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Rearrangement of *N*-Aryl-2-Vinylaziridines to Benzoazepines and Dihydropyrroles: A Synthetic and Theoretical Study

Simone Fantauzzi,[a] Emma Gallo,*[a] Alessandro Caselli,[a] Cristiana Piangiolino,[a] Fabio Ragaini,[a] Nazzareno Re,[b] and Sergio Cenini[a]

Abstract: Herein we report the one-pot synthesis of several N-heterocyclic compounds by rearrangement reactions of *N*-aryl-2-vinylaziridines. The optimization of the synthetic methodology employed allowed us to obtain differently substituted 2,5-dihydro-1*H*-benzo[b]azepines in good yields and purities. The relationship between the nature of the starting *N*-aryl-2-vinylaziridine and the obtained N-heterocycle was also investigated. Finally, to rationalize all the experimental results reported in this paper a theoretical study was performed that casts light on the reaction mechanism.

Keywords: azides · homogeneous catalysis · nitrogen heterocycles · porphyrinoids · ruthenium

Introduction

Aziridines have received special attention as intermediates[1–6] in the synthesis of nitrogen-containing compounds because of their high reactivity due to the three-membered ring strain responsible for ring opening or ring expansion reactions.[7,8] Moreover, if a vinylic functionality is present on the nitrogen [3,9–11] or on the carbon atom of the ring, the reactivity of the aziridine is enhanced by the contemporary presence of the aziridine ring and a double bond. Therefore, it is not surprising that vinylaziridines are extensively used as starting materials for the synthesis of both natural and non-natural products, such as alkaloids[12–16] and allylamines.[17–19] The chemical behavior of *C*-vinylaziridines is modulated by the nature of the substituent on the nitrogen atom and, in general, the presence of a benzyl group or of strong electronegative functionalities, such as a tosyl or acyl group, improves their reactivity towards nucleophiles.[4,5,7,20–22] *C*-Vinylaziridines can also undergo several pericyclic reactions in which a σ bond is shifted over a π system to yield heterocyclic compounds, such as 3-pyrrolines,[23,24] tetrahydropyridines,[14,25–28] lactams,[29–31] and benzoazepines. These last products are formed by [3,3]-Claisen rearrangements of the corresponding *N*-aryl-2-vinylaziridines. Although, this reaction has been known since 1967,[32–34] up to now its scope was not deeply investigated in spite of the scientific interest in developing new methodologies to afford benzoazepine derivatives[11,35–38] for their pharmaceutical activity in several psycho-diseases.[39–42] It should be noted that the limited literature on this subject is probably due to the great chemical instability of *N*-aryl-2-vinylaziridines that prevents their extensive use as starting materials. In addition to that, few methods have been reported for the preparation of this class of molecules.[43–45]

We have recently investigated the [Ru(CO)(porphyrin)]-catalyzed reactions of arylazides with unsaturated hydrocarbons to synthesize *N*-aryl-aziridines in very good yields.[46–49] Our methodology is very atom-efficient because the use of arylazide as a nitrogen donor allows the transfer of the nitrene functionality, "ArN", to the olefin with the generation of eco-friendly molecular nitrogen as the only reaction side product.[50] Therefore, we decided to extend the scope of the reaction by using conjugated dienes as starting materials and we obtained *N*-aryl-2-vinylaziridines in good yields and purities.[51]

[a] Dr. S. Fantauzzi, Prof. E. Gallo, Dr. A. Caselli, Dr. C. Piangiolino, Prof. F. Ragaini, Prof. S. Cenini
Dipartimento di Chimica Inorganica
Metallorganica e Analitica "Lamberto Malatesta"
Università degli Studi di Milano and ISTM-CNR
Via Venezian 21, I-20133 Milano (Italy)
Fax: (+39) 025-031-4405
E-mail: emma.gallo@unimi.it.

[b] Prof. N. Re
Dipartimento di Scienze del Farmaco
Università "G. d'Annunzio"
Via dei Vestini, 31, I-06100 Chieti (Italy)

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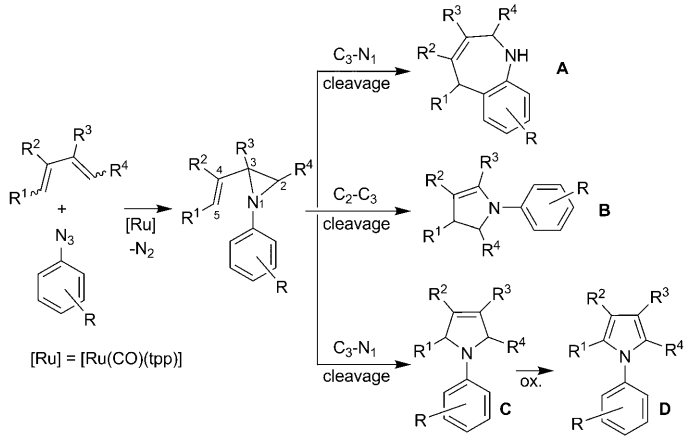
Here we report our results on the study of sigmatropic rearrangements of *N*-aryl-2-vinylaziridines for the synthesis of N-heterocyclic compounds. Several *N*-aryl-2-vinylaziridines with different substituents on the aziridine cycle and the vinyl moiety were considered and the experimental conditions were optimized to improve the chemoselectivity of the reaction. Moreover, density functional calculations were performed to predict the chemoselectivity of the rearrangement to N-heterocyclic compounds on the basis of the electronic and steric characteristics of the substituents and to gain insight into the mechanism of the sigmatropic rearrangement to benzoazepines.

Results and Discussion

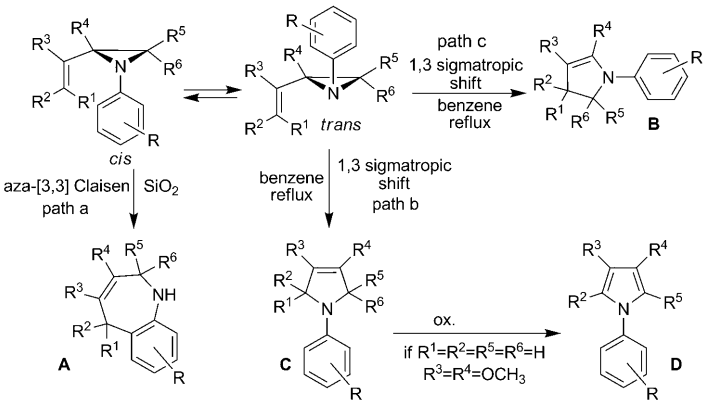
As we have recently reported,[51] *N*-aryl-2-vinylaziridines are very unstable when heated or treated in the presence of acidic species. The crucial step to obtain *N*-aryl-2-vinylaziridines is the purification procedure and a lowering of the yields can be observed during the chromatographic process even when using deactivated silica.[51] The great instability of *N*-aryl-2-vinylaziridines can be turned into an advantage by promoting isomerization processes to form new aza compounds.

Several dienes and arylazides were used to form *N*-aryl-2-vinylaziridines that were transformed into different N-heterocycles by adding a small quantity of silica to the reaction mixture or by increasing the reaction temperature (Scheme 1, Table 1). As reported in Table 1, the addition of silica to the in situ formed *N*-aryl-2-vinylaziridines, deriving from a diene containing at least a terminal double bond, facilitated an aza-[3,3]-Claisen rearrangement in which a C_3–N_1 (Scheme 1) bond cleavage of the aziridine moiety and a proton shift from the aryl moiety to the nitrogen atom occurred. This reaction pathway yielded differently substituted 2,5-dihydro-1*H*-benzo[b]azepines in yields up to 65% (Table 1, entries 1, 3, and 4). The slight lowering of the azepine yield observed by using 3,5-$(CF_3)_2$-phenylazide instead of 4-NO_2-phenylazide (compare entries 1 and 3) could be due to the presence of two substituents in *meta* positions on the aryl moiety which hampers the ring closure in the *ortho* position. A change of the chemoselectivity of the reaction was observed when, at the complete consumption of the arylazide, the reaction temperature was increased from 65 °C to reflux without adding silica to the reaction mixture. The temperature-mediated rearrangement of *N*-aryl-2-vinylaziridines **1** afforded lower yields of the corresponding benzoazepine because of the contemporary formation of 2,5-dihydropyrrole **C** (entry 2). Compound **C** is obtained by the cleavage of the C_3–N_1 bond, as shown for the synthesis of 2,5-dihydro-1*H*-benzo[b]azepines **A**, but the aryl group bonded to the aziridine nitrogen atom is not involved anymore in the rearrangement reaction.

If the starting olefin is an internal diene, the addition of silica gel to the corresponding *N*-aryl-2-vinylaziridine yielded the benzoazepine in a low yield when R^1 and R^4 (Scheme 1) are two methyl groups (Table 1, entry 6), whereas no trace of azepine was detected when using the *N*-aryl-2-vinylaziridine **11** of *trans*,*trans*-1,4-diphenyl-1,3-butadiene (entry 8). In this last case, the only organic product recovered at the end of the reaction was the 2,3-dihydropyrrole **12** formed by a C_2–C_3 bond cleavage (Scheme 1 and Scheme 2, path c).



Scheme 1. Synthesis of N-heterocycles by sigmatropic rearrangements of *N*-aryl-2-vinylaziridines.

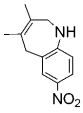
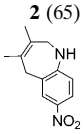
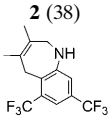
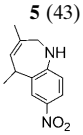
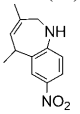
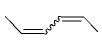
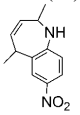
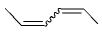
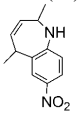
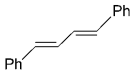
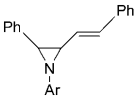
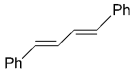
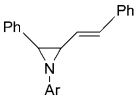
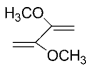
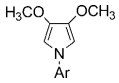


Scheme 2. Proposed reaction pathways for the formation of N-heterocyclic compounds.

The increase in the reaction temperature of the mixture containing *N*-aryl-2-vinylaziridines **8** or **11** resulted in the formation of a small amount of the 2,3-dihydropyrrole **10** and an increase in the yield of **12**, respectively. In both cases, product **C** (Scheme 1) was not detected in the organic mixture. These last results indicated that the steric hindrance at the double bonds influences the chemoselectivity of the reactions because it directs the cleavage of a C–N or a C–C bond.

As is well known, the pyramidal inversion of the aziridine nitrogen atom produces the two different N-invertomers, *cis* and *trans* (Scheme 2), which show a different distance between the aryl group and the double bond. Therefore, it is reasonable to propose that the steric hindrance of R groups

Table 1. Synthesis of N-heterocycles by sigmatropic rearrangements of in situ formed *N*-aryl-2-vinylaziridines.[a]

Entry	Diene	*N*-Aryl-2-vinyl aziridine	Ar	*t* [h][b]	Yield of **A** [%][c]	Yield of **B** [%][c]	Yield of **C** [%][c]	Yield of **D** [%][c]
1[d]			4-$NO_2C_6H_4$	8		–	–	–
		1			**2** (65)	–	–	–
2[e]			4-$NO_2C_6H_4$	8		–		–
		1			**2** (38)		**3** (53)	
3[d]			3,5$(CF_3)_2C_6H_3$	8		–	–	–
		4			**5** (43)			
4[d]			4-$NO_2C_6H_4$	12		–	–	–
		6[f]			**7** (58)			
5[e]			4-$NO_2C_6H_4$	20		–	traces	–
		6[f]			**7** (35)			
6[d]			4-$NO_2C_6H_4$	18		–	–	–
		8			**9** (27)			
7[e]			4-$NO_2C_6H_4$	48			–	–
		8			**9** (36)	**10** (7)		
8[d]			4-$NO_2C_6H_4$	8	–		–	–
		11				**12** (50)		
9[e]			4-$NO_2C_6H_4$	4	–		–	–
		11				**12** (70)		
10[e]			4-$NO_2C_6H_4$	36	–	–	–	
		13						**14** (60)

[a] General procedure for the reaction: [Ru(CO)(tpp)] (1.30×10^{-2} mmol) in benzene (30 mL) at 65 °C, molar ratio: catalyst/azide/olefin 1:50:250. [b] Time required to reach complete conversion of the intermediately formed *N*-aryl-2-vinylaziridines. [c] Isolated yield. [d] Silica gel (400 mg) was added after complete conversion of the arylazide. [e] The reaction temperature was increased from 65 °C to reflux after complete conversion of the arylazide. [f] The aziridine ring is formed in the terminal position.

present on the diene skeleton determines the position of the equilibrium *cis*⇄*trans* and consequentially the nature of the formed organic product.

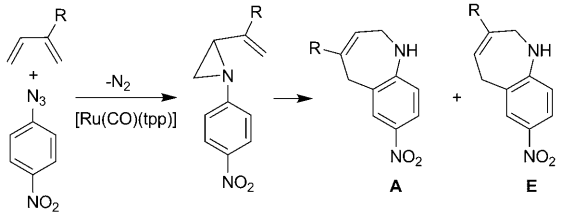
To study the interconversion between the two N-invertomers, *cis* and *trans*, we have obtained in CD_2Cl_2 a series of ^{1}H NMR spectra at several temperatures (RT→−90 °C) of *N*-aryl-2-vinylaziridine **1**, deriving from the terminal diene 2,3-dimethyl-1,3-butadiene, and of the *trans* isomer of **11**, synthesized from the internal diene *trans*,*trans*-1,4-diphenyl-1,3-butadiene. The ^{1}H NMR spectroscopic experiments run with **1** did not show any change in the pattern of signals. On the other hand, a broadening of the signals relative to com-

pound **11** was observed at −70 °C. No sharpening of the signals was observed by further lowering of the temperature down to −90 °C. These data pointed out that the energetic barriers relative to the inversion of *N*-aryl-2-vinylaziridines of internal and terminal dienes are different and this can explain the different chemoselection of the reactions observed using **1** or **11**. This aspect will be discussed in the theoretical paragraph (see below).

As reported in Table 1, the yield of 2,3-dihydropyrrole **B** increased from 7% (Table 1, entry 7, product **10**) to 70% (entry 9, product **12**) when the R^2 and R^5 methyl groups were replaced by two phenyl ones, which indicates again the dependence of the reaction products on the substituents present on the diene molecule. No reaction was observed when using 2,5-dimethylhexa-2,4-diene as the starting material due to the very high steric hindrance around the double bonds.

The reaction of 2,3-dimethoxy-1,3-butadiene with 4-nitrophenyl azide yielded the direct formation of pyrrole **14** (Table 1, entry 10) and it was impossible to recover the *N*-aryl-2-vinylaziridine **13** in a pure form. In fact, a TLC analysis of the reaction at 65 °C, at an arylazide conversion of 40%, already showed the presence of **14** as the only heterocyclic compound present in the mixture. Probably the first step of the aziridine rearrangement is the formation of the corresponding 2,5-dihydropyrrole **C**, which cannot be observed because, during the workup of the reaction, it is rapidly oxidized by air to **14** due to the presence of electrodonating methoxy groups.

A very different reaction scheme has to be envisaged when a terminal nonsymmetric diene, such as isoprene or myrcene, is used as starting material (Scheme 3). In fact, the



Scheme 3. Proposed mechanism for the formation of 2,5-dihydro-1*H*-benzo[b]azepines **E**.

thermal rearrangement of *N*-aryl-2-vinylaziridines **15** or **18** did not only afford the benzoazepine **A**, but new benzoazepines **E**, **17**, and **19**, were collected in good yield (Table 2, entries 1 and 3). The reaction mixture containing **15** was also treated with silica gel, as previously described, and again **17** was isolated.

The data reported in Table 2 were obtained by performing the reaction in situ without isolating the *N*-aryl-2-vinylaziridine. To clarify the contemporary formation of benzoazepines **A** and **E**, the *N*-aryl-2-vinylaziridine **15** was synthesized, isolated in a pure form, and its reactivity was studied.

Table 2. Synthesis of 2,5-dihydro-1*H*-benzo[b]azepines **E**.[a]

Entry	R	*N*-Aryl-2-vinylaziridine	*t* [h][b]	Yield of **A** [%][c]	Yield of **E** [%][c]
1[d]	$(CH_2)_2CH{=}C(CH_3)_2$	**15**	18	**16**, (17)	**17**, (43)
2[e]	$(CH_2)_2CH{=}C(CH_3)_2$	**15**	60	–	**17**, (55)
3[f]	CH_3	**18**	14	–	**19**, (65)

[a] General procedure for the reaction: [Ru(CO)(tpp)] (1.30×10^{-2} mmol) in benzene (30 mL) at 65 °C, molar ratio catalyst/azide/olefin 1:50:250. [b] Time required to reach complete conversion of the *N*-aryl-2-vinylaziridine. [c] Isolated yield. [d] The reaction temperature was increased from 65 °C to reflux after complete conversion of the arylazide. [e] Silica gel (400 mg) was added after complete conversion of the arylazide. [f] The reaction was performed by using 8.90×10^{-3} mmol of [Ru(CO)(tpp)] in benzene (10 mL) at 80 °C in a pressure tube due to the low boiling point of the diene, molar ratio: [Ru(CO)(tpp)]/azide/olefin 1:50:500.

Firstly, it was refluxed in benzene in the absence or presence of [Ru(CO)(tpp)] (tpp = dianion of tetraphenylporphyrin), and in both cases only benzoazepine **16** was recovered after 24 h. Then, the rearrangement of **15** was studied in the presence of silica or a silica/[Ru(CO)(TPP)] mixture and again only **16** was formed in 28 h. The same behavior was observed when using isoprene as the starting diene. In fact, the rearrangement of isolated **18**, run in the presence of silica or by increasing the temperature, afforded the corresponding benzoazepine **20** (see the Experimental Section) without the formation of **19**. All these experimental results indicate that **17** and **19** cannot be directly formed by an Aza-Claisen rearrangement of *N*-aryl-2-vinylaziridines **15** and **18** but that a different mechanism has to be involved.

Suspecting that the formation of **E** may be due to a radical process, we have repeated the aziridination reaction of myrcene at 65 °C in the presence of a stable radical species, 2,2,6,6-tetramethylpiperidine-*N*-oxide (TEMPO). By using these last experimental conditions, **17** was obtained in a high yield (60%) and in just 4 h, a very fast reaction time compared to the time (24 h) required for pure *N*-aryl-2-vinylaziridine **15** to rearrange to the benzoazepine **16**. This last result indicated that the formation of benzoazepines **E** is promoted by the presence of radical species and this could explain the data reported in Table 2. In fact, when the formation of the N-heterocyclic compound is performed by a one-pot reaction, it is reasonable to believe that small amounts of radical species deriving from the arylazide are present in the reaction medium, which cannot be present if isolated **15** or **18** are used as the starting materials.

Theoretical investigations: To predict the chemoselectivity of the rearrangement to N-heterocyclic compounds on the basis of the electronic and steric characteristics of the substituents and to gain insight into the mechanism of the sigmatropic rearrangement to benzoazepines, we carried out theoretical calculations by using DFT methods. We considered all *N*-aryl-2-vinylaziridines, the thermal conversions of which were explored in this work, that is, compounds **1**, **6**, **8**, **11**, **13**, and **18** (Tables 1 and 2). The rearrangement of **15** (Table 2) can be safely simulated by that of **18**.

Conformational analysis of *N*-aryl-2-vinylaziridines and rearrangement pathways: N-substituted aziridines are known to have a relatively large barrier to nitrogen inversion;[52,53] this gives rise to two distinguishable invertomers: one with the aryl substituent on the nitrogen atom *cis* to the vinyl group on the adjacent carbon atom, and another with a *trans* relationship between the two substituents (Scheme 2). However, since the barriers for configuration inversion experimentally[52,54] and theoretically[55,56] evaluated are below 30–35 kcal mol^{-1}, even for the sterically crowded *N*-aryl-substituted aziridines, the two invertomers are easily interchanged and, therefore, distributed according to a Boltzmann distribution at the reaction temperature of refluxing benzene (80 °C). A preliminary conformational search was performed on both *cis* and *trans* invertomers of all reactants **1**, **6**, **8**, **11**, **13**, and **18** at the semiempirical AM1 level, followed by DFT calculations on the lowest-energy conformations of each molecule. This was carried out by changing the dihedral angles around the C_3–C_4 and N_1–aryl bonds (see numbering in Scheme 1), and also those around the C_2–phenyl bond for **11** and the C_3–OMe bond for **13**. These searches allowed us to evaluate the relative energies of the main conformations that each *N*-aryl-2-vinylaziridine can adopt in both possible invertomers. Two main conformations could be identified for each invertomer (Scheme 2, Figure 1): for the *cis* invertomer we found one conformation with the vinyl group oriented towards the nitrogen aryl substituent (**a**) and one with the vinyl group pointing away (**b**) whereas for the *trans* isomer we found one conformation with the vinyl group oriented towards the nitrogen (**c**) and one with the vinyl group oriented towards the C_2 atom (**d**). All of these conformations have been confirmed as minima at the considered B3LYP/6-31+G* level of theory.

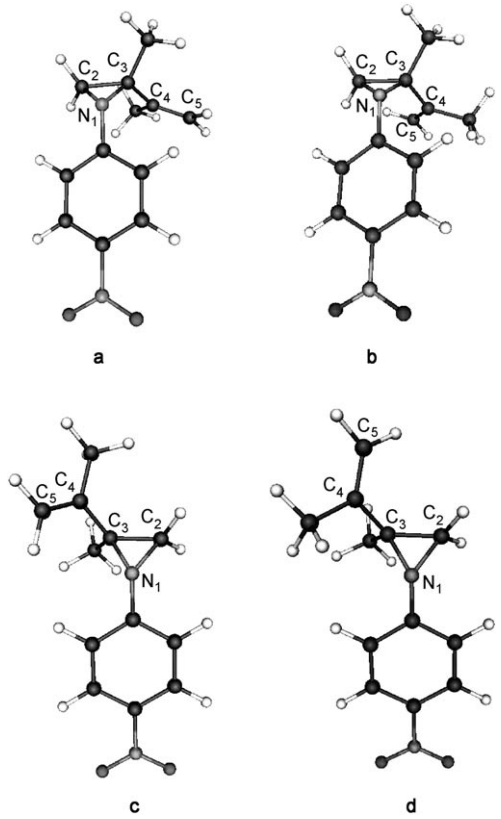


Figure 1. Lowest-energy conformations of the *cis* (**a** and **b**) and *trans* (**c** and **d**) invertomers of 2-isopropenyl-2-methyl-*N*-(4-nitrophenyl)aziridine **1**.

It is well-known that the rate of an intramolecular organic reaction depends upon the distance between reacting atoms in the starting reagent.[57,58] The optimized geometries of the above conformers show relatively short distances between the vinyl terminal carbon atom C_5 (see Scheme 1 and Figure 1) and 1) the *ortho* carbon atom of the *N*-aryl group for the conformer **a**, 2) the N_1 atom of the aziridine ring for the conformer **c**, and 3) the C_2 atom of the aziridine ring for the conformer **d**. For conformer **b** the vinyl group points out both from the aziridine ring and the *N*-aryl group. In conformers **a**, **c** and **d**, the vinyl group is, therefore, suitably oriented to attack the *ortho* carbon atom of the *N*-aryl group and the N_1 or the C_2 atoms of the aziridine ring, thus leading to the products **A**, **C**, and **B**, respectively. The relative energies of these conformers for all considered compounds are reported in Table 3. We see that for **1**, **6**, **8**, and **18** the three conformers are all within 1.9 kcal mol^{-1}, and thus almost equally accessible (see Table 3). On the other hand, for **11** and **13** the conformer **a**, leading preferentially to the benzoazepine **A**, is significantly higher in energy than the global minimum by 3.7 and 2.7 kcal mol^{-1}, respectively. These results can give a simple rationale for the experimental results, without requiring the exceedingly computationally expensive evaluation of the activation energy of the three concur-

Table 3. Relative energies [kcal mol^{-1}] of the lowest-energy conformations for both *cis* and *trans* invertomers of compounds **1**, **6**, **8**, **11**, **13**, and **18**.

Compound	Invertomer	Conformer	Energy
1	*cis*	**a**	0.7
1	*cis*	**b**	0.6
1	*trans*	**c**	0.0
1	*trans*	**d**	0.2
6	*cis*	**a**	0.2
6	*cis*	**b**	0.1
6	*trans*	**c**	0.0
6	*trans*	**d**	0.7
8	*cis*	**a**	1.9
8	*cis*	**b**	0.0
8	*trans*	**c**	0.4
8	*trans*	**d**	0.1
11	*cis*	**a**	3.7
11	*cis*	**b**	1.0
11	*trans*	**c**	0.6
11	*trans*	**d**	0.0
13	*cis*	**a**	2.7
13	*cis*	**b**	0.0
13	*trans*	**c**	1.3
13	*trans*	**d**	0.1
18	*cis*	**a**	0.6
18	*cis*	**b**	0.4
18	*trans*	**c**	0.0
18	*trans*	**d**	0.3

rent pathways, leading to **A**, **B**, and **C**, for all the considered compounds. Indeed, assuming for the reaction pathways leading to **A**, **B**, and **C** similar barrier heights, our conformational analysis showed that for compounds **1**, **6**, **8**, and **18**, conformer **a**, which more easily leads to **A**, is low in energy and thus thermally populated, whereas for compounds **11** and **13**, only conformers **c** and **d**, more easily leading to **C** and **B**, are thermally populated. This is in excellent agreement with the experimental evidence showing that a mixture, with a high contribution of the benzoazepine derivative **A** is observed for the thermal conversion of **1**, **6**, **8**, and **18**, whereas the thermal conversion of **11** and **13** did not yield to benzoazepines **A**.

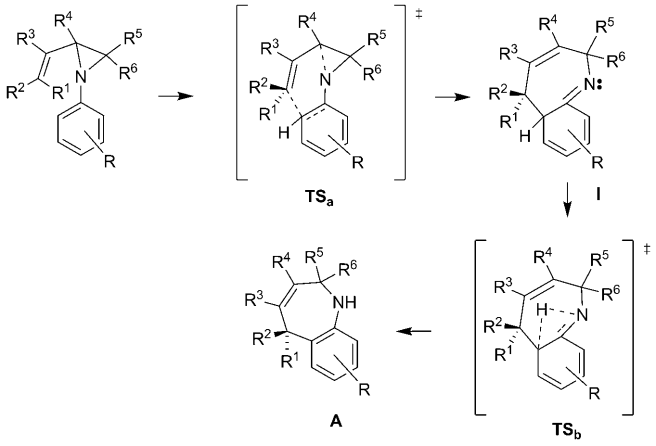
DFT calculations were then performed to study the thermodynamics of the rearrangement of the considered *N*-aryl-2-vinylaziridines to yield 2,5-dihydro-1*H*-benzo[b]azepines (**A**), 2,3-dihydropyrroles (**B**), or 2,5-dihydropyrroles (**C**) and the results are reported in Table 4. Although the selectivity

Table 4. Reaction energies for the sigmatropic rearrangements of *N*-aryl-2-vinylaziridines to the corresponding N-heterocyclic compounds, that is, 2,5-dihydro-1*H*-bezo[b]azepines (**A**), 2,3-dihydropyrroles (**B**), 2,5-dihydropyrroles (**C**), and pyrroles (**D**) plus H_2. Also reported are the energies of the imine intermediates (**I**) proposed for the rearrangement to **A**.

	A	B	C	D	I
1	−27.5	−28.0	−30.9	−13.1	+4.3
6	−22.6	−23.8	−26.0	−13.8	+7.3
8	−18.9	−22.1	−20.2	−11.0	+10.7
11	−11.8	−17.1	−14.6	−6.3	+16.1
13	−22.3	−21.7	−22.4	−18.2	+8.1
18	−28.1	−28.8	−31.9	−13.9	+3.9

of these rearrangements are expected to be kinetically determined, the data in Table 4 shows that while for **1**, **6**, and **18**, the three possible products have similar stabilities, with **C** slightly more stable, for compounds **8** and **11** product **B** is the most stable and, particularly for the latter compound, the benzoazepine derivatives are less stable. This is perfectly consistent with the experimental evidence, which shows that while the thermal conversion of **1** and **6** leads to a mixture of **A** and **C** and of **18** leads to **A**, that of **8** and **11** leads to a mixture of **A** and **B** or only to **B**, respectively. Moreover, for **13**, the oxidation product **D**, **14** is significantly more stable than all the other **D** compounds (Table 4), again in agreement with the experimental data.

Mechanism of the [3,3]-Claisen rearrangement: The mild reaction conditions under which the considered *N*-aryl-2-vinylaziridines transformed into the ring expanded benzoazepines raises the issue concerning the mechanism involved in this rearrangement. A cyclization through an aza-[3,3]-Claisen sigmatropic rearrangement[59] is proposed (Scheme 4), in analogy to the rearrangement of 2,3-divinylaziridines to azepines[60,61] and to the rearrangement of *N*-acyl-vinylaziridines to tetrahydroazepin-2-ones.[30,31] This sigmatropic rearrangement would involve the attack of the vinyl group to the aryl ring with a concomitant C–N bond cleavage of the aziridine



Scheme 4. Proposed mechanism for the aza-[3,3]-Claisen rearrangement of the considered *N*-aryl-2-vinylaziridines to benzoazepines.

moiety leading to an imine intermediate **I**, followed by an aromatization with a concomitant proton shift from the aryl moiety to the nitrogen atom and double-bond shift from the imine to the aryl ring to yield the final benzoazepine product **A** (Scheme 4).

DFT calculations were performed for the main stationary points on the potential-energy surface along this proposed reaction mechanism for the rearrangement of the simplest *N*-aryl-2-vinylaziridine **1**. Geometry optimization of the imine intermediate leads to a stable intermediate **1I**, with a half chair conformation, only 4.3 kcal mol^{-1} above the starting *N*-aryl-2-vinylaziridine **1**. We could also locate the transition states for the transformation of the compound **1** to **1I** and of **1I** to the product **2**, **1TS$_a$** and **1TS$_b$**, respectively. **1TS$_a$** shows a seven-membered half-chairlike conformation structure with a distance of 2.26 Å for the forming C–C bond and a distance of 1.79 Å for the breaking of the aziridine C–N bond and can, therefore, be characterized as an early and dissociative transition state, resembling more the reactant than the product (Figures 2 and 3).

1TS$_b$ actually corresponds to the expected transition state for the 1,2-proton shift from the *ortho* to the *ipso* position on the aryl ring formally leading to an unstable species which relaxes, without any barrier, through a further 1,2-hydrogen shift to the adjacent nitrogen atom. The shifting hydrogen atom is midway between the *ortho* and *ipso* aryl carbon atoms at 1.43 and 1.51 Å, respectively, with minor variations of the fused six and seven-membered rings with respect to **1I**. Figure 3 reports the whole energy profile calculated for the rearrangement of the *N*-aryl-2-vinylaziridine **1** to the corresponding benzoazepine **2**. An activation energy of 35.2 kcal mol^{-1} has been found for the **1** to **1I** step and one of only 22.1 kcal mol^{-1} for the final **1I** to **2** step, the overall energy barrier for the aza-[3,3]-Claisen rearrangement of the *N*-aryl-2-vinylaziridine to the corresponding benzoazepine, 35.2 kcal mol^{-1}, being consistent with the experimental conditions required for the thermal conversion, that is, refluxing in benzene.

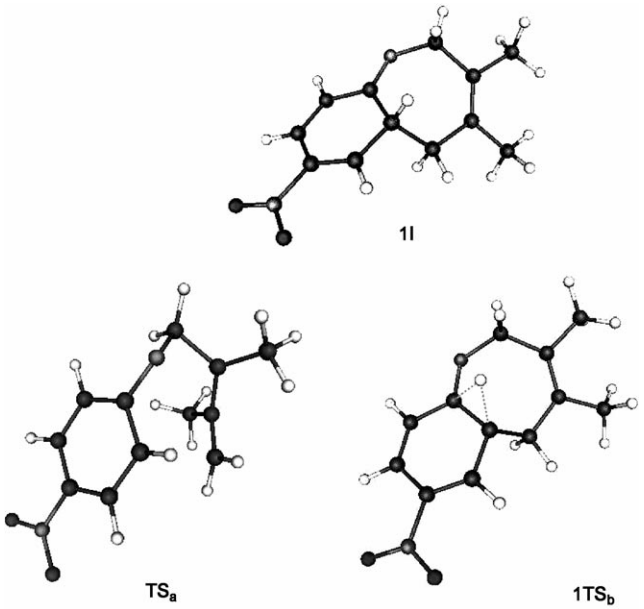


Figure 2. Optimized geometries of the intermediate **1I** and of the corresponding transition-states **1TS$_a$** and **1TS$_b$**.

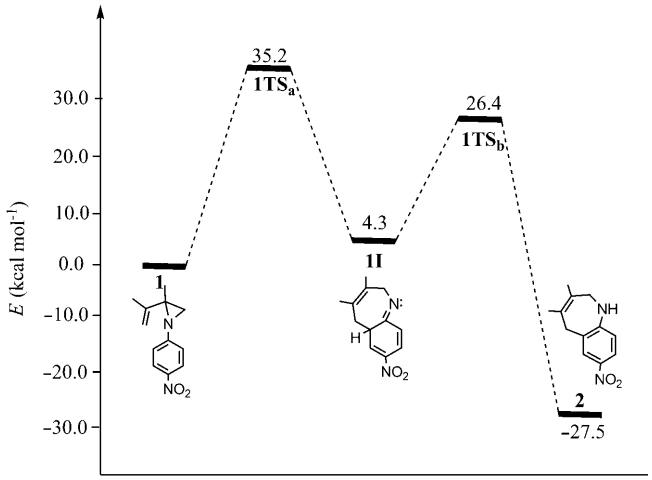


Figure 3. Energy profile for the rearrangement of the *N*-aryl-2-vinylaziridine **1** to the corresponding benzoazepine **2**.

Chemoselectivity of the rearrangement to N-heterocyclic compounds: In principle, a quantitative estimation of the effect of the substituents on the chemoselectivity of the *N*-aryl-2-vinylaziridines rearrangement to the three possible N-heterocyclic compounds **A**, **B**, and **C** would require the evaluation of the activation energies of the three corresponding pathways for all considered compounds. However, due to the high computational load of this task—which would also require a preliminary study of the mechanism of the rearrangements to the 2,3- and 2,5-dihydropyrroles **B** and **C**—these calculations are out of the goal of this work and were not accomplished.

A qualitative interpretation of the observed chemoselectivity in terms of the substituent effects on the relative stabilities of the lowest conformations of the starting *N*-aryl-2-vinylaziridines has been already discussed above. Here we notice that this approximate approach is supported by the nature of the transition state for the rate-determining step of the transformation of the *N*-aryl-2-vinylaziridine **1** to the corresponding benzoazepine **2**, **1TS$_a$**, characterized as early and dissociative, and thus resembling more the reactant than the product in accord with the Hammond postulate. To achieve a more quantitative estimate of substituent effects on the chemoselectivity of the *N*-aryl-2-vinylaziridines to benzoazepines rearrangement, we have tried to correlate the activation energies of the rate-determining step, **1** to **1I**, with the corresponding reaction energies. The activation energies of Claisen rearrangements have been shown to be related to the corresponding reaction energies[62] through Marcus theory.[63] Briefly, Marcus theory allows the separation of the energy barrier into intrinsic and thermodynamic contributions [Eq. (1)]:

$$\Delta E^{\neq} = \Delta E_0{}^{\neq} + 1/2\Delta E_R + (\Delta E_R)^2/(16\Delta E_0{}^{\neq}) \quad (1)$$

in which $\Delta E^{\neq}$ is the activation barrier for the reaction, ΔE_R is the reaction energy, and $\Delta E_0{}^{\neq}$ is the intrinsic barrier, corresponding to the barrier of a hypothetical thermoneutral process. The thermodynamic contribution is an estimate of the change in the activation energy due to the variation of reaction thermodynamics, which is based on an assumption that the hypersurface of potential energy behaves like two overlapping parabolas representing reactant and product energies. For the large activation energies (around the value of 35 kcal mol^{-1} calculated for **1**) and the relatively small reaction energies (4–16 kcal mol^{-1}, see below) expected for the considered **1** to **1I** step, the Marcus equation [Eq. (1)] approximately reduces to a free-energy relationship, $\Delta\Delta E^{\neq} = 1/2\Delta\Delta E_R$, determined empirically for a set of related reactions by Dimroth, Brønsted, and Bell–Evans–Polanyi.[64]

Therefore, we performed DFT calculations on the imine intermediates involved in the rearrangements of all the considered **1**, **6**, **8**, **11**, **13**, and **18** compounds and estimated the reaction energies for the *N*-aryl-2-vinylaziridines to the imine intermediate rearrangements, see Table 4. The results show that the reaction energies for the *N*-aryl-2-vinylaziridines to the imine intermediate rearrangements are all endothermic with small values, 3.9–7.3 kcal mol^{-1}, for **1**, **6**, and **18** and larger values, 10.7 and 16.1 kcal mol^{-1}, for **8** and **11**. We thus expect activation energies for **6** and **18** similar to those for **1**, that is, around 35 kcal mol^{-1}, whereas a significantly higher activation energy is expected for **8** and even more for **11**. These results are in good agreement with the experimental evidence showing that the thermal conversion of **1**, **6**, and **18** gives a mixture with a high contribution of the benzoazepine **A**, whereas this derivative is obtained in a mixture with compound **B** for the thermal conversion of **8**, and is not observed at all for the thermal conversion of **11**. Relatively low reaction energies are obtained for the *N*-aryl-2-vinylaziridine to imine intermediate rearrangements of **13**, but in this case the formation of the benzoazepine **A** could

be prevented by the preferential reaction to thermodynamically more favorable oxidation product **D** (see Tables 1 and 4).

Conclusion

In this paper, we have reported a new methodology that allows us to selectively obtain different heterocyclic compounds by a one-pot procedure without requiring any intermediate purification or workup. This reaction has been applied to a set of conjugated dienes and the heterocyclic compounds can be easily purified by flash chromatography. Among the obtained products, benzoazepines constitute the skeleton of several pharmaceutically active compounds employed in the treatment of psycho-diseases. The results achieved indicate that the chemoselectivity of the reaction strongly depends both on steric properties of the starting diene and on the experimental conditions employed for the rearrangement. The effect of the former could be nicely rationalized by theoretical calculations at the DFT level on the rearrangements of the intermediately formed *N*-aryl-2-vinylaziridines. Calculations identified the key role of the effects of the substituents on the relative stabilities of the starting *N*-aryl-2-vinylaziridine conformations allowing us to give a rationale of the experimentally observed chemoselectivity of the rearrangement to N-heterocyclic compounds. It should be pointed out that our study allows us to rationalize the aza-[3,3]-Claisen rearrangement of *N*-aryl-2-vinylaziridines to benzoazepines, a reaction already mentioned in the literature several years ago,[32–34] but never applied in a systematic way. In conclusion, we believe that this synthetic study, accompanied by a theoretical investigation, has allowed us to turn some isolated observations into an efficient and predictable synthetic methodology.

Experimental Section

General: Unless otherwise specified, all reactions were carried out under a nitrogen atmosphere employing standard Schlenk techniques and magnetic stirring. Benzene was dried over sodium prior to use and stored under nitrogen. All starting materials were commercial products and were used as received, unless otherwise reported. Arylazides[64] and [Ru(CO)(tpp)][65] were synthesized by methods reported in the literature or by using minor modifications of them. The catalyst was kept under vacuum at 120 °C for 3 h prior to use.[66] The purity of the azides and dienes employed was checked by ^{1}H NMR spectroscopic or GCMS analyses. ^{1}H NMR spectra were recorded on an Avance 300-DRX Bruker instrument, operating at 300 MHz for ^{1}H, at 75 MHz for ^{13}C, and at 282 MHz for ^{19}F NMR, or on an Avance 400-DRX Bruker instrument, operating at 400 MHz for ^{1}H and at 100 MHz for ^{13}C NMR. Unless otherwise specified, all the NMR spectra reported in the following were recorded at 300 K. Chemical shifts (ppm) are reported relative to TMS and *J* values are given in Hz. The ^{1}H NMR signals of compounds described in the following have been assigned by COSY and NOESY techniques. Assignments of the resonances in ^{13}C NMR spectra were made by using the APT pulse sequence, HSQC, and HMQC techniques. IR spectra were recorded on a Varian Scimitar FTS 1000 spectrophotometer. Elemental analyses and mass spectra were recorded in the analytical laboratories of Milan University.

(*Z*)-2,5-Dihydro-3,4-dimethyl-7-nitro-1*H*-benzo[b]azepine (2) and 2,5-dihydro-3,4-dimethyl-1-(4-nitrophenyl)-1*H*-pyrrole (3): [Ru(CO)(tpp)] (9.3 mg, 1.25×10^{-2} mmol) and 4-nitrophenyl azide (103.3 mg, 6.30×10^{-1} mmol) were added to a dry benzene solution (30.0 mL) of 2,3-dimethyl-1,3-butadiene (0.36 mL, 3.15 mmol). The resulting red solution was stirred at 65 °C in a preheated oil bath for 4 h. The consumption of the arylazide was monitored by TLC until the corresponding spot was no longer observable, and then by IR spectroscopy. The reaction was considered to be finished when the absorbance of the azide band at 2121 cm^{-1} in the IR spectrum of the solution, measured with a 0.5 mm thick cell, was at or below 0.03. Silica (400 mg) was then added to the reaction mixture and the suspension was stirred at 65 °C under nitrogen. The conversion of **1** was monitored by TLC (silica, *n*-hexane/ethyl acetate 8:2). After 8 h, the solvent was evaporated to dryness and the residue was purified by flash chromatography (*n*-hexane/ethyl acetate 9.5:0.5→7:3). Pure **2** was collected as a dark-yellow oil (65 %). The reaction for the isomerization of **1** was repeated by increasing the temperature to reflux when the starting arylazide was completely consumed. After 8 h, the crude was purified by flash chromatography (*n*-hexane/ethyl acetate 9.5:0.5→7:3) to give compounds **2** and **3** in 38 and 53 % yields, respectively.

Compound ***2***: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.83$ (dd, $J=8.9$, 2.5 Hz, 1H; ArH), 7.79 (d, $J=2.5$ Hz, 1H; ArH), 6.27 (d, $J=8.9$ Hz, 1H; ArH), 4.93 (br s, 1H; NH), 3.99 (s, 2H; NH-CH_2), 3.51 (s, 2H; CH_2), 1.84 (s, 3H; CH_3), 1.82 ppm (s, 3H; CH_3); ^{1}H NMR (300 MHz, C_6D_6): $\delta=7.96$ (dd, $J=8.9$, 2.6 Hz, 1H; ArH), 7.91 (d, $J=2.6$ Hz, 1H; ArH), 5.70 (d, $J=8.9$ Hz, 1H; ArH), 3.78 (br s, 1H; NH), 3.29 (m, 2H; NH−CH_2), 3.05 (s, 2H; CH_2), 1.55 (s, 3H; CH_3), 1.54 ppm (s, 3H; CH_3); ^{13}C NMR (100 MHz, C_6D_6): $\delta=153.1$ (C), 133.6 (C), 127.9 (CH), 126.5 (C), 124.3 (CH), 121.5 (C), 115.3 (CH), 47.5 (*C*H_2−NH), 38.9 (CH_2), 18.5 (CH_3), 18.2 ppm (CH_3); MS (ESI): *m*/*z* (%): 218 [M^+], 203 (73) [M^+-CH_3], 157 (100) [$M^+-CH_3-NO_2$]; elemental analysis calcd (%) for $C_{12}H_{14}N_2O_2$ (218.26): C 66.04, H 6.46, N 12.83; found: C 66.02, H 6.72, N 12.53.

Compound ***3***: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=8.17$ (d, $J=9.3$ Hz, 2H; ArH), 6.45 (d, $J=9.3$ Hz, 2H; ArH), 4.12 (s, 4H; CH_2), 1.78 ppm (s, 6H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=151.8$ (C), 137.3 (C), 127.2 (C), 127.1 (CH), 110.5 (CH), 59.7 (CH_2), 12.0 ppm (CH_3); MS (ESI): *m*/*z* (%): 218 [M^+], 203 (73) [M^+-CH_3], 171 [$M^+-CH_3-O_2$], 157 (100) [$M^+-CH_3-NO_2$]; elemental analysis calcd (%) for $C_{12}H_{14}N_2O_2$ (218.26): C 66.04, H 6.46, N 12.83; found: C 66.08, H 6.32, N 12.44.

(*Z*)-6,8-Bis(trifluoromethyl)-2,5-dihydro-3,4-dimethyl-1*H*-benzo[b]azepine (5): [Ru(CO)(tpp)] (10.9 mg, 1.47×10^{-2} mmol) and 3,5-bis(trifluoromethyl)phenyl azide (188.3 mg, 7.38×10^{-1} mmol) were added to a dry benzene solution (30.0 mL) of 2,3-dimethyl-1,3-butadiene (0.40 mL, 3.54 mmol). The resulting red solution was stirred at 65 °C in a preheated oil bath. The reaction was considered to be finished when the absorbance of the azide band at 2116 cm^{-1} in the IR spectrum of the solution, measured with a 0.5 mm thick cell, was at or below 0.03 (1.5 h). Silica (400 mg) was then added to the reaction mixture and the suspension was left stirring at 65 °C. The conversion of **4** was monitored by TLC (silica, *n*-hexane/ethyl acetate 8:2). After 8 h, the solvent was evaporated to dryness and the residue was purified by flash chromatography (*n*-hexane/ethyl acetate 9.5:0.5→7:3). Pure **5** was collected as a dark-yellow oil (43 %). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.32$ (s, 1H; ArH), 7.00 (s, 1H; ArH), 4.24 (br s, 1H; NH), 3.87 (s, 2H; NH-CH_2), 3.68 (s, 2H; CH_2), 1.84 (s, 3H; CH_3), 1.68 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=149.7$ (C), 132.8 (q, $^2J_{C\text{-}F}=32.5$ Hz; *C*−CF_3), 129.9 (q, $^2J_{C\text{-}F}=31.9$ Hz; *C*−CF_3), 127.7 (q, $J_{C\text{-}F}=191.1$ Hz; *C*F_3), 126.8 (q, $J_{C\text{-}F}=191.0$ Hz; *C*F_3), 118.7 (CH), 114.0 (br; CH), 51.5 (CH_2), 33.6 (CH_2), 20.3 (CH_3), 19.1 ppm (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$): $\delta=-58.81$, −63.38 ppm; MS (ESI): *m*/*z*: 309 [M^+], 294 [M^+-CH_3]; elemental analysis calcd (%) for $C_{14}H_{13}NF_6$ (309.25): C 54.37, H 4.24, N 4.53; found: C 54.18, H 4.21, N 4.38.

(*Z*)-2,5-Dihydro-3,5-dimethyl-7-nitro-1*H*-benzo[b]azepine (7): [Ru(CO)(tpp)] (10.2 mg, 1.38×10^{-2} mmol) and 4-nitrophenyl azide (106 mg, 6.46×10^{-1} mmol) were added to a dry benzene solution (30 mL) of *trans*-2-

methyl-1,3-pentadiene (0.38 mL, 3.28 mmol). The resulting red solution was first stirred at 65 °C in a preheated oil bath for 11 h and for 12 h after adding silica (400 mg). The rest of the procedure was identical to that described for **2** (**7**, 58 %). The reaction was repeated by increasing the temperature to reflux after the arylazide had been completely consumed. Compound **7** was recovered in 35 % yield after 20 h and column purification (silica gel, *n*-hexane/ethyl acetate 9.5:0.5→8:2). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.95$ (d, $J = 2.4$ Hz, 1H; ArH), 7.91 (dd, $J = 8.7$, 2.4 Hz, 1H; ArH), 6.49 (d, $J = 8.7$ Hz, 1H; ArH), 5.54 (dd, $J = 6.4$, 1.5 Hz, 1H; C*H*=C(CH_3)), 4.37 (dd, $J = 15.3$, 1.5 Hz, 1H; CH_2), 4.04 (m, 1H; C*H*(CH_3)), 3.51 (d, $J = 15.3$ Hz, 1H; CH_2), 1.78 (s, 3H; CH=C(*C*H_3)), 1.45 ppm (d, $J = 6.4$ Hz, 3H; CH(*C*H_3)); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta =$ 131.4 (CH), 124.2 (CH), 123.0 (CH), 117.3 (CH), 48.8 (CH_2), 34.5 (CH), 23.0 (CH_3), 19.3 ppm (CH_3); MS (ESI): *m/z*: 216 [$M^+ - 2$H], 201 [$M^+ - 2$H$-CH_3$], 155 [$M^+ - 2$H$-CH_3-NO_2$]; elemental analysis calcd (%) for $C_{12}H_{14}N_2O_2$ (218.26): C 66.04, H 6.47, N 12.84; found: C 66.11, H 6.78, N 12.53.

***cis*- and *trans*-2-Methyl-*N*-(4-nitrophenyl)-3-propenyl aziridine (8)**: [Ru(CO)(tpp)] (10.0 mg, 1.35×10^{-2} mmol) and 4-nitrophenyl azide (106.1 mg, 6.47×10^{-1} mmol) were added to a dry benzene solution (30.0 mL) of 2,4-hexadiene (0.50 mL, 3.90 mmol). The resulting red solution was stirred at 65 °C in a preheated oil bath. The consumption of the arylazide was monitored by TLC, until the corresponding spot was no longer observable, and then by IR spectroscopy (40 h). The reaction was considered to be finished when the absorbance of the azide band at 2121 cm^{-1} in the IR spectrum of the solution, measured with a 0.5 mm thick cell, was at or below 0.03. The obtained red solution was evaporated to dryness and the residue was purified by flash chromatography on deactivated silica gel with the use of Et_3N in *n*-hexane (10 %) during the packing of the column (*n*-hexane/ethyl acetate 10:0→9:1) to give compound **8** (53 %, *trans*-**8**/*cis*-**8** 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): *trans*-**8**: $\delta = 8.09$ (d, $J = 8.8$ Hz, 2H; ArH), 7.00 (d, $J = 8.8$ Hz, 2H; ArH), 5.93 (m, 1H; CH=C*H*(CH_3)), 5.45 (m, 1H; C*H*=CH(CH_3)), 2.73 (m, 1H; N−C*H*(CH_3)), 2.49 (m, 1H; N−C*H*(CH=CH(CH_3))), 1.80 (m, 3H; (CH=CH-(*C*H_3))), 1.36 ppm (m, 3H; N−CH(*C*H_3)); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 161.9$ (C), 142.9 (C), 131.1 (CH), 126.1 (CH), 125.6 (CH), 120.4 (CH), 46.4 (CH), 41.9 (CH), 18.4 (CH_3), 14.2 ppm (CH_3); *cis*-**8**: $\delta = 8.11$ (d, $J =$ 8.8 Hz, 2H; ArH), 7.02 (d, $J = 8.8$ Hz, 2H; ArH), 5.85 (m, 1H; CH=C*H*-(CH_3)), 5.35 (m, 1H; C*H*=CH(CH_3)), 2.99 (m, 1H; N−C*H*(CH_3)), 2.51 (m, 1H; N−C*H*(CH=CH(CH_3))), 1.82 (m, 3H; (CH=CH(*C*H_3))), 1.38 ppm (m, 3H; N−CH(*C*H_3)); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 161.7$ (C), 143.0 (C), 130.2 (CH), 126.1 (CH), 125.6 (CH), 120.6 (CH), 42.3 (CH), 41.8 (CH), 14.6 (CH_3), 14.2 ppm (CH_3); MS (EI): *cis*- + *trans*-**8**: *m/z:* 218 [M^+]; elemental analysis calcd (%) for $C_{12}H_{14}N_2O_2$ (218.26): C 66.04, H 6.47, N 12.84; found: C 66.19, H 6.61, N 12.69.

(*Z*)-2,5-Dihydro-2,5-dimethyl-7-nitro-1*H*-benzo[b]azepine (9) and *cis*- and *trans*-2,3-dihydro-2,3-dimethyl-1-(4-nitrophenyl)-1*H*-pyrrole (10): The product **8** was synthesized as described above and then silica (400 mg) was added to the reaction mixture before the isolation of **8**. *N*-aryl-2-vinylaziridines were totally consumed in 18 h. The reaction mixture was then evaporated to dryness and purified by flash chromatography (*n*-hexane/ethyl acetate 9.8:0.2→8:2) (**9**, 27 %). The same procedure was repeated by increasing the reaction temperature to reflux once the arylazide was completely consumed. After 48 h, the reaction was stopped and the mixture was purified by flash chromatography (*n*-hexane/ethyl acetate 9.8:0.2→8:2) (**9**, 36 %; **10**, 7 %, *cis*/*trans* 2:1).

Compound ***9***: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.93$ (d, $J = 2.6$ Hz, 1H; ArH), 7.88 (dd, $J = 8.5$, 2.6 Hz, 1H; ArH), 6.41 (d, $J = 8.5$ Hz, 1H; ArH), 5.71 (m, 1H; C*H*=CH), 5.38 (m, 1H; C*H*=CH), 4.64 (m, 1H; NH−C*H*-(CH_3)), 4,11 (m, 2H; C*H*(CH_3)+N*H*), 1.44 (m, 3H; NH−CH(*C*H_3)), 1.34 ppm (m, 3H; CH(*C*H_3)); ^{1}H NMR (300 MHz, C_6D_6): $\delta = 8.05$ (d, $J =$ 2.3 Hz, 1H; ArH), 7.96 (dd, $J = 8.8$, 2.3 Hz, 1H; ArH), 5.80 (d, $J = 8.8$ Hz, 1H; ArH), 5.46 (m, 1H; C*H*=CH), 5.08 (m, 1H; C*H*=CH), 4.00 (m, 1H; NH−C*H*(CH_3)), 3.63 (m, 1H; C*H*(CH_3)), 3.25 (brs, 1H; N*H*), 1.15 (m, 3H; CH_3), 0.82 ppm (m, 3H; CH_3); ^{13}C NMR (100 MHz, C_6D_6): $\delta = 135.2$ (CH), 129.4 (CH), 123.8 (CH), 123.1 (CH), 118.1 (CH), 49.1 (*C*H(CH_3)–NH), 35.0 (*C*H(CH_3)), 22.4 (CH(*C*H_3)–NH), 18.7 ppm (CH(*C*H_3)); MS (EI): *m/z:* 218 [M^+]; elemental analysis calcd (%) for $C_{12}H_{14}N_2O_2$ (218.26): C 66.04, H 6.47, N 12.84; found: C 66.18, H 6.69, N 12.66.

Compounds cis- *and* trans-***10***: ^{1}H NMR (300 MHz, $CDCl_3$): *cis*-**10**: $\delta =$ 8.11 (d, $J = 8.8$ Hz, 2H; ArH), 6.92 (d, $J = 8.8$ Hz, 2H; ArH), 5.93 (m, 1H; CH=C*H*−CH(CH_3)), 4.84 (m, 1H; N-C*H*=CH), 2.74 (m, 1H; CH−C*H*(CH_3)−CH(CH_3)), 2.40 (m, 1H; CH(CH_3)−C*H*(CH_3)−N), 1.72 (m, 3H; CH−CH(*C*H_3)−CH(CH_3)), 1.35 ppm (m, 3H; CH(CH_3)−CH(*C*H_3)−N); ^{13}C NMR (75 MHz, $CDCl_3$): *cis*-**10**: $\delta = 157.6$ (C), 142.6 (C), 131.6 (CH), 127.8 (CH), 125.4 (CH), 120.9 (CH), 48.4 (*C*H(CH_3)), 42.7 (*C*H-(CH_3)), 18.4 (CH_3), 17.1 ppm (CH_3); ^{1}H NMR (300 MHz, $CDCl_3$): *trans*-**10**: $\delta = 8.11$ (d, $J = 8.8$ Hz, 2H; ArH), 6.90 (d, $J = 8.8$ Hz, 2H; ArH), 5.79 (m, 1H; CH=C*H*−CH(CH_3)), 4.69 (m, 1H; N−C*H*=CH), 3.03 (m, 1H; CH−C*H*(CH_3)−CH(CH_3)), 2.40 (m, 1H; CH(CH_3)−C*H*(CH_3)−N), 1.88 (m, 3H; CH−CH(*C*H_3)−CH(CH_3)), 1.41 ppm (m, 3H; CH(CH_3)−CH-(*C*H_3)−N); ^{13}C NMR (75 MHz, $CDCl_3$): *trans*-**10**: $\delta = 157.4$ (C), 142.6 (C), 130.8 (CH), 126.7 (CH), 125.4 (CH), 120.9 (CH), 43.7 (*C*H(CH_3)), 43.1 (*C*H(CH_3)), 17.4 (CH_3), 13.8 ppm (CH_3); MS (EI): *cis*- + *trans*-**10**: *m/z*: 218 [M^+]; elemental analysis calcd (%) for $C_{12}H_{14}N_2O_2$ (218.26): C 66.04, H 6.47, N 12.84; found: C 66.21, H 6.42, N 12.86.

***cis*-2,3-Dihydro-1-(4-nitrophenyl)-2,3-diphenyl-1*H*-pyrrole (12)**: [Ru(CO)(tpp)] (10.5 mg, 1.42×10^{-2} mmol) and 4-nitrophenyl azide (107 mg, 6.53×10^{-2} mmol) were added to a dry benzene solution (30.0 mL) of *trans*,*trans*-1,4-diphenyl-1,3-butadiene (730 mg, 3.54 mmol). The resulting red solution was first stirred at 65 °C in a preheated oil bath for 4 h and then for 8 h more after adding silica (400 mg). The rest of the procedure was identical to that described for **2** (**12**, 50 %). The reaction was repeated by increasing the temperature to reflux after 4 h when the arylazide had been completely consumed. Compound **12** was recovered after 4 h more (70 %). ^{1}H NMR (300 MHz, C_6D_6): $\delta = 7.94$ (d, $J = 9.2$ Hz, 2H; ArH), 7.03–6.63 (m, 10H; ArH), 6.55 (d, $J = 4.2$ Hz, 1H; N-C*H*=CH), 6.21 (d, 2H, $J = 9.2$ Hz; ArH), 5.00 (dd, $J = 4.2$, 2.2 Hz, 1H; N−CH=C*H*), 4.87 (d, $J = 10.8$ Hz, 1H; N-C*H*(Ph)−CH(Ph)), 4.52 ppm (dd, $J = 10.8$, 2.2 Hz, 1H; N−CH(Ph)−C*H*(Ph)); ^{13}C NMR (75 MHz, C_6D_6): $\delta = 145.27$ (C), 138.2 (C), 136.7 (C), 132.1 (C), 129.7 (CH), 127.5 (CH), 127.1 (CH), 126.0 (CH), 112.5 (CH), 110.4 (C), 68.9 (CH), 54.8 ppm (CH); MS (ESI): *m/z*: 342 [M^+], 310 [$M^+ - 2$O]; elemental analysis calcd (%) for $C_{22}H_{18}N_2O_2$ (342.40): C 77.17, H 5.31, N 8.18; found: C 77.51, H 5.20, N 7.93.

3,4-Dimethoxy-1-(4-nitrophenyl)-1*H*-pyrrole (14): [Ru(CO)(tpp)] (9.5 mg, 1.28×10^{-2} mmol) and 4-nitrophenyl azide (102.5 mg, 6.25×10^{-1} mmol) were added to a dry benzene solution (30.0 mL) of 2,3-dimethoxy-1,3-butadiene (0.40 mL, 3.13 mmol). The resulting dark solution was stirred at 65 °C in a preheated oil bath. The consumption of the arylazide was monitored by TLC, until its spot was no longer observable, and then by IR spectroscopy (36 h). After chromatographic purification, pure pyrrole **14** was obtained as an orange solid in 60 % yield. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.25$ (d, $J = 9.2$ Hz, 2H; ArH), 7.32 (d, $J = 9.2$ Hz, 2H; ArH), 6.63 (s, 2H; CH), 3.83 ppm (s, 6H; OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 145.8$ (C), 143.4 (C), 142.8 (C), 126.1 (CH), 116.8 (CH), 99.6 (CH), 58.7 ppm (OCH_3); MS (ESI): *m/z*: 248 [M^+], 233 [$M^+ - CH_3$]; elemental analysis calcd (%) for $C_{12}H_{12}N_2O_4$ (248.24): C 58.06, H 4.87, N 11.28; found: C 58.10, H 4.94, N 11.44.

(*Z*)-2,5-Dihydro-4-(4-methylpent-3-enyl)-7-nitro-1*H*-benzo[b]azepine (16) and (*Z*)-2,5-dihydro-3-(4-methylpent-3-enyl)-7-nitro-1*H*-benzo[b]-azepine (17)

Method A: [Ru(CO)(tpp)] (10.4 mg, 1.40×10^{-2} mmol) and 4-nitrophenyl azide (107 mg, 6.53×10^{-1} mmol) were added to a dry benzene solution (30 mL) of myrcene (0.57 mL, 3.35 mmol). The resulting red solution was stirred first at 65 °C for 12 h in a preheated oil bath and then for 18 h more after adding silica (400 mg). The obtained red solution was evaporated to dryness and the residue was purified by flash chromatography on deactivated silica gel with use of Et_3N in *n*-hexane (10 %) during the packing of the column (*n*-hexane/ethyl acetate 9:1→8:2) (**17**, 55 %).

Method B: The reaction was repeated by increasing the temperature to reflux after the starting arylazide had been completely consumed. A mixture of **17** (43 %) and **16** (17 %) was recovered after 60 h as already described for method A.

Method C: [Ru(CO)(tpp)] (9.7 mg, 1.31×10^{-2} mmol), TEMPO (3.2 mg, 2.05×10^{-2} mmol), and 4-nitrophenyl azide (103.5 mg, 6.31×10^{-1} mmol) were added to a dry benzene solution (30 mL) of myrcene (0.57 mL, 3.35 mmol). The resulting red solution was stirred at 65°C for 4 h in a preheated oil bath. The isolation of **16** and **17** was performed as already described for method A (**16**, 13%; **17**, 60%).

Compound ***16***: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.83$ (d, $J=8.8$ Hz, 1H; ArH), 7.81 (s, 1H; ArH), 6.31 (d, $J=8.8$ Hz, 1H; ArH), 5.61 (t, $J=6.9$ Hz, 1H; $CH_2-CH=C$), 5.04 (brs, 1H; $CH=C(CH_3)_2$), 4.88 (brs, 1H; NH), 3.96 (s, 2H; CH_2), 3.53 (d, $J=6.9$ Hz, 2H; CH_2), 2.19–2.12 (s, 4H; CH_2-CH_2), 1.65 (s, 3H; CH_3), 1.55 ppm (s, 3H; CH_3); ^{1}H NMR (300 MHz, C_6D_6): $\delta=7.83$ (d, $J=9.0$ Hz, 1H; ArH), 7.81 (s, 1H; ArH), 5.60 (d, $J=9.0$ Hz, 1H; ArH), 5.25 (t, $J=6.6$ Hz, 1H; CH_2-CH-C), 5.04 (m, 1H; $CH-C(CH_3)_2$), 3.60 (brs, 1H; NH), 3.20 (d, $J=6.6$ Hz, 2H; CH_2), 3.02 (s, 2H; CH_2), 1.95 (m, 4H; CH_2-CH_2), 1.62 (s, 3H; CH_3), 1.45 ppm (s, 3H; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=153.1$ (C), 145.8 (C), 137.5 (C), 132.1 (C), 126.7 (CH), 124.3 (CH), 123.4 (CH), 120.6 (C), 118.7 (CH), 115.4 (CH), 41.4 (CH_2), 37.5 (CH_2), 36.7 (CH_2), 26.2 (CH_2), 25.6 (CH_3), 17.7 ppm (CH_3); MS (EI): m/z: 272 [M^+]; elemental analysis calcd (%) for $C_{16}H_{20}N_2O_2$ (272.35): C 70.56, H 7.40, N 10.29; found: C 70.34, H 7.63, N 10.45.

Compound ***17***: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.84$ (dd, $J=8.8$, 2.5 Hz, 1H; ArH), 7.81 (d, $J=2.5$ Hz, 1H; ArH), 6.33 (d, $J=8.8$ Hz, 1H; ArH), 5.88 (t, $J=6.9$ Hz, 1H; CH_2-CH-C), 5.08 (brs, 1H; $CH=C(CH_3)_2$), 4.76 (brs, 1H; NH), 4.01 (s, 2H; CH_2), 3.49 (d, $J=6.9$ Hz, 2H; CH_2), 2.14 (s, 4H; CH_2-CH_2), 1.67 (s, 3H; CH_3), 1.60 ppm (s, 3H; CH_3); ^{1}H NMR (300 MHz, C_6D_6): $\delta=7.83$ (dd, $J=9.1$, 2.6 Hz, 1H; ArH), 7.81 (d, $J=2.6$ Hz, 1H; ArH), 5.77 (d, $J=9.1$ Hz, 1H; ArH), 5.51 (t, $J=7.0$ Hz, 1H; CH_2-CH-C), 5.10 (m, 1H; $CH=C(CH_3)_2$), 3.96 (brs, 1H; NH), 3.35 (s, 2H; CH_2), 2.94 (d, $J=7.0$ Hz, 2H; CH_2), 2.00 (m, 2H; CH_2-CH_2), 1.95 (m, 2H; CH_2-CH_2), 1.62 (s, 3H; CH_3), 1.51 ppm (s, 3H; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=154.8$ (C), 140.5 (C), 139.2 (C), 133.7 (C), 128.1 (CH), 126.1 (CH), 125.9 (CH), 124.9 (CH), 123.4 (C), 116.3 (CH), 46.4 (CH_2), 37.5 (CH_2), 32.9 (CH_2), 28.0 (CH_2), 26.6 (CH_3), 18.5 ppm (CH_3); MS (ESI): m/z: 272 [M^+], 203 [$M^+-CH_2CHC(CH_3)_2$], 157 [$M^+-CH_2CHC(CH_3)_2-NO_2$]; elemental analysis calcd (%) for $C_{16}H_{20}N_2O_2$ (272.35): C 70.56, H 7.40, N 10.29; found: C 70.29, H 7.68, N 10.03.

(*Z*)-2,5-Dihydro-3-methyl-7-nitro-1*H*-benzo[b]azepine (19): This reaction was run in a pressure tube under a nitrogen atmosphere. [Ru(CO)(tpp)] (6.6 mg, 8.90×10^{-3} mmol) and 4-nitrophenyl azide (76.0 mg, 4.64×10^{-1} mmol) were added to a dry benzene solution (10 mL) of isoprene (0.44 mL, 4.40 mmol). The resulting red solution was stirred at 80°C in a preheated oil bath for 14 h. After this time, the red solution was evaporated to dryness and the residue was purified by flash chromatography (*n*-hexane/ethyl acetate 9.5:0.5→7:3) (**19**, 51%). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.88$ (dd, $J=8.7$, 2.6 Hz, 1H; ArH), 7.84 (d, $J=2.6$ Hz, 1H; ArH), 6.48 (d, $J=8.7$ Hz, 1H; ArH), 5.85 (t, $J=6.6$ Hz, 1H; $CH=C(CH_3)$), 4.63 (brs, 1H; NH), 3.97 (s, 2H; CH_2), 3.50 (d, $J=6.6$ Hz, 2H; CH_2), 1.83 ppm (s, 3H; CH_3); ^{1}H NMR (300 MHz, C_6D_6): $\delta=7.94$ (dd, $J=8.9$, 2.4 Hz, 1H; ArH), 7.83 (d, $J=2.4$ Hz, 1H; ArH), 5.74 (d, $J=8.9$ Hz, 1H; ArH), 5.52 (m, 1H; $CH=C(CH_3)$), 3.40 (brs, 1H; NH), 3.21 (s, 2H; CH_2), 2.97 (m, 2H; CH_2), 1.55 ppm (s, 3H; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=153.1$ (C), 138.8 (C), 133.6 (C), 126.7 (CH), 124.7 (CH), 124.4 (CH), 116.8 (CH), 47.6 (CH_2), 32.4 (CH_2), 22.9 ppm (CH_3); MS (ESI): m/z: 204 [M^+], 203 [M^+-H], 157 [M^+-CH_3-2O], 143 [$M^+-CH_3-NO_2$]; elemental analysis calcd (%) for $C_{11}H_{12}N_2O_2$ (204.23): C 64.69, H 5.92, N 13.72; found: C 64.42, H 5.61, N 13.95.

(*Z*)-2,5-Dihydro-4-methyl-7-nitro-1*H*-benzo[b]azepine (20): Compound **18**[51] (10 mg, 4.90×10^{-2} mmol) was dissolved under nitrogen in distilled benzene (10 mL). Silica (100 mg) was then added and the yellow solution was left stirring at 65°C under nitrogen. The conversion of **18** was monitored by TLC (silica, *n*-hexane/ethyl acetate 8:2). After 24 h, the solvent was evaporated to dryness and the residue was purified by flash chromatography (*n*-hexane/ethyl acetate 9.5:0.5→7:3) to give **20** (75%). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.86$ (d, $J=8.8$ Hz, 1H; ArH), 7.84 (s, 1H; ArH), 6.32 (d, $J=8.8$ Hz, 1H; ArH), 5.65 (m, 1H; $CH=C(CH_3)$), 4.70 (brs, 1H; NH), 3.97 (m, 2H; CH_2), 3.50 (s, 2H; CH_2), 1.91 ppm (s, 3H; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=153.4$ (C), 142.4 (C), 138.3 (C), 127.1 (CH), 124.7 (CH), 121.1 (C), 119.5 (CH), 116.0 (CH), 42.0 (CH_2), 38.1 (CH_2), 23.8 ppm (CH_3); MS (EI): m/z: 204 [M^+]; elemental analysis calcd (%) for $C_{11}H_{12}N_2O_2$ (204.23): C 64.69, H 5.92, N 13.72; found: C 64.47, H 5.81, N 13.65.

Theoretical calculations: All calculations were performed with the Jaguar 6.0 quantum chemistry package,[67] by using DFT with the B3LYP hybrid functional,[68,69] which is known to give good descriptions of reaction profiles for pericyclic reactions.[70] All molecules were optimized in gas phase by employing a 6-31G(d) basis set.[71] Frequency calculations were performed to verify the correct nature of the stationary points (and to estimate zero-point energy (ZPE) and vibrational entropy corrections at room temperature). Intrinsic reaction coordinate (IRC) calculations were employed to correctly locate reagents and products. The energies of all stationary points have been revaluated with single-point calculations by using the larger 6-311++G(d,p) set.[72] For the considered *N*-aryl-2-vinylaziridines, a preliminary conformational search was performed on both *cis*- and *trans* invertomers at the semiempirical AM1 level; each conformer was subsequently submitted to geometry optimization and energy re-evaluation at the DFT levels described above.

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