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Dearomative Electrocyclization

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

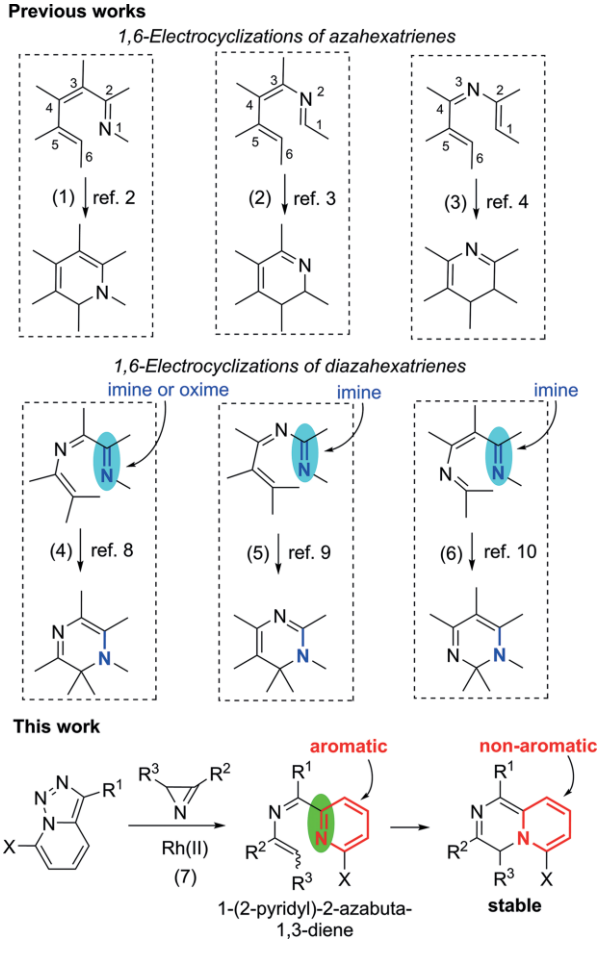
Ilya P. Filippov,[a] Mikhail S. Novikov,[a] Alexander F. Khlebnikov,[a] and Nikolai V. Rostovskii*[a]

Abstract: The 1,6-electrocyclization of 1-(2-pyridyl)-2-azabuta-1,3-dienes obtained by Rh^{II}-catalyzed reaction of pyridotriazoles with 2*H*-azirines affords stable non-aromatic 4*H*-pyrido[1,2-*a*]-pyrazines despite the fact that the reaction proceeds with irreversible dearomatization of the pyridine aromatic system. This pseudopericyclic cyclization occurs when the 2-azabutadiene contains H, alkyl, or Ph at the C4 atom and an electron-withdrawing substituent at the C1 atom. A number of stable 4*H*-pyrido[1,2-*a*]pyrazines as well as 1*H*-pyrazino[1,2-*a*]quinoline and 4*H*-benzo[4,5]oxazolo[3,2-*a*]pyrazine derivatives were synthesized. Whereas 4-alkyl-substituted pyridopyrazines are stable at room temperature, 4-phenyl-substituted pyridopyrazines exist in ring–chain valence equilibrium with 1-(2-pyridyl)-2-azabutadienes. Thermodynamic stability of the 4*H*-pyrido[1,2-*a*]-pyrazine decreases with increasing size of the substituent at the C6 atom.

Introduction

The aza-1,6-electrocyclization is a powerful and atom-economic approach to the formation of N-heterocyclic compounds such as pyridines, quinolines, and isoquinolines, including natural products and medicines.[1] Thus, the 1,6-electrocyclization of 1-aza-,[2] 2-aza-,[3] and 3-azahexa-1,3,5-trienes[4] leads to the formation of 1,2-, 2,3-, and 3,4-dihydropyridines (Scheme 1, reactions 1–3). Such cyclization easily occurs when none of the double bonds of the azatriene fragment are included in the aromatic cycle.[2a–2e,3a,3b,4a–4d,5] When one of the double bonds of starting azatriene is a part of an aromatic system, 1,6-electrocyclization can occur reversibly (if aromatization of the primary dihydropyridine product is impossible)[6] or irreversibly (if aromatization of the primary dihydropyridine intermediate into pyridine is plausible).[2f–2j,3c–3f,4e]

The examples of the 1,6-electrocyclization of diazahexa-1,3,5-trienes are much rarer.[7] The 1,6-electrocyclization of diazahexa-1,3,5-trienes occurs when the C=N-termini of the diazahexatriene is a part of an imine or oxime group, and does not occur when the C=N-termini is included in an aromatic system. In particular, in recent studies it has been shown on many examples that the 1,6-cyclization of 1,4-diazatrienes leads to 1,2-dihydropyrazines[8] (Scheme 1, reaction 4) which in some cases undergo aromatization to give pyrazines.[8c–8h] Similarly, the



Scheme 1. 1,6-Electrocyclizations of aza- and diazahexa-1,3,5-trienes.

[a] *I. P. Filippov, Prof. Dr. M. S. Novikov, Prof. Dr. A. F. Khlebnikov, Dr. N. V. Rostovskii*
St. Petersburg State University, Institute of Chemistry, 7/9 Universitetskaya nab., St. Petersburg 199034, Russia
E-mail: n.rostovskiy@spbu.ru

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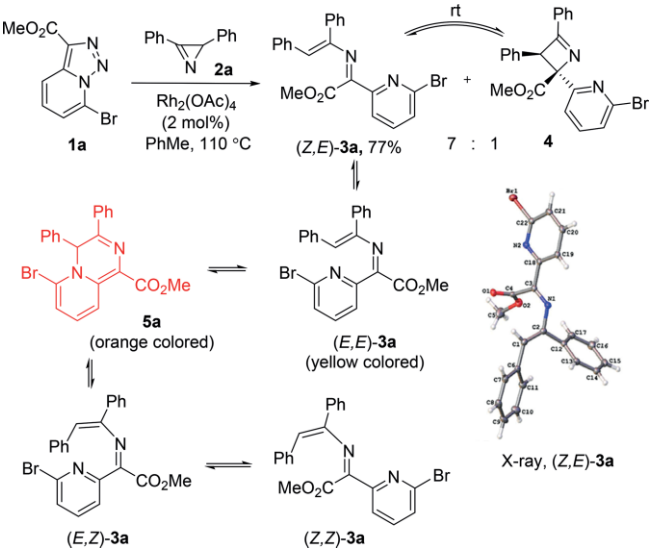
1,6-cyclizations of 1,3-diazatrienes[9] and 1,5-diazatrienes[10] (reactions 5 and 6) afford dihydropyrimidines. Conversely, several 1-(2-pyridyl)-2-azabuta-1,3-dienes are known,[11] but the dearomative cyclization of these compounds involving a pyridine ring was not mentioned anywhere in the literature. Thus, no thermodynamically favorable 1,6-electrocyclizations of aza- and diazahexatrienes accompanied by dearomatization[12] and formation of a stable non-aromatic product were published till now.

In this work, we were able to demonstrate that such processes indeed exist. We studied 1,6-electrocyclizations of 1-(2-pyridyl)-2-azabuta-1,3-dienes as representatives of 1,4-diazahexatrienes with the C=N bond incorporated in aromatic pyridine system. It was found that these cyclizations could afford stable 4*H*-pyrido[1,2-*a*]pyrazines despite the fact that the reaction proceeded with irreversible dearomatization of the pyridine aromatic system (Scheme 1, reaction 7). The factors affecting stability of the diazatriene and pyridopyrazine forms were identified, and a number of stable 4*H*-pyrido[1,2-*a*]pyrazines were isolated. These findings significantly expand the scope of the 1,6-electrocyclization in organic synthesis.



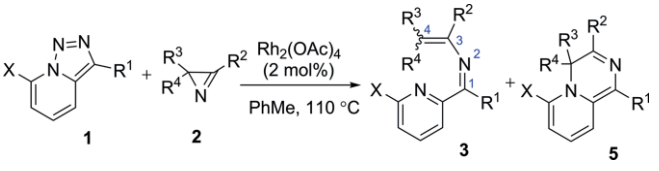
Scheme 2. The reaction of pyridotriazole **1a** with azirine **2a**.

Results and Discussion

In previous works, we have developed the convenient method for the synthesis of 2-azabutadienes via the reactions of 2*H*-azirines with Rh^{II} carbenoids derived from diazo compounds.[13] In order to synthesize 1-(2-pyridyl)-2-azabuta-1,3-dienes for our study, we exploited a similar approach in which pyridotriazoles[14] were used as precursors of carbenoids. The advantage of this approach is that it permits to prepare the desired 1-(2-pyridyl)-2-azabuta-1,3-dienes with a different substitution pattern in one synthetic operation. In our initial experiment, we performed the reaction of pyridotriazole **1a** with 2,3-diphenylazirine **2a** at 110 °C in the presence of $Rh_2(OAc)_4$ (2 mol-%) (Scheme 2). The products of the reaction were 1-(2-pyridyl)-2-azabutadiene (*Z*,*E*)-**3a** and 2,3-dihydroazete **4**, the product of 4π-electrocyclization[13c,13e,13g,13h] of (*Z*,*E*)-**3a** (the first stereodescriptor refers to the configuration of the C=N bond, the second one to the C=C bond). These products were separated by rapid column chromatography, but all attempts to record NMR spectra of analytically pure samples of these compounds failed because of their rather fast interconversion in solution at room temperature. In order to determine the configurations of the double bonds in (*Z*,*E*)-**3a**, we used X-ray diffraction analysis of the crystals obtained from the mixture of (*Z*,*E*)-**3a** and **4** by slow evaporation of their Et_2O solution (Scheme 2). Pure samples of compound (*Z*,*E*)-**3a** were obtained as yellow crystals using column chromatography followed by slow crystallization.

It was found that the solution of a mixture of azadiene (*Z*,*E*)-**3a** and dihydroazete **4** gradually turned orange upon keeping at room temperature in $CDCl_3$. A detailed analysis of the reaction mixture by ^1H NMR (two doublets of doublets at 6.75 and 6.86 ppm) and TLC (red-orange spot) led us to the conclusion about the presence of pyrido[1,2-*a*]pyrazine **5a** in the solution (Scheme 2). An attempt to increase the content of pyridopyrazine **5a** by keeping the above solution at room temperature for long period (14 days) led to an equilibrium mixture of azadiene (*Z*,*E*)-**3a**, pyridopyrazine **5a**, azadiene (*Z*,*Z*)-**3a**, and dihydroazete **4** in a 10.8:3:1:2.5 ratio. Heating at higher temperature (70 °C) for 36 h resulted in an equilibrium mixture of azadiene (*Z*,*E*)-**3a**, pyridopyrazine **5a**, and azadiene (*Z*,*Z*)-**3a** in a 1:4.4:6.5 ratio. This reaction mixture was subjected to chromatographic separation. However, both isolated products, pyridopyrazine **5a** and azadiene (*Z*,*Z*)-**3a**, were rapidly interconverted.

Encouraged by the formation of pyridopyrazine **5a**, we studied the influence of various substituents in pyridotriazoles **1** and azirines **2** on the reaction outcome (Scheme 3). The main goal was to find out which substituents shifted the equilibrium **3** ⇄ **5** toward pyridopyrazine **5**. The results obtained are summarized in Table 1.



Scheme 3. The reactions of pyridotriazoles **1** with azirines **2**.

The variation of substituents in azirines **2** showed that 2-methyl-substituted azirine **2b** gave pyridopyrazines **5b**–**d** as a major product (Table 1, entries 2–4). These reactions provided the equilibrium mixtures of 4-methyl-2-azabutadienes **3b**–**d** and 4-methylpyridopyrazines **5b**–**d**. However, the latter were stable in pure form at room temperature and did not isomerize to azadienes **3b**–**d** in solid state and solution. Pyridopyrazines **5b**–**d** were characterized by the data of NMR spectroscopy and HRMS. The structure of pyridopyrazine **5d** was confirmed by X-ray diffraction analysis (Figure 1).

The optimization of the reaction conditions for the preparation of pyridopyrazine **5c** [$Rh_2(OAc)_4$, $Rh_2(Piv)_4$, and $Rh_2(esp)_2$; toluene and 1,2-dichloroethane; 110 and 140 °C] did not allow to increase the yield of the product. In contrast, a noticeable decrease in yield was observed when using an excess of pyrido-

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Table 1. The results of the reactions of pyridotriazoles **1** with azirines **2**.[a]

Entry	Pyridotriazole	X	R^1	Azirine	R^2	R^3	R^4	Yield of **3** [%]	Yield of **5** [%]
1	**1a**	Br	CO_2Me	**2a**	Ph	Ph	H	77 [(*Z*,*E*)-**3a**]	–
2	**1a**	Br	CO_2Me	**2b**	Ph	Me	H	17 (**3b**)[b]	60 (**5b**)
3	**1b**	Cl	CO_2Me	**2b**	Ph	Me	H	15 (**3c**)[c]	60 (**5c**)
4	**1c**	MeO	CO_2Me	**2b**	Ph	Me	H	18 (**3d**)[d]	39 (**5d**)
5	**1b**	Cl	CO_2Me	**2c**	Ph	CH_2CO_2Me	H	63 (**3e**)[e]	15 (**5e**)
6	**1b**	Cl	CO_2Me	**2d**	4-$NO_2C_6H_4$	H	H	–	65 (**5f**)
7	**1d**	H	CN	**2b**	Ph	Me	H	–	31 (**5g**)
8	**1e**	H	CO_2Me	**2b**	Ph	Me	H	– (**3h**)	– (**5h**)
9	**1b**	Cl	CO_2Me	**2e**	Ph	Me	Me	77 (**3i**)	trace
10	**1a**	Br	CO_2Me	**2f**	Ph	CO_2Me	H	89 (**3j**)[f]	–
11[g]	**1f**	H	Ph	**2a**	Ph	Ph	H	26 (**3k**)	–
12	**1b**	Cl	CO_2Me	**2g**	Ph	(*E*)-CH=$CHCO_2Me$	H	61 [(*E*)-**3l**][h]	–

[a] Isolated yields. [b] A 1:1 mixture of (*Z*)- and (*E*)-isomers. [c] A 5:1 mixture of (*Z*)- and (*E*)-isomers. [d] A 2:1 mixture of (*Z*)- and (*E*)-isomers. [e] A 1.6:1 mixture of (*Z*)- and (*E*)-isomers. [f] A 1: 1.6 mixture of (*Z*)- and (*E*)-isomers. [g] $Rh_2(esp)_2$ (1 mol-%) was used as a catalyst at 140 °C. [h] Dimethyl 2-(6-chloropyridin-2-yl)-6-phenyl-1,2-dihydropyridine-2,3-dicarboxylate **6** (yield 17 %) was isolated as a by-product.

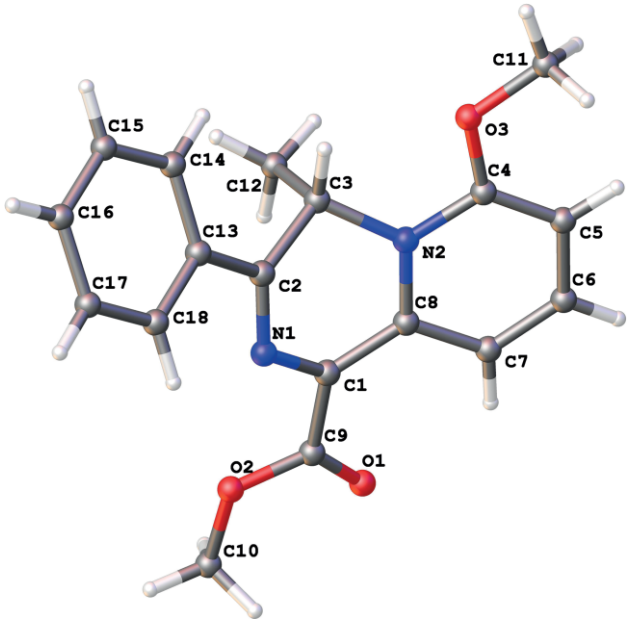

Figure 1. X-ray structure of 4*H*-pyrido[1,2-*a*]pyrazine **5d**.

triazole **1b** or 1 mol-% of $Rh_2(OAc)_4$ probably due to significantly increased reaction time.

The change of methyl to CH_2CO_2Me substituent at the C4 position of the 2-azabutadiene decreased the yield of pyridopyrazine (**5e**) (Table 1, entry 5). Like pyridopyrazines **5b**–**d**, compound **5e** was stable at room temperature.

We also performed the reaction of pyridotriazole **1b** with 3-(4-nitrophenyl)azirine **2d**. The product, pyrido[1,2-*a*]pyrazine **5f**, turned out to be quite stable and it was obtained in good yield (Table 1, entry 6).

In the reaction of azirine **2b** with pyridotriazole **1d** having the unsubstituted C7 position, the only product was pyrido-[1,2-*a*]pyrazine **5g** (Table 1, entry 7), the corresponding 2-azadiene was not observed in the reaction mixture. The low yield of the product **5g** is related to the low reactivity of pyridotriazole **1d**. For example, pyridotriazole **1d** and azirine **2b** were not fully consumed even in 4 h at 140 °C in toluene in the presence of 2 mol-% of $Rh_2(esp)_2$ or 5 mol-% of $Rh_2(OAc)_4$. Naturally, the long-term reaction at such high temperature resulted in the formation of by-products. A slow dropwise addition of pyridotriazole **1d** as well as the use of microwave irradiation did not increase the yield of pyridopyrazine **5g**. In view of recent publications,[14a,14f,14h–14j] we also tested copper(II) compounds [$Cu(acac)_2$, $Cu(tfacac)_2$, and $Cu(OTf)_2$] as catalysts. However, they were inactive, and pyridopyrazine **5g** in these reactions was not detected at all. Another C7-unsubstituted pyridotriazole **1e** gave complex mixture of unstable products (Table 1, entry 8). The introduction of two methyl groups at the C4 position of 2-azadiene (**3i**) only led to traces of the corresponding pyridopyrazine (Table 1, entry 9).

Finally, some reactions led to azadienes **3** which did not cyclize to pyrido[1,2-*a*]pyrazines **5** even under heating (Table 1, entries 10,11). These azadienes contain ester or phenyl substituents at the C1 and C4 positions of the azabutadiene fragment (R^1 and R^3). Under harsh conditions (*o*-xylene, 165 °C) azadiene (*E*)-**3j** slowly isomerized across the C=C bond to azadiene (*Z*)-**3j**, and no traces of the desired cyclization product were detected. 1-Phenyl-substituted 2-azadiene **3k** was obtained in low yield, which was due to an extremely low reactivity of pyridotriazole **1f**. This led to a low conversion of the starting compounds and the formation of unidentifiable by-products under long-term heating. For azadiene **3l**, the 6π-electrocyclization of the 2-azahexa-1,3,5-triene fragment to the 2,3-dihydropyridine derivative followed by tautomerization to 1,2-dihydropyridine **6** was more preferable than cyclization onto the pyridine ring (Table 1, entry 12).

An attempt to synthesize pyrido[1,2-*a*]pyrazine **5m** with benzoyl substituent at the C1 atom failed due to 2-azadiene **3m** underwent 1,6-cyclization onto the C=O bond to give 2*H*-1,4-oxazine **7** more readily than 1,6-cyclization onto the pyridine C=N bond (Scheme 4).

We also studied the reactions of azirine **2b** with triazoloquinoline **1h** and diazo compound **1i** bearing benzoxazole substituent (Scheme 5). The reaction of triazoloquinoline **1h** gave pyrazinoquinoline **5n** in 50 % yield. The moderate yield in this case was due to low conversion of triazoloquinoline **1h**. The reaction of diazo compound **1i** with azirine **2b**, to our delight, afforded benzo[4,5]oxazolo[3,2-*a*]pyrazine derivative **5o**. Unlike triazolo-

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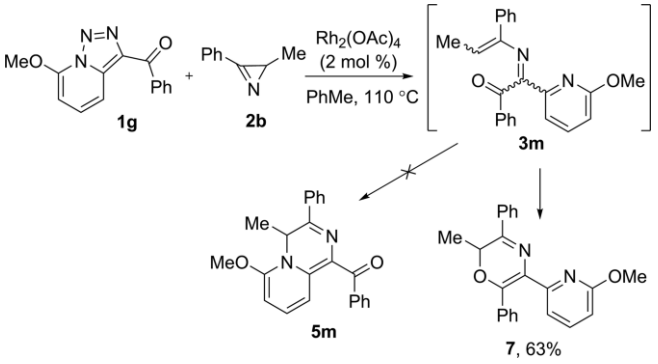
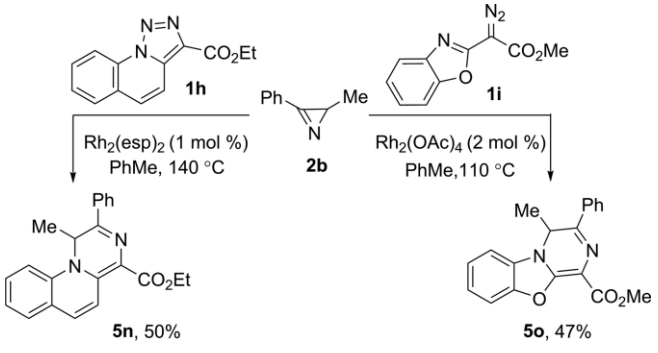


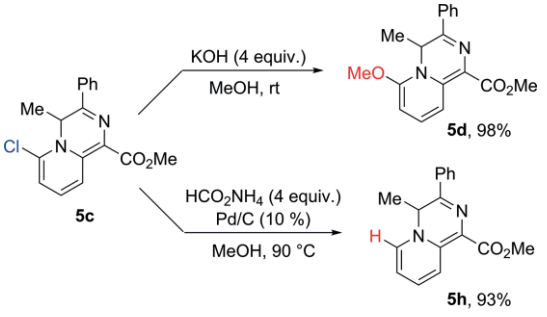
Scheme 4. The reaction of 3-benzoylpyridotriazole **1g** with azirine **2b**.

quinoline **1h**, diazo compound **1i** was quite active, but its reaction was accompanied by the formation of some quantities of by-products which decreased the yield of product **5o**. In both reactions, the formation of the corresponding azadienes was not observed.



Scheme 5. Synthesis of 1*H*-pyrazino[1,2-*a*]quinoline **5n** and 4*H*-benzo[4,5]oxazolo[3,2-*a*]pyrazine **5o**.

Since pyrido[1,2-*a*]pyrazines are known only either in fully hydrogenated[15] or 4-oxo-substituted form,[16] it was of interest to explore some chemical properties of novel 4*H*-pyrido[1,2-*a*]-pyrazines **5** obtained (Scheme 6). The halogen atom at the C6 position of pyridopyrazines **5** can be replaced by an alkoxy group that was demonstrated for 6-chloro-substituted pyridopyrazine **5c**. When treated with KOH in methanol solution, this compound quantitatively transformed to 6-methoxy-substituted pyridopyrazine **5d**. The reduction of pyridopyrazine **5c** by ammonium formate in the presence of Pd/C led to the removal of chlorine and formation of C6-unsubstituted pyridopyrazine **5h**. This reaction proved to be of particular interest to us in the light of unsuccessful experiments on the synthesis of pyridopyrazine **5h** directly from azirine **2b** and pyridotriazole **1e** (Table 1, entry 8). Unexpectedly, C6-unsubstituted pyridopyrazine **5h** turned out to be quite stable: it did not undergo ring opening into the corresponding pyridylazadiene even when heated.



Scheme 6. Modification of the C6 position of 6-chloropyridopyrazine **5c**.

The results obtained show that the nature of the C6-substituent in pyridopyrazines **5** is one of critical factors affecting the equilibrium **3** ⇄ **5**. The question arises whether this substituent affects only the equilibrium position or the cyclization rate as well. Another issue to be clarified is whether the isomerization of azadienes **3** around the C=N bond (N-inversion) affects the yield of pyridopyrazines **5**. To shed some light on these problems, the DFT calculations (wB97XD/cc-pvtz, PCM for toluene, 383K) of activation barriers for 1,6-electrocyclization and N-inversion of azadienes *E,Z*- and *E,E*-**3c**,**h** were performed (Figure 2, blue lines correspond to R = Cl (c), red lines to R = H (h)).

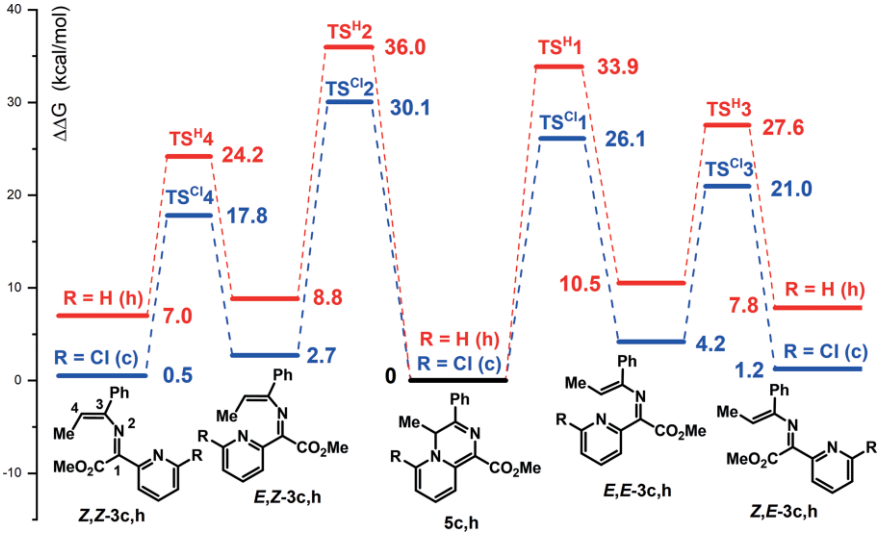


Figure 2. Energy diagram for 1,6-electrocyclization and *E*/*Z* isomerization of azadienes *E,Z*- and *E,E*-**3c**,**h** (wB97XD/cc-pvtz, PCM for toluene, 383K).

An analysis of the structures of the transition states for the 1,6-electrocyclizations (TS^H1, TS^H2, $TS^{Cl}1$, and $TS^{Cl}2$) revealed that these transformations are pseudopericyclic reactions.[17,18] The fact that the π-orbital of the pyridine C=N bond is not involved in bonding follows from the small deviation of the dihedral angle ∠C4–N5–C6–C7 from 180°. The dihedral angle values for all the transition states are in the range of 164.4–175.7° (Figure 3, TS^H1 and TS^H2).

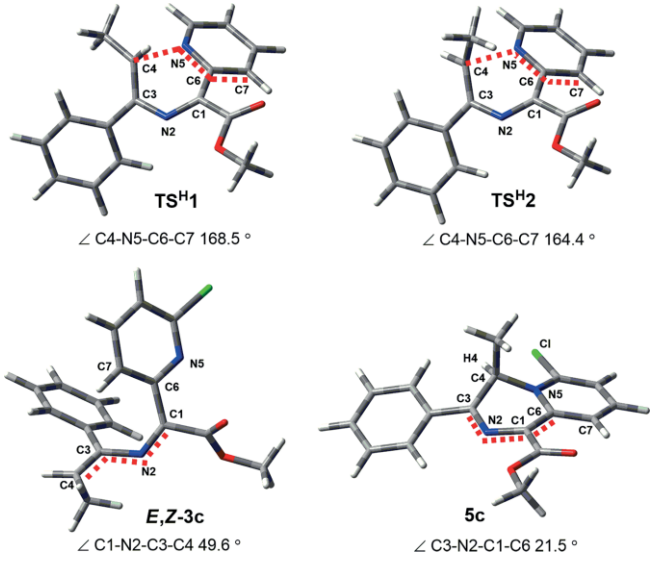


Figure 3. The calculated structures of TS^H1, TS^H2, *E,Z*-**3c**, and **5c**.

According to the calculations (Figure 2), the activation barriers for the cyclizations of *E,E*-**3c** and *E,E*-**3h** to the corresponding pyridopyrazines ($TS^{Cl}1$ and TS^H1) are close in value (21.9 and 23.4 kcal/mol). Both these barriers are lower than that for the cyclizations of *E,Z*-**3c** and *E,Z*-**3h** (27.4 and 27.2 kcal/mol). The configuration of the C=C bond in compounds **3**, thus, has greater effect on the cyclization to **5** than the nature of a substituent in the α-position of the pyridine ring. The activation barriers for N-inversions in azadienes **3c** ($TS^{Cl}3$ and $TS^{Cl}4$) and **3h** (TS^H3 and TS^H4) are lower than the barriers for their cyclization to **5** by 4.9–12.3 kcal/mol (Figure 2). From this it follows that the equilibrium between the N-invertomers, *E,E*⇄*Z,E* and *E,Z*⇄*Z,Z*, is rapidly attained already at room temperature, and, therefore, these isomerizations should not affect the formation of pyridopyrazines **5**.

The relative energies of chlorinated pyridopyrazine **5c** and four isomers of **3c** are close to each other (Figure 2). Compound **5c** and the most stable azadienes, *Z,Z*-**3c** and *Z,E*-**3c**, thus, can be in equilibrium at elevated temperatures. Such equilibrium was indeed observed experimentally (Table 1, entry 3). In contrast, non-chlorinated pyridopyrazine **5h** is much more stable than azadienes **3h**. This fact, along with rather high barriers for the ring opening of pyridopyrazine **5h** (33.9 and 36.0 kcal/mol), makes the 1,6-cyclizations of azadienes *E,Z*- and *E,E*-**3h** into **5h** irreversible. The destabilization of the cyclic form and a decrease in the barrier for the ring opening, caused by the introduction of a chlorine atom in the α-position of the pyridine ring, can be explained by the steric repulsion between the H4 atom and the chlorine atom. According to the calculation for **5c**, the distance between the H4 and Cl atoms is just 0.244 nm (Figure 3, compound **5c**).

As can be seen in Table 1 and Scheme 2, the position of the equilibrium **3**⇄**5** is also affected by the nature of the substituent at C4 of the pyridopyrazine (**5a**). The introduction of a phenyl substituent at the C4 position shifts the equilibrium toward azadiene **3a** and increases the rate of the isomerization, which occurs even at room temperature (Scheme 2). All this can be rationalized in terms of the energetically favorable conjugation of the aromatic substituent with the π-system of the azadiene. Probably for the same reason, pyridopyrazines **5** were not observed in some other reactions (Table 1, entries 10–12).

In order to clarify the reasons for the thermodynamic stability of 4-methyl-substituted pyridopyrazines **5** relative to the corresponding azadienes **3**, we used the data of X-ray diffraction for compounds (*Z,E*)-**3a** and **5d** and the quantum chemical calculations. According to these data, there is a weak conjugation of unsaturated fragments in 2-azadienes **3**. For example, the values of the dihedral angle $\angle C^1–N^2–C^3–C^4$ (Figure 3, compound *E,Z*-**3c**) in the calculated optimized geometries of isomers **3c,h** are in the range of 39.2–58.8°. According to X-ray diffraction analysis, the same angle in azadiene (*Z,E*)-**3a** is 61.1°. In contrast, all pyridopyrazines **5** contain nearly flat conjugated 8-amino-1-azaoctatetraene system (Figure 1 and Figure 3, compound **5c**) with the C1- and C3-substituents being in the effective conjugation with the pyridopyrazine π-system. Thus, the extended conjugated system of non-aromatic pyridopyrazine **5** is more beneficial than weakly conjugated 2-azadiene **3** containing an aromatic pyridine substituent.

Due to the extended conjugated system, compounds **5** are colored. Their color varies from yellow (for **5o**) to purple (for **5f**). We recorded the absorption spectra of compounds **5**, which are presented in Figure 4. For pyridopyrazines obtained, the intensive absorption band lies in the visible region: for most compounds long wave maximum is in the range of 464–488 nm. The exceptions are pyridopyrazine **5f** (λ_{max} = 530 nm) containing a nitro group in aryl substituent and benzoxazolopyrazine **5o** (λ_{max} = 401 nm). The maximum extinction coefficients

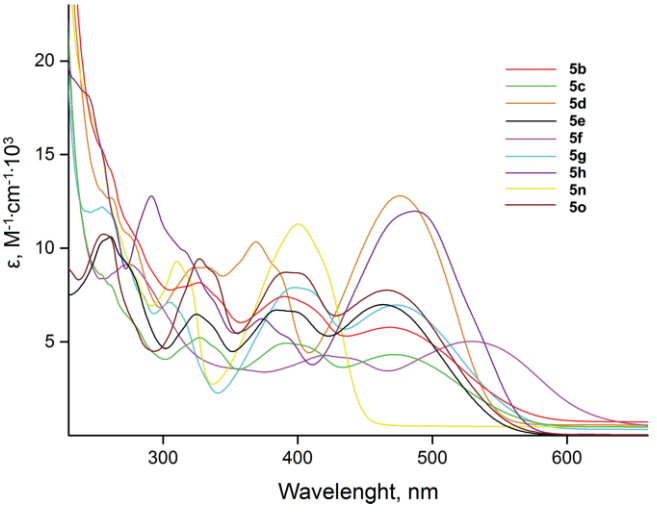


Figure 4. Absorption spectra of compounds **5b**–**h**,**n**,**o**.

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(ε = 11300–12800 $mol^{-1}\,cm^{-1}$) were observed for pyridopyrazine **5d** bearing an electron-donating methoxy group, as well as for compounds **5n**,**o**, possessing additional fused benzene ring.

Conclusion

1-(2-Pyridyl)-2-azabuta-1,3-dienes were synthesized by Rh^{II}-catalyzed reaction of pyridotriazoles with 2*H*-azirines, and their pseudopericyclic 1,6-cyclization involving dearomatization of a pyridine ring was studied. The 2-azadienes containing H, alkyl, or Ph at the C4 atom and an electron-withdrawing substituent at the C1 atom were able to undergo 1,6-electrocyclization to 4*H*-pyrido[1,2-*a*]pyrazine derivatives. A number of stable 4*H*-pyrido[1,2-*a*]pyrazines mainly containing methyl group at the C4 atom were synthesized. Whereas 4-alkyl-substituted pyridopyrazines are stable at room temperature, 4-phenyl-substituted pyridopyrazines exist in ring–chain valence equilibrium with the corresponding 2-azadienes. Thermodynamic stability of the 4*H*-pyrido[1,2-*a*]pyrazine decreases with increasing the steric volume of a substituent at the C6 atom. The 1,6-cyclization was also expanded to the synthesis of 1*H*-pyrazino[1,2-*a*]quinoline and 4*H*-benzo[4,5]oxazolo[3,2-*a*]pyrazine derivatives. The 2-azadienes containing phenyl or ester groups at both the C1 and the C4 positions did not cyclize to the pyridopyrazines.

Experimental Section

General Information

Melting points were determined on a melting point apparatus SMP30. ^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded on a Bruker AVANCE 400 spectrometer in $CDCl_3$. Chemical shifts (δ) are reported in parts per million downfield from tetramethylsilane. Electrospray ionization (ESI) mass spectra were recorded on a Bruker MaXis mass spectrometer. UV/Vis spectra were recorded on a Shimadzu UV-1800 spectrometer in 1,2-dichloroethane (DCE). Single crystal X-ray data for (*Z*,*E*)-**3a** and **5d** were collected by means of a SuperNova, Single source at offset/far, HyPix3000 diffractometer at 100 K using monochromated Cu-K_α radiation. Thin-layer chromatography (TLC) was conducted on aluminum sheets precoated with SiO_2 ALUGRAM SIL G/UV254. Column chromatography was performed on Macherey-Nagel silica gel 60 M (0.04–0.063 mm). Toluene was distilled and stored over sodium metal. 1,2-Dichloroethane and dichloromethane were washed with concentrated H_2SO_4 and water, distilled from P_2O_5, and stored over anhydrous K_2CO_3. Pyridotriazole **1f** was prepared by the reported procedure.[14b] Azirines **2a**,[19] **2b**,[20] **2c**,[21] **2d**,[22] **2e**,[23] **2f**,[24] and **2g**[25] were prepared by the reported procedures.

CCDC 1844058 [for (*Z*,*E*)-**3a**], and 1980147 (for **5d**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

2-(6-Methoxypyridin-2-yl)-1-phenylethanone: This compound (0.90 g, yield 40 %) was obtained according to the literature procedure.[26] Yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ: [*keto form*] 3.88 (s, 3H), 4.39 (s, 2H), 6.62 (d, *J* = 8.3 Hz, 1H), 6.89 (d, *J* = 7.2 Hz, 1H), 7.38–7.44 (m, 2H), 7.48 (t, *J* = 7.6 Hz, 2H), 8.11–8.13 (m, 2H); [*enol form*] 4.05 (s, 3H), 6.09 (s, 1H), 6.55 (d, *J* = 8.2 Hz, 1H), 6.72 (d, *J* = 7.5 Hz, 1H), 7.51–7.53 (m, 1H), 7.55–7.59 (m, 3H), 7.83–7.85 (m, 2H), 14.08 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (both forms): 48.1, 53.2, 53.5, 95.7, 106.4, 108.6, 114.0, 116.5, 125.2, 128.3, 128.4, 128.9, 129.1, 133.0, 135.8, 136.7, 138.9, 139.6, 152.7, 155.9, 160.4, 161.8, 163.7, 197.0. HRMS (ESI): calcd. for $C_{14}H_{13}NNaO_2^+$, $[M + Na]^+$: 250.0838, found 250.0836.

General Procedure for the Synthesis of Pyridotriazoles 1a–e,g–i: To a dichloromethane (DCM) solution (10 mL) of the corresponding (2-pyridyl)acetate (1 equiv.) and TsN_3 (1.1 equiv.) a solution of 1,8-diazabicyclo[5.4.0]undec-7-ene (1.1 equiv.) in DCM (5 mL) was added dropwise at 0 °C. The mixture was stirred at room temperature until consumption of the (2-pyridyl)acetate, and the reaction mixture was poured into saturated NH_4Cl solution. The water layer was extracted with DCM, combined organic layers were washed with water, brine and dried with Na_2SO_4. The DCM was evaporated in vacuo, and the residue was purified by column chromatography on silica gel.

Methyl 7-Bromo-[1,2,3]triazolo[1,5-*a*]pyridine-3-carboxylate (1a):[14k] Compound **1a** (322 mg, yield 34 %) was obtained according to the general procedure. Colorless solid, m.p. 149–150 °C (decomp.). ^1H NMR (400 MHz, $CDCl_3$) δ: 4.06 (s, 3H), 7.41 (br s, 1H), 7.47 (t, *J* = 8.0 Hz, 1H), 8.31 (br s, 1H).

Methyl 7-Chloro-[1,2,3]triazolo[1,5-*a*]pyridine-3-carboxylate (1b):[14b] Compound **1b** (624 mg, yield 85 %) was obtained according to the general procedure. Beige solid, m.p. 143–145 °C (lit.[14c] 147 °C). ^1H NMR (400 MHz, $CDCl_3$) δ: 4.05 (s, 3H), 7.23 (br s, 1H), 7.55 (t, *J* = 8.0 Hz, 1H), 8.27 (br s, 1H).

Methyl 7-Methoxy-[1,2,3]triazolo[1,5-*a*]pyridine-3-carboxylate (1c): Compound **1c** (127 mg, yield 80 %) was obtained according to the general procedure. Colorless solid, 138–139 °C (decomp.). ^1H NMR (400 MHz, $CDCl_3$, 233K) δ: 4.03 (s, 3H), 4.26 (s, 3H), 6.48 (d, *J* = 7.5 Hz, 1H), 7.61 (t, *J* = 8.1 Hz, 1H), 7.87 (d, *J* = 8.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, 233K) δ = 52.3, 57.3, 92.9, 110.1, 128.7, 131.9, 136.2, 149.3, 161.8. HRMS (ESI): calcd. for $C_9H_9N_3NaO_3^+$, $[M + Na]^+$: 230.0536, found 230.0543.

[1,2,3]Triazolo[1,5-*a*]pyridine-3-carbonitrile (1d):[27] Compound **1d** (1.42 g, yield 94 %) was obtained according to the general procedure. Colorless solid, m.p. 143–145 °C (lit.[27] 146 °C). ^1H NMR (400 MHz, $CDCl_3$) δ: 7.28 (td, *J* = 6.9, 1.1 Hz, 1H), 7.67 (ddd, *J* = 8.9, 6.9, 1.0 Hz, 1H), 7.96 (dt, *J* = 8.9, 1.1 Hz, 1H), 8.91 (dt, *J* = 6.9, 1.0 Hz, 1H).

Methyl [1,2,3]Triazolo[1,5-*a*]pyridine-3-carboxylate (1e):[14k] Compound **1e** (1.01 g, yield 80 %) was obtained according to the general procedure. Colorless solid, m.p. 139–141 °C (lit.[14c] 140–141 °C). ^1H NMR (400 MHz, $CDCl_3$) δ: 4.05 (s, 3H), 7.18 (td, *J* = 6.9, 1.2 Hz, 1H), 7.57 (ddd, *J* = 8.9, 6.9, 0.9 Hz, 1H), 8.29 (dt, *J* = 8.9, 1.2 Hz, 1H), 8.85 (dt, *J* = 6.9, 0.9 Hz, 1H).

(7-Methoxy-[1,2,3]triazolo[1,5-*a*]pyridin-3-yl)(phenyl)methanone (1g): Compound **1g** (784 mg, yield 84 %) was obtained according to the general procedure. Colorless solid, m.p. 135–137 °C (decomp.). ^1H NMR (400 MHz, $CDCl_3$) δ: 4.24 (s, 3H), 6.51 (d, *J* = 7.6 Hz, 1H), 7.54–7.58 (m, 2H), 7.61–7.67 (m, 2H), 8.17–8.19 (m, 2H), 8.41 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$/$[D_6]$DMSO, 233K) δ = 57.1, 93.7, 111.1, 128.1, 130.0, 132.6, 132.8, 136.3, 136.8, 136.9, 149.2, 186.4. HRMS (ESI): calcd. for $C_{14}H_{11}N_3NaO_2^+$, $[M + Na]^+$: 276.0743, found 276.0753.

Ethyl [1,2,3]Triazolo[1,5-*a*]quinoline-3-carboxylate (1h): Compound **1h** (185 mg, yield 47 %) was obtained according to the general procedure. Pale-yellow solid, m.p. 168–169 °C. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.53 (t, *J* = 7.1 Hz, 3H), 4.57 (q, *J* = 7.1 Hz, 2H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.82 (d, *J* = 9.3 Hz, 1H), 7.86 (t, *J* = 7.9 Hz,

1H), 7.95 (d, *J* = 8.0 Hz, 1H), 8.12 (d, *J* = 9.3 Hz, 1H), 8.89 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.4, 61.2, 115.5, 116.5, 123.9, 127.7, 128.6, 130.2, 130.8, 131.3, 131.5, 133.5, 161.5. HRMS (ESI): calcd. for $C_{13}H_{11}N_3NaO_2^+$, $[M + Na]^+$: 264.0743, found 264.0747.

Methyl 2-(Benzo[*d*]oxazol-2-yl)-2-diazoacetate (1i):[28] Compound **1i** (160 mg, yield 88 %) was obtained according to the general procedure. Yellow solid, m.p. 126–127 °C (lit.[28] 127–128 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.99 (s, 3H), 7.28–7.36 (m, 2H), 7.54–7.56 (m, 1H), 7.68–7.70 (m, 1H).

General Procedure for the Reaction of Pyridotriazoles 1 with Azirines 2: 2*H*-azirine **2** (1 equiv.), pyridotriazole **1** or diazo compound **1i** (0.6–1.5 equiv.), rhodium carboxylate (1–5 mol-% on azirine), and dry toluene (0.5 mL) were placed into a screw-cap glass tube and heated at 110 °C or 140 °C (oil bath temperature) whilst stirring until gas evolution had ceased. The solvent was evaporated in vacuo, and the residue was purified by column chromatography on silica gel.

(*Z*)-Methyl 2-(6-Bromopyridin-2-yl)-2-{[(*E*)-1,2-diphenylvinyl]-imino}acetate [(*Z*,*E*)-3a] and (2*RS*,3*SR*)-Methyl 2-(6-Bromopyridin-2-yl)-3,4-diphenyl-2,3-dihydroazete-2-carboxylate (4): Azadiene (*Z*,*E*)-**3a** (230 mg, yield 77 %) and dihydroazete **4** (27 mg, yield 9 %) were obtained according to the general procedure from pyridotriazole **1a** (200 mg, 0.78 mmol) and azirine **2a** (137 mg, 0.7 mmol) [110 °C, 1 min, $Rh_2(OAc)_4$ (2 mol-%, 6.2 mg), eluent for chromatography EtOAc/hexane, 1:5]. Just after isolation both compounds were identified by TLC as pure but due to rapid interconvertion in solution their NMR spectra contained signals of both compounds. Pure (*Z*,*E*)-**3a** in crystal form was obtained by slow evaporation of the Et_2O solution of (*Z*,*E*)-**3a** and **4** mixture.

Compound (*Z*,*E*)-3a: Orange solid, m.p. 106–109 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.87 (s, 3H), 6.25 (s, 1H), 7.07–7.08 (m, 2H), 7.16–7.17 (m, 2H), 7.33–7.35 (m, 4H), 7.40–7.42 (m, 2H), 7.58 (d, *J* = 7.9 Hz, 1H), 7.66 (t, *J* = 7.9 Hz, 1H), 8.14 (d, *J* = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 52.1, 115.6, 120.9, 126.9, 128.1, 128.5, 128.5, 129.3, 129.5, 130.0, 135.5, 135.7, 138.8, 141.3, 149.6, 154.0, 157.1, 164.7. HRMS (ESI): calcd. for $C_{22}H_{18}{}^{79}BrN_2O_2^+$, $[M + H]^+$: 421.0547, found 421.0545.

Compound 4: Pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (identified signals): 3.28 (s, 3H), 5.77 (s, 1H), 7.80 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (identified signals): 56.9, 121.5, 126.8, 128.7, 128.9, 132.3, 188.6.

(*Z*)-Methyl 2-(6-Bromopyridin-2-yl)-2-{[(*Z*)-1,2-diphenylvinyl]-imino}acetate [(*Z*,*Z*)-3a] and Methyl 6-Bromo-3,4-diphenyl-4*H*-pyrido[1,2-*a*]pyrazine-1-carboxylate (5a): Azadiene (*Z*,*Z*)-**3a** (35 mg, yield 35 %) and pyridopyrazine **5a** (52 mg, yield 52 %) were obtained by heating solution of azadiene (*Z*,*E*)-**3a** (100 mg) in $CDCl_3$ (0.5 mL) in a sealed tube at 70 °C for 36 h followed by rapid column chromatography (eluent EtOAc/hexane, 1:4).

Compound (*Z*,*Z*)-3a: Orange solid. This compound is rapidly transformed to **5a**. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.48 (s, 3H), 6.43 (s, 1H), 7.19 (t, *J* = 7.3 Hz, 1H), 7.29–7.31 (m, 2H), 7.36–7.41 (m, 5H), 7.49 (d, *J* = 7.0 Hz, 2H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 8.33 (d, *J* = 7.6 Hz, 1H).

Compound 5a: Red solid. This compound is rapidly transformed to (*Z*,*Z*)-**3a**. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.86 (s, 3H), 6.75 (dd, *J* = 6.9, 1.0 Hz, 1H), 6.86 (dd, *J* = 9.4, 6.9 Hz, 1H), 7.16–7.18 (m, 2H), 7.22–7.27 (m, 3H), 7.36 (s, 1H), 7.39–7.42 (m, 1H), 7.46 (t, *J* = 7.4 Hz, 2H), 8.00 (d, *J* = 7.3 Hz, 2H), 8.41 (d, *J* = 9.3 Hz, 1H).

Mixture of (*Z*,*Z*)-3a and 5a: ^{13}C NMR (100 MHz, $CDCl_3$) δ: 51.4 (**5a**), 51.8, 57.0 (**5a**), 113.3 (**5a**), 115.0, 117.5 (**5a**), 120.6, 125.3 (**5a**), 126.5 (**5a**), 126.6 (**5a**), 126.65, 126.69 (**5a**), 128.1, 128.2, 128.27, 128.33, 128.65 (**5a**), 128.74 (**5a**), 128.8 (**5a**), 129.2 (**5a**), 129.4, 130.4, 131.6 (**5a**), 134.8 (**5a**), 136.0, 136.9 (**5a**), 137.5 (**5a**), 137.7, 139.0, 140.4 (**5a**), 141.5, 146.3, 153.6, 160.4, 163.9, 165.7 (**5a**). HRMS (ESI): calcd. for $C_{22}H_{17}{}^{79}BrN_2NaO_2^+$, $[M + Na]^+$: 443.0366, found 443.0360.

Methyl 2-(6-Bromopyridin-2-yl)-2-[(1-phenylprop-1-en-1-yl)-imino]acetate (3b) and Methyl 6-Bromo-4-methyl-3-phenyl-4*H*-pyrido[1,2-*a*]pyrazine-1-carboxylate (5b): Azadiene **3b** (5 mg, yield 17 %) and pyridopyrazine **5b** (17 mg, yield 60 %) were obtained according to the general procedure from pyridotriazole **1a** (24 mg, 0.09 mmol) and azirine **2b** (16 mg, 0.08 mmol) [110 °C, 30 min, $Rh_2(OAc)_4$ (2 mol-%, 0.7 mg), eluent for chromatography EtOAc/hexane, 1:6].

Compound 3b: (mixture of *Z* and *E* isomers in 1:1 ratio). Unstable yellow oil which is rapidly transformed to **5b**. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.71 (d, *J* = 7.1 Hz, 3H, *Z*), 1.79 (d, *J* = 7.2 Hz, 3H, *E*), 3.73 (s, 3H, *Z*), 3.82 (s, 3H, *E*), 5.44 (q, *J* = 7.2 Hz, 1H, *E*), 5.52 (q, *J* = 7.1 Hz, 1H, *Z*), 7.30–7.34 (m, 3H), 7.38–7.45 (m, 7H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.62 (t, *J* = 7.7 Hz, 2H), 7.70 (t, *J* = 7.8 Hz, 1H), 8.10 (d, *J* = 7.6 Hz, 1H, *E*), 8.26 (d, *J* = 7.0 Hz, 1H, *Z*).

Compound 5b: Red solid, m.p. 97–98 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.22 (d, *J* = 6.8 Hz, 3H), 3.91 (s, 3H), 6.32 (q, *J* = 6.7 Hz, 1H), 6.67 (d, *J* = 6.9 Hz, 1H), 6.85 (dd, *J* = 9.3, 7.0 Hz, 1H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.44 (t, *J* = 7.4 Hz, 2H), 7.92 (d, *J* = 7.4 Hz, 2H), 8.45 (d, *J* = 9.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.0, 51.4, 52.2, 111.0, 117.7, 120.3, 125.2, 126.0, 128.8, 129.1, 132.2, 135.8, 139.0, 140.4, 166.1. HRMS (ESI): calcd. for $C_{17}H_{16}{}^{79}BrN_2O_2^+$, $[M + H]^+$: 359.0390, found 359.0402. λ_{max} (DCE, ε): 390 (7400), 470 (5800).

Methyl 2-(6-Chloropyridin-2-yl)-2-[(1-phenylprop-1-en-1-yl)-imino]acetate (3c) and Methyl 6-Chloro-4-methyl-3-phenyl-4*H*-pyrido[1,2-*a*]pyrazine-1-carboxylate (5c): Azadiene **3c** (13 mg, yield 15 %) and pyridopyrazine **5c** (52 mg, yield 60 %) were obtained according to the general procedure from pyridotriazole **1b** (55 mg, 0.25 mmol) and azirine **2b** (33 mg, 0.25 mmol) [110 °C, 30 min, $Rh_2(OAc)_4$ (2 mol-%, 2.2 mg), eluent for chromatography EtOAc/hexane, 1:6].

Compound 3c: (mixture of *Z* and *E* isomers in 5:1 ratio). Unstable yellow oil which is rapidly transformed to **5c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.72 (d, *J* = 7.1 Hz, 15H, *Z*), 1.79 (d, *J* = 7.2 Hz, 3H, *E*), 3.74 (s, 15H, *Z*), 3.83 (s, 3H, *E*), 5.44 (q, *J* = 7.2 Hz, 1H, *E*), 5.52 (q, *J* = 7.1 Hz, 5H, *Z*), 7.29–7.34 (m, 13H), 7.38–7.41 (m, 16H), 7.44–7.48 (m, 7H), 7.73 (t, *J* = 7.8 Hz, 1H, *E*), 7.81 (t, *J* = 7.8 Hz, 5H, *Z*), 8.07 (d, *J* = 7.7 Hz, 1H, *E*), 8.24 (d, *J* = 7.1 Hz, 5H, *Z*).

Compound 5c: Red solid, m.p. 121–123 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.23 (d, *J* = 6.8 Hz, 3H), 3.90 (s, 3H), 6.31 (q, *J* = 6.7 Hz, 1H), 6.47 (dd, *J* = 7.0, 1.1 Hz, 1H), 6.94 (dd, *J* = 9.4, 7.0 Hz, 1H), 7.36 (m, 1H), 7.43 (m, 2H), 7.91 (m, 2H), 8.40 (dd, *J* = 9.4, 0.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.1, 48.9, 51.3, 110.6, 113.0, 119.6, 125.9, 128.7, 129.0, 132.0, 134.9, 135.7, 138.5, 140.1, 166.2. HRMS (ESI): calcd. for $C_{17}H_{16}{}^{35}ClN_2O_2^+$, $[M + H]^+$: 315.0895, found 315.0910. λ_{max} (DCE, ε): 327 (5200), 472 (4300).

Methyl 2-(6-Methoxypyridin-2-yl)-2-[(1-phenylprop-1-en-1-yl)-imino]acetate (3d) and Methyl 6-Methoxy-4-methyl-3-phenyl-4*H*-pyrido[1,2-*a*]pyrazine-1-carboxylate (5d): Azadiene **3d** (17 mg, yield 18 %) and pyridopyrazine **5d** (37 mg, yield 39 %) were obtained according to the general procedure from pyridotriazole **1c** (63 mg, 0.3 mmol) and azirine **2b** (40 mg, 0.3 mmol) [110 °C, 30 min, $Rh_2(OAc)_4$ (2 mol-%, 2.7 mg), eluent for chromatography EtOAc/hexane, 1:4]. Pyridopyrazine **5d** was also obtained in 98 % yield by stirring pyridopyrazine **5c** in saturated solution of potas-

sium hydroxide (4 equiv.) in methanol at room temperature for 24 h followed by chromatographic purification on silica gel.

Compound 3d: (mixture of *Z* and *E* isomers in 1.9:1 ratio). Unstable yellow oil which is rapidly transformed to **5d**. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.72 (d, *J* = 7.1 Hz, 5.7H, *Z*), 1.79 (d, *J* = 7.2 Hz, 3H, *E*), 3.73 (s, 3.7H, *Z*), 3.81 (s, 3H, *E*), 3.91 (s, 3H, *E*), 3.92 (s, 5.7H, *Z*), 5.42 (q, *J* = 7.2 Hz, 1H, *E*), 5.52 (q, *J* = 7.0 Hz, 1.9H, *Z*), 6.82 (d, *J* = 8.1 Hz, 1H, *E*), 6.89 (d, *J* = 8.2 Hz, 1.9H, *Z*), 7.31–7.46 (m, 16H), 7.63–7.67 (m, 1H, *E*), 7.71–7.77 (m, 3H), 7.93 (d, *J* = 7.3 Hz, 1H, *Z*).

Compound 5d: Orange solid, m.p. 175–177 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.20 (d, *J* = 6.7 Hz, 3H), 3.89 (s, 3H), 3.96 (s, 3H), 5.78 (dd, *J* = 7.5, 0.9 Hz, 1H), 6.23 (q, *J* = 6.7 Hz, 1H), 7.11 (dd, *J* = 9.3, 7.5 Hz, 1H), 7.29–7.34 (m, 1H), 7.37–7.42 (m, 2H), 7.88–7.91 (m, 2H), 8.09 (dd, *J* = 9.3, 0.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.7, 44.3, 51.1, 56.7, 89.6, 108.0, 112.4, 125.6, 128.3, 128.5, 134.6, 136.3, 137.3, 139.8, 154.6, 166.5. HRMS (ESI) [M + H]$^+$: calcd. for $C_{18}H_{19}N_2O_3^+$, 311.1391, found 311.1398. λ_{max} (DCE, ε): 369 (10300), 476 (12800).

Methyl 4-{[1-(6-Chloropyridin-2-yl)-2-methoxy-2-oxoethylidene]amino}but-3-enoate (3e) and Methyl 6-Chloro-4-(2-methoxy-2-oxoethyl)-3-phenyl-4*H*-pyrido[1,2-*a*]pyrazine-1-carboxylate (5e): Azadiene **3e** (114 mg, yield 63 %) and pyridopyrazine **5e** (28 mg, yield 15 %) were obtained according to the general procedure from pyridotriazole **1b** (116 mg, 0.55 mmol) and azirine **2c** (89 mg, 0.5 mmol) [110 °C, 15 min, $Rh_2(OAc)_4$ (2 mol-%, 4.4 mg), eluent for chromatography EtOAc/hexane, 1:5].

Compound 3e: (mixture of *Z* and *E* isomers in 1:1.6 ratio). Unstable orange oil which is rapidly transformed to **5e**. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.16–3.20 (m, 5.2H), 3.71–3.73 (m, 11H), 3.92 (s, 5H, *E*), 5.41 (t, *J* = 7.7 Hz, 1.6H, *E*), 5.68 (t, *J* = 7.1 Hz, 1H, *Z*), 7.32–7.48 (m, 16H), 7.74 (t, *J* = 7.8 Hz, 1.6H, *E*), 7.82 (t, *J* = 7.8 Hz, 1H, *Z*), 8.07 (d, *J* = 7.7 Hz, 1.6H, *E*), 8.21 (d, *J* = 7.7 Hz, 1H, *Z*). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 32.8 (*Z*), 33.7 (*E*), 51.8 (*Z*), 51.9 (*E*), 52.0 (*E*), 52.1 (*Z*), 104.6 (*Z*), 106.9 (*E*), 120.3 (*Z*), 120.4 (*E*), 125.9 (*E*), 126.2 (*E*), 126.7 (*Z*), 128.3 (2C, *Z*), 128.4 (*E*), 128.5 (*Z*), 128.7 (*E*), 134.7 (*E*), 136.0 (*Z*), 139.1 (*E*), 139.3 (*Z*), 148.2 (*Z*), 150.8 (*E*), 151.0 (*Z*), 151.5 (*E*), 152.7 (*Z*), 153.4 (*E*), 157.2 (*E*), 160.5 (*Z*), 164.3 (*Z*), 164.5 (*E*), 171.8 (*E*), 171.9 (*Z*).

Compound 5e: Red solid, m.p. 132–134 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.33 (dd, *J* = 15.6, 4.0 Hz, 1H), 2.83 (dd, *J* = 15.6, 9.7 Hz, 1H), 3.60 (s, 3H), 3.93 (s, 3H), 6.55 (dd, *J* = 6.9, 1.1 Hz, 1H), 6.73 (dd, *J* = 9.7, 4.0 Hz, 1H), 6.99 (dd, *J* = 9.4, 7.0 Hz, 1H), 7.37–7.42 (m, 1H), 7.46 (t, *J* = 7.4 Hz, 2H), 7.94–7.99 (m, 2H), 8.39–8.44 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 29.8, 48.8, 51.5, 52.0, 112.5, 113.1, 119.6, 126.3, 128.6, 129.3, 131.6, 134.9, 135.2, 135.8, 139.4, 165.7, 169.9. HRMS (ESI): calcd. for $C_{19}H_{18}{}^{35}ClN_2O_4$, [M + H]$^+$: 373.0950, found 373.0939. λ_{max} (DCE, ε): 464 (7000).

Methyl 6-Chloro-3-(4-nitrophenyl)-4*H*-pyrido[1,2-*a*]pyrazine-1-carboxylate (5f): Pyridopyrazine **5f** (56 mg, yield 65 %) was obtained according to the general procedure from pyridotriazole **1b** (43 mg, 0.2 mmol) and azirine **2d** (40 mg, 0.25 mmol) [110 °C, 5 min, $Rh_2(OAc)_4$ (1 mol-%, 0.9 mg), eluent for chromatography EtOAc/hexane, 1:4]. Purple solid, m.p. 156–158 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.89 (s, 3H), 4.84 (s, 2H), 6.65 (d, *J* = 7.0 Hz, 1H), 7.10 (dd, *J* = 9.2, 7.2 Hz, 1H), 8.02 (d, *J* = 8.7 Hz, 2H), 8.23 (d, *J* = 8.7 Hz, 2H), 8.31 (d, *J* = 9.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 44.2, 51.4, 113.7, 114.2, 119.2, 124.0, 126.5, 129.2, 133.4, 135.0, 141.7, 142.6, 147.1, 165.5. HRMS (ESI): calcd. for $C_{16}H_{13}{}^{35}ClN_3O_4^+$, [M + H]$^+$: 346.0590, found 346.0598. λ_{max} (DCE, ε): 275 (9200), 530 (5000).

4-Methyl-3-phenyl-4*H*-pyrido[1,2-*a*]pyrazine-1-carbonitrile (5g): Pyridopyrazine **5g** (17 mg, yield 31 %) was obtained according to the general procedure from pyridotriazole **1d** (44 mg, 0.38 mmol) and azirine **2b** (33 mg, 0.25 mmol) [140 °C, 3 h, $Rh_2(OAc)_4$ (5 mol-%, 5.5 mg), eluent for chromatography EtOAc/PhH, 1:10]. Red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.33 (d, *J* = 6.7 Hz, 3H), 5.39 (q, *J* = 6.7 Hz, 1H), 6.38 (dt, *J* = 7.0, 4.0 Hz, 1H), 7.09 (d, *J* = 3.6 Hz, 2H), 7.13 (d, *J* = 6.8 Hz, 1H), 7.35–7.43 (m, 3H), 7.81–7.85 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 15.8, 55.0, 91.5, 112.7, 118.7, 120.6, 125.4, 128.7, 129.0, 133.6, 135.0, 135.1, 137.8, 139.9. HRMS (ESI): calcd. for $C_{16}H_{14}N_3^+$, [M + H]$^+$: 248.1183, found 248.1179. λ_{max} (DCE, ε): 400 (7900), 474 (7000).

Methyl 4-Methyl-3-phenyl-4*H*-pyrido[1,2-*a*]pyrazine-1-carboxylate (5h): A solution of pyridopyrazine **5c** (12 mg, 0.04 mmol) in methanol (0.5 mL) was added to the mixture of ammonia formate (25 mg, 10 equiv.) and Pd/C (1.2 mg, 10 mass. % on **5c**) and heated at 90 °C for 1 h in a screw-cap glass tube. Methanol was evaporated in vacuo, and the product was purified by column chromatography on silica gel to give pyridopyrazine **5h** (11 mg, yield 93 %). Red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.30 (d, *J* = 6.8 Hz, 3H), 3.91 (s, 3H), 5.39 (q, *J* = 6.7 Hz, 1H), 6.48 (t, *J* = 6.3 Hz, 1H), 7.16–7.20 (m, 2H), 7.35 (t, *J* = 7.2 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.89 (d, *J* = 7.5 Hz, 2H), 8.49 (d, *J* = 9.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 15.2, 51.2, 55.7, 107.8, 113.4, 121.1, 125.5, 128.6 (2C), 133.6, 134.8, 135.9, 136.0, 139.1, 166.4. HRMS (ESI): calcd. for $C_{17}H_{17}N_2O_2$, [M + H]$^+$: 281.1285, found 281.1292. λ_{max} (DCE, ε): 327 (9400), 466 (7800).

Methyl 2-(6-Chloropyridin-2-yl)-2-[(2-methyl-1-phenylprop-1-en-1-yl)imino]acetate (3i): Azadiene **3i** (26 mg, yield 77 %) was obtained according to the general procedure from pyridotriazole **1b** (26 mg, 0.12 mmol) and azirine **2e** (15 mg, 0.1 mmol) [140 °C, 5 min, $Rh_2(OAc)_4$ (2 mol-%, 0.9 mg), eluent for chromatography EtOAc/hexane, 1:15]. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.78 (s, 3H), 2.04 (s, 3H), 3.46 (s, 3H), 7.24–7.27 (m, 2H), 7.29–7.31 (m, 1H), 7.33–7.37 (m, 3H), 7.72 (t, *J* = 7.8 Hz, 1H), 8.15 (d, *J* = 7.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 20.2, 21.5, 51.6, 119.6, 125.5, 127.4, 127.8, 129.3, 130.3, 137.1, 138.8, 141.3, 150.6, 154.7 (2C), 165.4. HRMS (ESI): calcd. for $C_{18}H_{18}{}^{35}ClN_2O_2$, [M + H]$^+$: 329.1052, found 329.1059.

(*E*)-Methyl 3-{[1-(6-Bromopyridin-2-yl)-2-methoxy-2-oxoethylidene]amino}-3-phenylacrylate [(*E*)-3j] and (*Z*)-Methyl 3-{[1-(6-Bromopyridin-2-yl)-2-methoxy-2-oxoethylidene]amino}-3-phenylacrylate [(*Z*)-3j]: Azadiene (*E*)-**3j** (46 mg, yield 33 %) and unseparated mixture of (*E*)-**3j** and (*Z*)-**3j** in 1:1.6 ratio (79 mg, yield 56 %) were obtained according to the general procedure from pyridotriazole **1a** (116 mg, 0.46 mmol) and azirine **2f** (61 mg, 0.35 mmol) [140 °C, 1 min, $Rh_2(OAc)_4$ (5 mol-%, 7.7 mg), eluent for chromatography EtOAc/hexane, 1:4].

Compound (*E*)-3j: Yellow solid, m.p. 116–119 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.64 (s, 3H), 3.96 (s, 3H), 5.46 (s, 1H), 7.40–7.43 (m, 3H), 7.53–7.55 (m, 2H), 7.60 (d, *J* = 7.9 Hz, 1H), 7.67 (t, *J* = 7.8 Hz, 1H), 8.06–8.08 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 51.3, 52.3, 102.1, 121.2, 127.9, 128.6, 129.6, 130.6, 134.0, 138.9, 141.5, 152.9, 156.3, 163.0, 163.2, 165.9.

Compound (*Z*)-3j: [not separated from (*E*)-**3j**]. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.69 (s, 3H), 3.81 (s, 3H), 5.71 (s, 1H), 7.40–7.42 (m, 3H), 7.56–7.58 (m, 2H), 7.61–7.63 (m, 1H), 7.72 (t, *J* = 7.8 Hz, 1H), 8.22 (d, *J* = 7.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 51.3, 52.3, 97.6, 121.9, 126.6, 128.7, 130.4, 134.7, 139.0, 141.4, 152.9, 158.0, 160.1, 162.7, 163.0, 166.0. HRMS (ESI) of the mixture of (*E*)-**3j** and (*Z*)-**3j**: calcd. for $C_{18}H_{15}{}^{79}BrN_2NaO_4^+$, [M + Na]$^+$: 425.0108, found 425.0111.

1,2-Diphenyl-*N*-[phenyl(pyridin-2-yl)methylene]ethenamine (3k): Azadiene **3k** (47 mg, yield 26 %) was obtained according to the general procedure from pyridotriazole **1f** (150 mg, 0.77 mmol) and azirine **2a** (114 mg, 0.6 mmol) [140 °C, 3 h, $Rh_2(esp)_2$ (1 mol-%,

4.5 mg), eluent for chromatography EtOAc/hexane, 1:6]. Unstable yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.20 (s, 1H), 7.12–7.28 (m, 7H), 7.40–7.54 (m, 9H), 7.87–7.95 (m, 2H), 8.41 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 112.0, 123.0, 124.6, 125.9, 126.1, 127.5, 128.1, 128.1, 128.2, 128.3, 128.4, 128.9, 131.0, 132.9, 135.0, 137.0, 137.2, 147.8, 148.5. HRMS (ESI): calcd. for $C_{26}H_{21}N_2^+$, $[M + H]^+$: 361.1700, found 361.1714.

(2*E*,4*E*)-Methyl 5-{[1-(6-Chloropyridin-2-yl)-2-methoxy-2-oxoethylidene]amino}-5-phenylpenta-2,4-dienoate [(*E*)-3l] and Dimethyl 6′-Chloro-6-phenyl-1,2-dihydro-[2,2′-bipyridine]-2,3-dicarboxylate (6): Azatriene (*E*)-**3l** (47 mg, yield 61 %) and dihydropyridine **6** (13 mg, yield 17 %) were obtained according to the general procedure from pyridotriazole **1b** (42 mg, 0.2 mmol) and azirine **2g** (40 mg, 0.2 mmol) [110 °C, 1 min, $Rh_2(OAc)_4$ (2 mol-%, 1.8 mg), eluent for chromatography EtOAc/hexane, 1:5].

Compound (*E*)-3l: Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.73 (s, 3H), 3.87 (s, 3H), 5.98 (dd, *J* = 16.5, 13.6 Hz, 2H), 6.00 (d, *J* = 15.4 Hz, 1H), 7.42–7.49 (m, 7H), 7.76 (t, *J* = 7.8 Hz, 1H), 8.07 (d, *J* = 7.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 51.4, 52.3, 112.3, 120.7, 121.5, 126.7, 128.5, 129.1, 129.4, 134.2, 139.2, 141.1, 151.0, 152.8, 156.8, 157.2, 164.0, 167.4. HRMS (ESI): calcd. for $C_{20}H_{18}{}^{35}ClN_2O_4^+$, $[M + H]^+$: 385.0950, found 385.0966.

Compound 6: Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.76 (s, 3H), 3.84 (s, 3H), 5.44 (dd, *J* = 6.7, 1.8 Hz, 1H), 5.93 (s, 1H), 7.24 (dd, *J* = 7.8, 0.5 Hz, 1H), 7.42–7.46 (m, 4H), 7.55 (d, *J* = 6.7 Hz, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.70–7.74 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 51.6, 53.3, 67.7, 95.2, 110.6, 121.1, 123.3, 127.0, 128.9, 130.4, 135.0, 137.8, 138.7, 149.4, 150.0, 162.2, 166.3, 172.9. HRMS (ESI): calcd. for $C_{20}H_{18}{}^{35}ClN_2O_4^+$, $[M + H]^+$: 385.0950, found 385.0969.

Ethyl 1-Methyl-2-phenyl-1*H*-pyrazino[1,2-*a*]quinoline-4-carboxylate (5n): Pyrazinoquinoline **5n** (77 mg, yield 50 %) was obtained according to the general procedure from triazoloquinoline **1h** (125 mg, 0.5 mmol) and azirine **2b** (60 mg, 0.45 mmol) [140 °C, 3 h, $Rh_2(esp)_2$ (1 mol-%, 3.4 mg), eluent for chromatography EtOAc/hexane, 1:4]. Red solid, m.p. 78–80 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.30 (d, *J* = 6.7 Hz, 3H), 1.49 (t, *J* = 7.1 Hz, 3H), 4.35–4.50 (m, 2H), 6.20 (q, *J* = 6.7 Hz, 1H), 7.22 (t, *J* = 7.4 Hz, 1H), 7.30 (d, *J* = 9.8 Hz, 1H), 7.40–7.52 (m, 5H), 7.64 (d, *J* = 8.6 Hz, 1H), 8.03 (d, *J* = 7.4 Hz, 2H), 8.46 (d, *J* = 9.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.8, 14.6, 45.9, 60.0, 111.7, 112.2, 120.9, 123.3, 125.5, 125.9, 128.4, 128.6, 129.1, 130.3, 131.8, 136.1, 136.8, 137.4, 140.7, 166.3. HRMS (ESI): calcd. for $C_{22}H_{21}N_2O_2^+$, $[M + H]^+$: 345.1598, found 345.1603. λ_{max} (DCE, ε): 291 (12800), 487 (12000).

Methyl 4-Methyl-3-phenyl-4*H*-benzo[4,5]oxazolo[3,2-*a*]pyrazine-1-carboxylate (5o): Oxazolopyrazine **5o** (60 mg, yield 47 %) was obtained according to the general procedure from diazo compound **1i** (96 mg, 0.44 mmol) and azirine **2b** (53 mg, 0.4 mmol) [110 °C, 5 min, $Rh_2(OAc)_4$ (2 mol-%, 3.5 mg), eluent for chromatography EtOAc/hexane, 1:2]. Yellow solid, m.p. 97–100 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.49 (d, *J* = 6.6 Hz, 3H), 3.96 (s, 3H), 5.91 (q, *J* = 6.5 Hz, 1H), 7.19–7.25 (m, 2H), 7.29–7.33 (m, 1H), 7.37–7.48 (m, 4H), 7.96 (d, *J* = 7.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 16.1, 50.2, 51.3, 95.1, 108.1, 111.3, 123.8, 124.9, 126.0, 128.6, 129.0, 129.2, 135.5, 140.3, 147.7, 154.0, 164.7. HRMS (ESI): calcd. for $C_{19}H_{17}N_2O_3^+$, $[M + H]^+$: 321.1234, found 321.1246. λ_{max} (DCE, ε): 310 (9300), 401 (11300).

5-(6-Methoxypyridin-2-yl)-2-methyl-3,6-diphenyl-2*H*-1,4-oxazine (7): Oxazine **7** (112 mg, yield 63 %) was obtained according to the general procedure from pyridotriazole **1g** (139 mg, 0.55 mmol) and azirine **2b** (66 mg, 0.5 mmol) [110 °C, 15 min, $Rh_2(OAc)_4$ (2 mol-%, 4.4 mg), eluent for chromatography EtOAc/hexane, 1:3]. Yellow solid, m.p. 168–169 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.59 (d, *J* = 6.8 Hz, 3H), 3.26 (s, 3H), 5.66 (q, *J* = 6.8 Hz, 1H), 6.53 (d, *J* = 8.0 Hz, 1H), 7.30–7.33 (m, 3H), 7.45–7.53 (m, 5H), 7.58 (t, *J* = 7.8 Hz, 1H), 7.65 (d, *J* = 7.2 Hz, 1H), 8.01–8.04 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 15.0, 52.4, 67.0, 108.5, 114.0, 126.6, 126.7, 127.7, 128.6, 128.7, 130.0, 130.3, 134.9, 135.1, 138.5, 142.2, 151.8, 153.2, 162.5. HRMS (ESI): calcd. for $C_{23}H_{21}N_2O_2^+$, $[M + H]^+$: 357.1598, found 357.1605.

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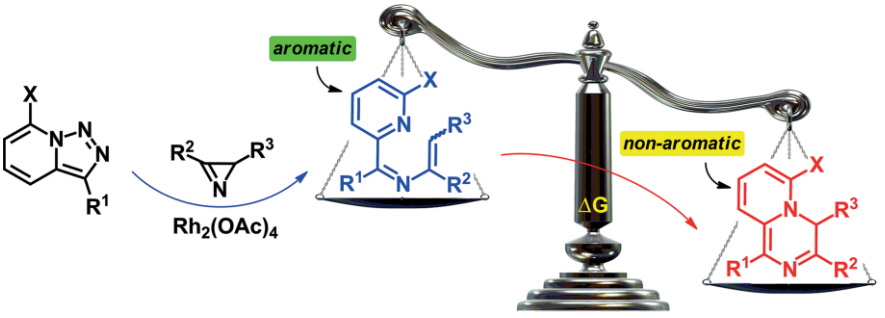
Dearomative Electrocyclization

I. P. Filippov,
M. S. Novikov,
A. F. Khlebnikov,
*N. V. Rostovskii** 1–11

Pseudopericyclic Dearomative 1,6-Cyclization of 1-(2-Pyridyl)-2-aza-buta-1,3-dienes: Synthesis and Ring–Chain Valence Equilibria of 4*H*-Pyrido[1,2-*a*]pyrazines



The 1,6-electrocyclization of 1-(2-pyridyl)-2-azabuta-1,3-dienes, obtained by Rh^{II}-catalyzed reaction of pyridotriazoles with 2*H*-azirines, affords stable non-aromatic 4*H*-pyrido[1,2-*a*]pyrazines despite the fact that the reaction proceeds with irreversible dearomatization of the pyridine aromatic system.

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