. Khaidarov, A.R.; Rostovskii, N.V.; Zolotarev, A.A.; Khlebnikov, A.F.; Novikov, M.S. Synthesis of 1-(2-Aminovinyl)indoles and 1,3′-Biindoles by Reaction of 2,2-Diaryl-Substituted 2*H*-Azirines with α-Imino Rh(II) Carbenoids. *J. Org. Chem.* **2019**, *84*, 3743–3753. [CrossRef]
58. Khaidarov, A.R.; Rostovskii, N.V.; Starova, G.L.; Khlebnikov, A.F.; Novikov, M.S. Synthesis of spirocyclic 3*H*-pyrrol-4-amines from 2*H*-azirines and 1-sulfonyl-1,2,3-triazoles. *Chem. Heterocycl. Compd.* **2018**, *54*, 946–950. [CrossRef]
59. Loy, N.S.Y.; Singh, A.; Xu, X.; Park, C.-M. Synthesis of Pyridines by Carbenoid-Mediated Ring Opening of 2*H*-Azirines. *Angew. Chem. Int. Ed.* **2013**, *52*, 2212–2216. [CrossRef] [PubMed]
60. He, Y.-T.; Wang, Q.; Zhao, J.; Liu, X.-Y.; Xu, P.-F.; Liang, Y.-M. The copper-catalyzed synthesis of β-trifluoromethylated acrylonitriles and trifluoromethyl-substituted 2*H*-azirines. *Chem. Commun.* **2015**, *51*, 13209–13212. [CrossRef] [PubMed]
61. Manning, J.R.; Davies, H.M.L. One-Pot Synthesis of Highly Functionalized Pyridines via a Rhodium Carbenoid Induced Ring Expansion of Isoxazoles. *J. Am. Chem. Soc.* **2008**, *130*, 8602–8603. [CrossRef] [PubMed]
62. Strelnikova, J.O.; Rostovskii, N.V.; Khoroshilova, O.V.; Khlebnikov, A.F.; Novikov, M.S. An Efficient Synthesis of Functionalized 2*H*-1,3,5-Oxadiazines via Metal-Carbenoid-Induced 1,2,4-Oxadiazole Ring Cleavage. *Synthesis* **2021**, *53*, 348–358.
63. Koronatov, A.N.; Rostovskii, N.V.; Khlebnikov, A.F.; Novikov, M.S. Synthesis of 3-Alkoxy-4-Pyrrolin-2-ones via Rhodium(II)-Catalyzed Denitrogenative Transannulation of 1*H*-1,2,3-Triazoles with Diazo Esters. *Org. Lett.* **2020**, *22*, 7958–7963. [CrossRef] [PubMed]
64. Koronatov, A.N.; Afanaseva, K.K.; Sakharov, P.A.; Rostovskii, N.V.; Khlebnikov, A.F.; Novikov, M.S. Rh(II)-Catalyzed denitrogenative 1-sulfonyl-1,2,3-triazole–1-alkyl-1,2,3-triazole cross-coupling as a route to 3-sulfonamido-1*H*-pyrroles and 1,2,3-triazol-3-ium ylides. *Org. Chem. Front.* **2021**, *8*, 1474–1481. [CrossRef]