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Kinetic and Mechanistic Studies of Base-Catalyzed Phenylselenoetherification of (*Z*)- and (*E*)-Hex-4-en-1-ols

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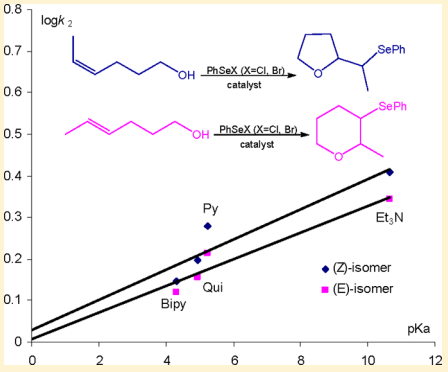
Supporting Information

ABSTRACT: The mechanism of phenylselenoetherification of (*Z*)- and (*E*)-hex-4-en-1-ols using some bases (triethylamine, pyridine, quinoline, 2,2′-bipyridine) as catalysts and some solvents [tetrahydrofuran (THF) and CCl_4] as reaction media was examined through studies of kinetics of the cyclization by UV−vis spectrophotometry. It was demonstrated that the intramolecular cyclization is facilitated in the presence of bases as a result of the hydrogen bond between the base and the alkenol's OH group. The rate constants in the base-catalyzed reactions are remarkably influenced by the bulkiness and basicity of the base used and the nature of the considered nitrogen donors. The obtained values for rate constants show that the reaction with triethylamine is the fastest one. THF with higher polarity and higher basic character is better as a solvent than CCl_4. Quantum-chemical calculations [MP2(fc)/6-311+G**//B3LYP/6-311+G** + ZPE(B3LYP/6-311+G**] show that the cyclization of (*Z*)-hex-4-en-1-ol to a tetrahydrofuranoid five-membered ring is kinetically controlled, while the cyclization of (*E*)-hex-4-en-1-ol to the tetrahydropyranoid six-membered ring is thermodynamically controlled. This is in accordance with previous experimental findings.

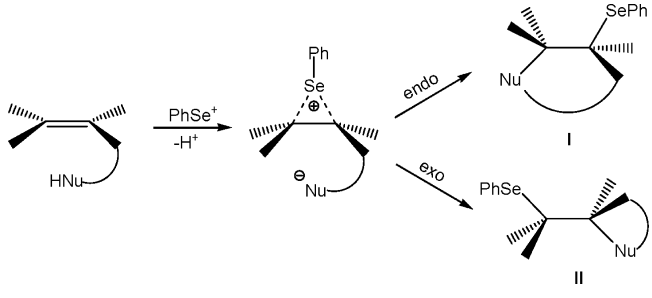


INTRODUCTION

Cycloetherifications induced by electrophilic reagents are important tools in the synthesis of complex organic molecules.[1] Selenium electrophiles are quite powerful and able to react with double bonds to generate, after an addition of nucleophile, the corresponding addition products.[2] This is a two-step mechanism that involves the formation of a seleniranium intermediate followed by nucleophilic attack to yield the final product. These reactions exhibit anti stereoselectivity, with the nucleophile attacking usually at the more highly substituted carbon atom (Markownikoff stereoselectivity). The products of these selenenylations are very useful because wide ranges of alkenes and nucleophiles can be employed in these transformations and many different subsequent reactions are possible.[3] The presence of internal nucleophiles leads to cyclization reactions, which have been employed in various syntheses for a long time.[4] Cyclofunctionalizations of alkenols promoted by PhSeX (X = Cl, Br) reagents are advantageous in the preparation of tetrahydrofuran (THF)- and tetrahydropyran-type rings because of the mild conditions and low temperatures required for these reactions, which usually allow high stereoselectivity.[5] Depending on the chain length and the substitution pattern on the alkenol, the reaction can occur by an endo or an exo pathway, leading to cyclic products **I** and/or **II**, respectively. As shown in Scheme 1, the cyclization reactions are stereospecific anti additions.

In the past few years, we have investigated the influence of steric hindrance on the yields and regio- and stereoselectivities of phenylselenoetherification reactions of unsaturated Δ^4- and Δ^5-alcohols.[6] For that purpose, we performed cyclization reactions of some alkenols with mono-, di-, and trialkyl-substituted double bonds and/or carbinol carbon atoms.

Scheme 1. Cycloetherification of Unsaturated Alcohols



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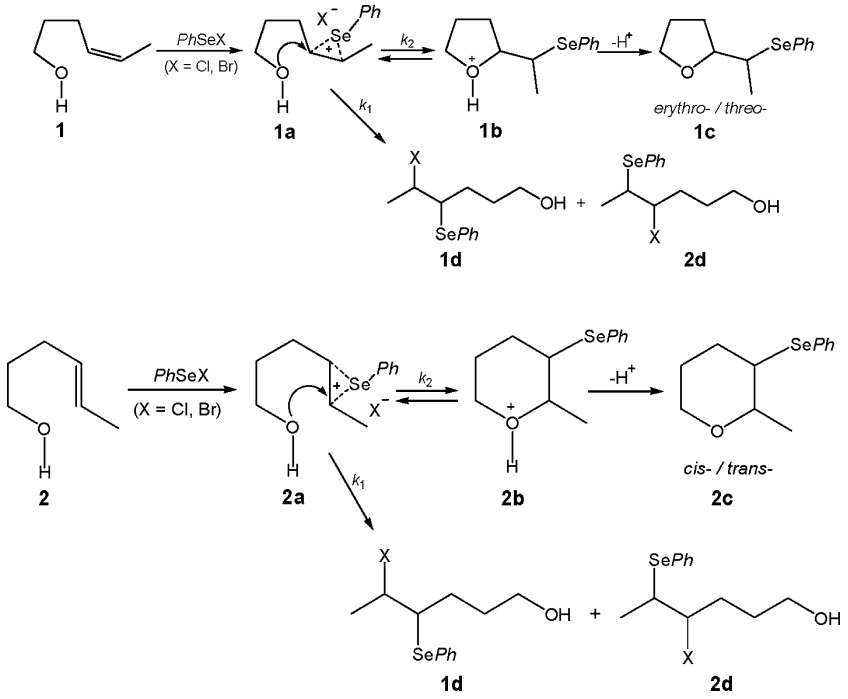
Scheme 2. Cycloetherifications of (*Z*)- and (*E*)-Hex-4-en-1-ol



Intramolecular heterocyclization is the main reaction in the case of all of the investigated primary and secondary alkenols, while tertiary alkenols, under the same experimental conditions, are converted into cyclic products not at all by PhSeBr and in only small amounts by PhSeCl. On the other hand, in the presence of some Lewis bases (triethylamine, pyridine, quinoline, 2,2′-bipyridine) and Lewis acids ($SnCl_2$, $CoCl_2$, Ag_2O, $AlCl_3$, $FeCl_3$) all of the alkenols (primary, secondary, and tertiary) cyclized in excellent yields with both reagents.[7]

Two geometric isomeric alcohols, (*Z*)-hex-4-en-1-ol (**1**) and (*E*)-hex-4-en-1-ol (**2**) are very interesting substrates in terms of stereo- and regioselectivity. In our previous work, we examined the regio- and stereoselectivities in cyclization reactions of these two alkenols with PhSeX (X = Cl, Br) in the presence of various additives.[7a] Very high regioselectivity was determined by steric effects of the methyl group in these two geometric isomers, and the careful selection of the additive (Lewis acid or base) was found to lead to the appearance of high stereoselectivity in these reactions. In the presence of a Lewis base, the main product of the cyclization of alkenol **1** was the erythro isomer, and the alkenol **2** gave the cis isomer in excess. The best results were obtained in the presence of Et_3N. When the reaction of alkenol **1** was performed in the presence of Et_3N, a single erythro stereoisomer was obtained, while in the case of other bases it was formed in excess. With alkenol **2**, the unexpected product (cis isomer) was indeed obtained in good yield, but this was accompanied by considerable amounts of the trans product. With Lewis acids as additives, alkenol **1** gave the threo isomer as the main product, and in the case of alkenol **2**, the trans isomer predominated. The best results with both alkenols (**1** and **2**) and both reagents (PhSeCl and PhSeBr) were obtained when $SnCl_2$ was used as an additive. The cyclic ether product was obtained in almost quantitative yield; in the case of alkenol **1**, the threo isomer was formed in large excess, while alkenol **2** gave the trans isomer as the main product. $CoCl_2$ as an additive also gave cyclic ether products in high yields, but in the reaction with alkenol **1**, stereoselectivity was lower than with $SnCl_2$ as the additive.

The scope of this work is to determine the kinetics and mechanism of these reactions and the catalytic role of the additive. For detailed discussion and confirmation of the mechanism of these reactions, we used a conventional kinetic method to determine the values of the rate constants. To investigate the single steps from the seleniranium ion to the cyclic isomers we applied quantum-chemical methods. It was also of interest in the present work to compare the influences of two different solvents (THF and CCl_4) on the values of the rate constants. Also, we examined the roles of the bulkiness and basicity of the additive on the catalytic activity in these reactions.

EXPERIMENTAL SECTION

UV−Vis Spectrophotometric Study. A conventional kinetic method for determination of the values of the rate constants and thermodynamic parameters was used, regarding the reaction as a nucleophilic displacement of the hydroxyl group on the C atom in the seleniranium intermediate (**1a** or **2a**; see Scheme 2).[8] Kinetic measurements were performed on a PerkinElmer Lambda 35 UV−vis spectrophotometer equipped with a water-thermostatted cell. For the determination of the activation parameters and the reaction mechanism, reactions were followed at 308, 298, and 288 K, and for investigation of the catalytic activity of Lewis bases, the reaction temperature was thermostatted at 288 K. The solutions of reactants were prepared by measuring calculated amounts of substances in THF and CCl_4 as solvents. In a quartz cuvette, a certain volume of alcohol solution and then the additive were added, and the reaction was initiated by adding phenylselenenyl halide (PhSeX, X = Cl, Br). The concentration of PhSeX was kept constant (1×10^{-4} M), and the alcohol concentrations of 2.5×10^{-3}, 2×10^{-3}, 1.5×10^{-3}, and 1×10^{-3} M were used. When the concentration of alcohol was 5 ×

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10^{-4} M, to maintain pseudo-first-order kinetic conditions, the concentration of PhSeX was lowered to 5×10^{-5} M. In the reactions with additives present, their concentrations were equal to the PhSeX concentration.

After preliminary repetitive scan experiments in the 600−220 nm range to search for isosbestic points and spectral changes, the kinetics was studied by measuring the changing absorbance at a suitable wavelength as a function of time.

The pseudo-first-order rate constants (k_{obs}) were determined according to eq 1 (see below) by fitting each of the kinetic runs to a single-exponential function. Second-order rate constants (k_2) were determined by linear regression of the k_{obs} values versus the alkenol concentration. The observed pseudo-first-order rate constants were calculated as averages of two to five independent kinetic runs using the computer programs Microsoft Excel and Origin 6.1. The obtained experimental data are reported in Tables 1−3.

Quantum-Chemical Calculations. All of the structures were fully optimized at the B3LYP/6-311+G** level[9] and characterized as minima or transition-state structures by computation of vibrational frequencies [for minima, all frequencies are positive, and the number of imaginary frequencies (N_{imag}) is equal to zero; for transition-state structures, exactly one imaginary frequency is present (N_{imag} = 1)]. Being well aware of the limitations of DFT calculations,[10] we evaluated the energies using MP2(fc)/6-311+G** calculations [MP2(fc)/6-311+G**//B3LYP/6-311+G** + ZPE-(B3LYP/6-311+G**), further denoted as MP2(f)-SP].[11] The Gaussian 03 suite of programs[12] was used throughout.

RESULTS AND DISCUSSION

The reaction between alcohol **1** or **2** and the phenylselenenyl halide starts with electrophilic attack of the phenylselenenyl group on the double bond of the alkenol, which results in the formation of a seleniranium cation (**1a** or **2a**; Scheme 2). In the next phase of the reaction, this seleniranium intermediate can be trapped by an internal nucleophile (the hydroxyl group of the alcohol) to give the cyclizated oxonium ion (**1b** or **2b**) or by an external nucleophile (the halide ion of PhSeX) to give the addition product (**1d** or **2d**). Finally, the generation of the five- or six-membered cyclic phenylseleno ether (**1c** or **2c**, respectively) ensues upon elimination of the proton from the oxonium ion. The attack on the seleniranium cation by the internal or external nucleophile is the rate-determining step.[13,14] The *Z* isomer produces only THF- type rings, while the *E* isomer gives only tetrahydropyran-type ones.

The reactions between PhSeX (X = Cl, Br) and (*Z*)-hex-4-en-1-ol (**1**) and (*E*)-hex-4-en-1-ol (**2**) in the presence or absence of various additives were studied under pseudo-first-order conditions in CCl_4 or THF as the solvent by UV−vis spectrophotometry. The wavelengths at which the kinetic measurements were performed were predetermined spectrophotometrically by recording the UV−vis spectral changes of the alkenol and reagent solutions over the 600−220 nm range. Pseudo-first-order rate constants (k_{obs}) were obtained from analysis of the single-exponential kinetic traces (Figure 1) by online nonlinear least-squares fits of the experimental data to eq 1:

$$A_t = A_0 + (A_0 - A_\infty) \exp(-k_{obs} t) \quad (1)$$

where A_0, A_t, and A_∞ represent the absorbance of the reaction mixture initially, at time t, and at the end of the reaction, respectively.

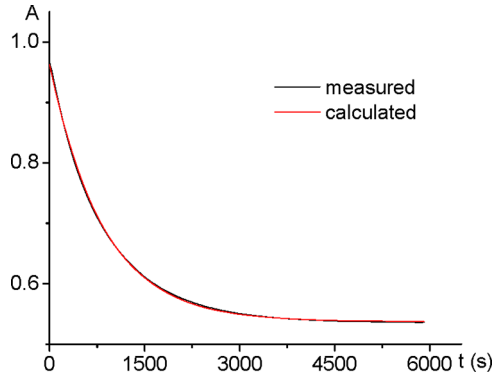

Figure 1. Kinetic traces for the reaction between (*Z*)-hex-4-en-1-ol (C = 1.5 mM) and PhSeBr (C = 0.1 mM) in THF as a solvent at 288 K, λ = 250 nm.

The values of k_{obs} increased linearly with increasing alkenol concentration, as shown typically in Figures 2 and 3 (the data are given in Tables S.1−S.4 in the Supporting Information). The k_{obs} values as a function of total alkenol concentration can be described by eq 2:

$$k_{obs} = k_1 + k_2[\text{alkenol}] \quad (2)$$

where k_2 is the second-order rate constant for the forward reaction, whose rate depends on the alkenol concentration, and k_1 is rate constant for the parallel substitution reaction (Scheme 2), whose rate is independent of the alkenol concentration.[8] The values of k_1 and k_2 determined from the intercepts and slopes, respectively, of the plots of k_{obs} versus [alkenol] obtained for reactions at different temperatures in the presence or absence of pyridine (Figure 2 for **1** and Figure 3 for **2**) are summarized in Table 1. These values were used to construct Eyring plots (e.g., Figure 4), from which values of the enthalpy ($\Delta H^{\ddagger}$) and entropy ($\Delta S^{\ddagger}$) of activation were determined (see Table 1). The negative values of $\Delta S^{\ddagger}$ indicate that the reactions of PhSeX (X = Cl, Br) with (*Z*)- and (*E*)-hex-4-en-1-ol in the presence or absence of pyridine follow the mechanism of bimolecular nucleophilic substitution (S_N2 pathway). The results in Table 1 confirm the catalytic role of pyridine in these reactions. All of the reactions performed in the presence of pyridine were on average 2 times faster than those without pyridiine. Also, reactions with PhSeCl as a reagent were 4 times faster than those with PhSeBr. It was observed in previous work[7a] that compared with reactions performed with PhSeCl, the use of PhSeBr as a reagent affords lower yields of cyclic ether products, while the yields of the side reaction increase. The reason for this behavior can be explained by the higher nucleophility of the bromide ion, which preferentially forms an ion pair with the carbon atom of the seleniranium intermediate and then with selenium, interfering with the approach of the oxygen of the hydroxyl group. Therefore, the lower values of k_2 in reactions with PhSeBr are another validation of the synthetic results.

As described in our previous work,[7a] the role of the Lewis base (e.g., pyridine) in this reaction is to increase the nucleophilicity of the oxygen atom of the hydroxyl group by creating a hydrogen bond with its proton. In this way, the concurrent influence of the halide ion nucleophile is diminished, which is reflected in a decrease in k_1, the rate constant for the parallel reaction (Tables 1 and 3 and Figures 2 and 3).

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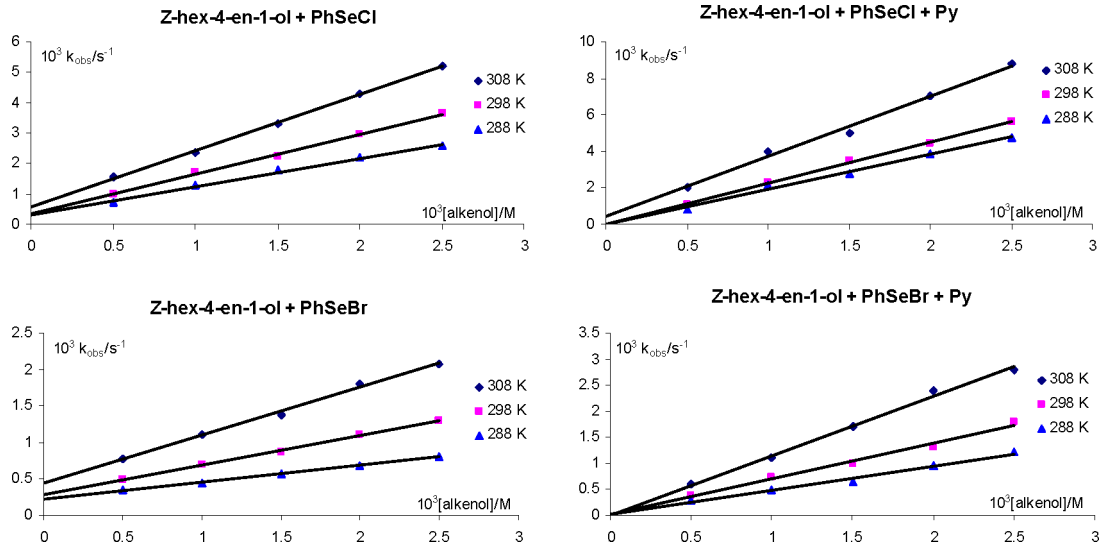

Figure 2. Pseudo-first-order rate constant k_{obs} as a function of the alkenol concentration and the temperature for the reactions between PhSeX (X = Cl, Br) and (*Z*)-hex-4-en-1-ol in THF as the solvent in the presence or absence of pyridine.

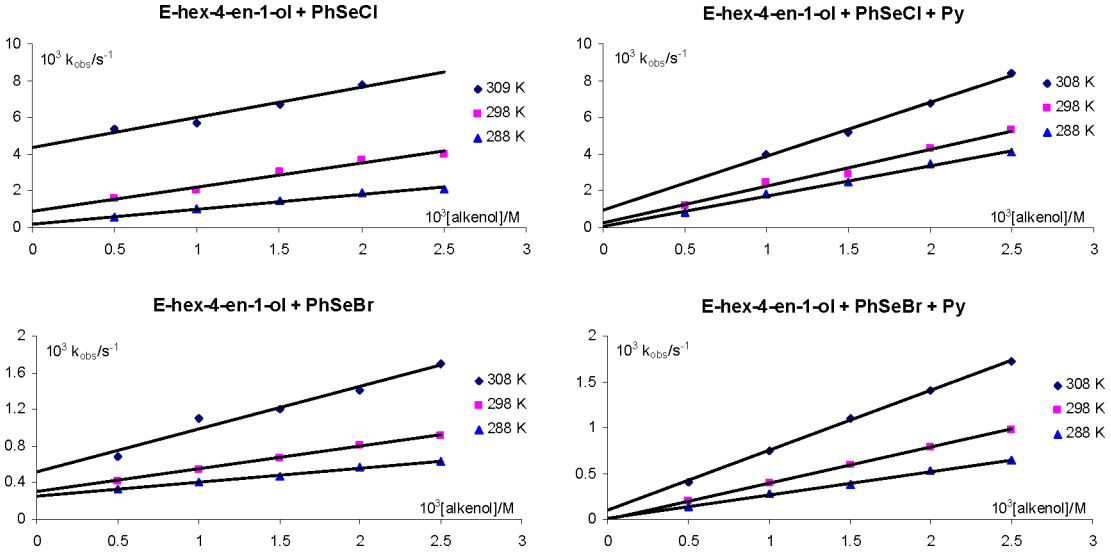

Figure 3. Pseudo-first-order rate constant k_{obs} as a function of the alkenol concentration and the temperature for the reaction between PhSeX (X = Cl, Br) and (*E*)-hex-4-en-1-ol in THF as the solvent in the presence or absence of pyridine.

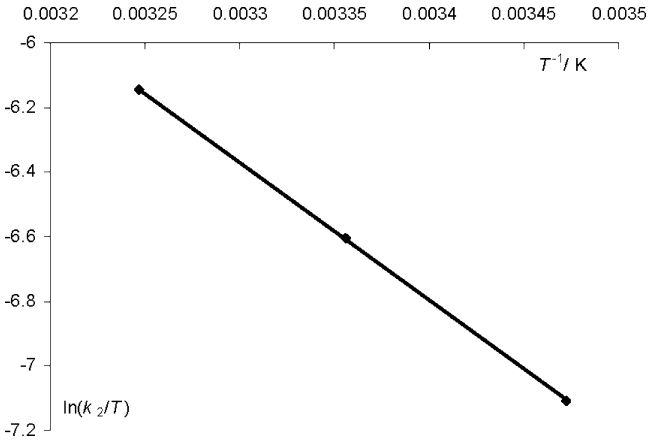

Figure 4. Eyring plot for the PhSeBr-induced cyclization of (*Z*)-hex-4-en-1-ol in THF.

Table 2 presents the values of k_2 in the presence of various base catalysts in THF as the solvent. The values of k_1 in these reactions were insignificantly small and therefore are not presented in Table 2. The k_2 values in base-catalyzed reactions are remarkably influenced by the nature of the nitrogen donor. Pyridine and quinoline have very similar pK_a values (5.23 and 4.94, respectively) and donor numbers (DN) (33.1 and 32.0, respectively) but quite different catalytic activities. This behavior is even more noticeable in the case of triethylamine. For such a high pK_a value (pK_a = 10.64, DN = 61.0), k_2 is increased by only 35% relative to that for the pyridine-catalyzed reaction. These results can be ascribed to the different steric effects of these bases in the transition state. Hydrogen bonding of the base to the hydroxyl group makes the approach of oxygen in the ring-closing phase more difficult, which results in a lower rate constant (Figure 5). This phenomenon is even more distinct in the base-catalyzed intramolecular cyclization of 6-methylhept-5-en-2-ol (**3**).[14] Without additive present, the phenylselenoetherification of this secondary alkenol with the

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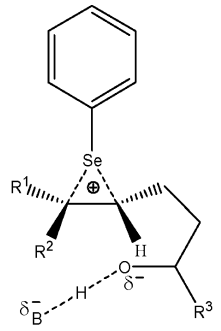
Table 1. Rate Constants and Activation Parameters for the Reactions between PhSeX and Isomeric (*Z*)- and (*E*)-Hex-4-en-1-ol in the Presence or Absence of Pyridine in THF as the Solvent

		PhSeCl					PhSeBr				
	T (K)	λ (nm)	k_2 (M^{-1} s^{-1})	k_1 (s^{-1})	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J K^{-1} mol^{-1})	λ (nm)	k_2 (M^{-1} s^{-1})	k_1 (s^{-1})	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J K^{-1} mol^{-1})
(*Z*)-hex-4-en-1-ol	288	245	0.93 ± 0.03	(3.1 ± 0.6) × 10^{-4}	22.9 ± 0.5	−181 ± 2	250	0.236 ± 0.008	(2.2 ± 0.1) × 10^{-4}	35.5 ± 0.3	−149 ± 1
	298		1.31 ± 0.03	(3.4 ± 0.5) × 10^{-4}				0.404 ± 0.009	(2.9 ± 0.2) × 10^{-4}		
	308		1.85 ± 0.03	(5.6 ± 0.6) × 10^{-4}				0.66 ± 0.03	(4.4 ± 0.4) × 10^{-4}		
(*Z*)-hex-4-en-1-ol + pyridine	288	246	1.9 ± 0.1	–	18 ± 0.5	−190 ± 20	251	0.47 ± 0.03	–	30 ± 4	−162 ± 13
	298		2.24 ± 0.05	–				0.68 ± 0.04	–		
	308		3.3 ± 0.2	(4 ± 3) × 10^{-4}				1.14 ± 0.05	–		
(*E*)-hex-4-en-1-ol	288	245	0.79 ± 0.05	(2.2 ± 0.8) × 10^{-4}	24 ± 6	−180 ± 20	250	0.153 ± 0.007	(2.5 ± 0.1) × 10^{-4}	39 ± 4	−141 ± 14
	298		1.3 ± 0.1	(9 ± 2) × 10^{-4}				0.248 ± 0.007	(3.0 ± 0.1) × 10^{-4}		
	308		1.6 ± 0.3	(44 ± 4) × 10^{-4}				0.47 ± 0.05	(5.1 ± 0.9) × 10^{-4}		
(*E*)-hex-4-en-1-ol + pyridine	288	245	1.64 ± 0.08	–	18 ± 5	−190 ± 20	251	0.254 ± 0.008	–	32 ± 2	−160 ± 7
	298		2.0 ± 0.2	(2 ± 3) × 10^{-4}				0.392 ± 0.002	–		
	308		3.0 ± 0.1	(9 ± 3) × 10^{-4}				0.65 ± 0.01	–		

Table 2. Rate Constants for Phenylselenoetherification of (*Z*)-Hex-4-en-1-ol (1), (*E*)-Hex-4-en-1-ol (2), and 6-Methylhept-5-en-2-ol (3) with PhSeCl in THF at 288 K in the Presence of Various Lewis Bases

		k_2 (M^{-1} s^{-1})		
additive	pK_a	**1**	**2**	**3**[a]
triethylamine	10.64	2.56 ± 0.05	2.20 ± 0.05	0.77 ± 0.03
pyridine	5.23	1.9 ± 0.1	1.64 ± 0.08	0.55 ± 0.02
quinoline	4.94	1.57 ± 0.06	1.43 ± 0.05	0.49 ± 0.01
2,2-bipyridine	4.3	1.4 ± 0.1	1.32 ± 0.09	0.48 ± 0.02
no additive		0.93 ± 0.03	0.79 ± 0.05	0.63 ± 0.02

[a]Data taken from ref 14.



(*Z*)-hex-4-en-1-ol R^1= Me; R^2 = H; R^3 = H

(*E*)-hex-4-en-1-ol R^1= H; R^2 = Me; R^3 = H

6-Me-hept-5-en-2-ol R^1= Me; R^2 = Me; R^3 = Me

Figure 5. Steric hindrance in ring-closing phase.

trisubstituted double bond exclusively gives a five-membered ring (anti-Markownikoff's rule). In the presence of a Lewis base, because of the greater steric hindrance in the transition state, the creation of the six-membered ring can occur. Besides the effects on the regioselectivity, the Lewis base also influences the reaction by decreasing the reaction rate (except for Et_3N; Table 2). Compared to (*Z*)- and (*E*)-hex-4-en-1-ol, 6-methylhept-5-en-2-ol as a more substituted alkenol is more sensitive to steric bulkiness in the rate-determining cyclization step and therefore exhibits lower rate constants with or without base present.

As presented in Figure 6, a linear relationship between log k_2 and pK_a exists; therefore, the base additive increases the rate and yield of reaction with the same reaction mechanism. The

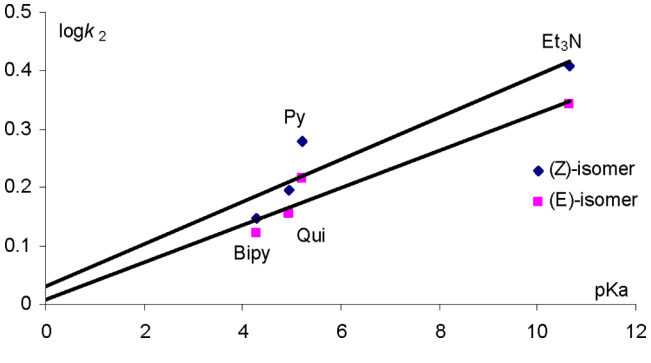


Figure 6. Plots of log k_2 vs pK_a of the base catalyst used in the phenylselenoetherification of (*Z*)- and (*E*)-hex-4-en-1-ol with PhSeCl in THF as the solvent.

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Table 3. Rate Constants for Phenylselenoetherification of (*Z*)- and (*E*)-Hex-4-en-1-ol with PhSeX with or without Pyridine in CCl_4 at 288 K

	PhSeCl			PhSeBr		
	λ (nm)	k_2 (M^{-1} s^{-1})	k_1 (s^{-1})	λ (nm)	k_2 (M^{-1} s^{-1})	k_1 (s^{-1})
(*Z*)-hex-4-en-1-ol	280	0.64 ± 0.03	(6 ± 0.09) × 10^{-4}	262	0.178 ± 0.004	(1.63 ± 0.08) × 10^{-4}
(*Z*)-hex-4-en-1-ol + pyridine	280	1.74 ± 0.08	–	262	0.40 ± 0.01	–
(*E*)-hex-4-en-1-ol	261	0.58 ± 0.01	(8.2 ± 0.2) × 10^{-4}	261	0.108 ± 0.008	(2.8 ± 0.1) × 10^{-4}
(*E*)-hex-4-en-1-ol + pyridine	261	1.10 ± 0.06	–	261	0.22 ± 0.01	–

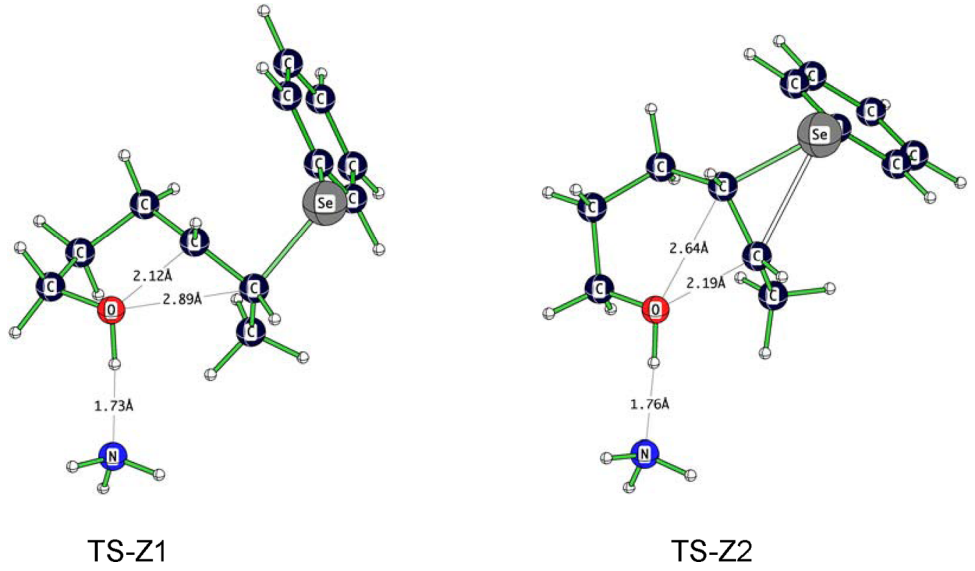

Figure 7. B3LYP/6-311+G**-calculated transition-state structures for the cyclization of (*Z*)-hex-4-en-1-ol.

slopes (β) obtained from the linear fits for the two isomeric alkenols are slightly different: β = 0.04 ± 0.01 for the *Z* isomer and β = 0.032 ± 0.007 for the *E* isomer. The higher β value for the *Z* isomer reflects the higher sensitivity of the reaction rate to the base catalyst.[15]

Table 3 presents the rate constants for phenylseleno-induced cyclization of (*Z*)- and (*E*)-hex-4-en-1-ol in the presence or absence of pyridine in CCl_4 at 288 K. Tetrachlorometane (ε = 2.2, DN = 0) as a nonpolar solvent proved to be a worse reaction medium than THF (ε = 7.6, DN = 20), resulting in lower reaction rates. Therefore, these results illustrate that solvents with higher polarity and higher basicity (THF vs CCl_4) can better stabilize the charged transition state and increase the reaction rate. Besides its polarity, the possibility that THF can form a hydrogen bond with the hydroxyl group's proton seems to be quite significant for its positive influence on the reaction rate.

To learn more about the reactions on a molecular level, we performed quantum-chemical calculations on the reaction pathways leading to the five- and six-membered-ring species. Therefore, we calculated results for (*Z*)- and (*E*)-hex-4-en-1-ol with NH_3 as the base.

Inspection of all of the possible cyclization products, still hydrogen-bonded to NH_4^+ and attached to the PhSe fragment, already gives first mechanistic ideas. Cyclization of (*E*)-hex-4-en-1-ol (**2**) results experimentally in the six-membered-ring tetrahydropyranoid structure, which at the MP2(f)-SP level is favored by 4 kcal mol^{-1} relative to the alternative five-membered heterocycle. In contrast, (*Z*)-hex-4-en-1-ol (**1**) reacts to give the five-membered tetrahydrofuranoid ring. The two possible reaction products are nearly energetically equivalent, favoring the tetrahydropyranoid form by a hardly significant 0.6 kcal mol^{-1} at the MP2(f)-SP level.

Starting the mechanistic investigation of **1** at the seleniranium **1a** leads to two transition states, one forming the five-membered ring and one forming the six-membered oxane. While the formation of the tetrahydrofuranoid ring passes an energy barrier of 7.5 kcal mol^{-1}, the barrier for the molecular rearrangement to the six-membered ring is 8.7 kcal mol^{-1} at the MP2(f)-SP level. The preference for the five-membered ring is already present in the structure of the seleniranium intermediate **1a**. The distance between the O and C4 atoms is only 2.71 Å, while the O−C5 distance is 3.31 Å. The distances of the forming O−C bonds in the transition state are consequently reduced, while the second O−C distance is elongated. Therefore, the O−C4 distance in the transition state for the formation of the furanoid form is 2.12 Å (O−C5: 2.89 Å; Figure 7, TS-Z1), and the corresponding transition state for the developing pyranoid form has an O−C5 distance of 2.19 Å (O−C4: 2.64 Å; Figure 7, TS-Z2). One can conclude that the transition state for the oxane-like structure is closer to the product and affords more structural rearrangement than the furan-like transition state. Therefore, the furan-like transition state is a bit earlier and a bit more stable. The final formation of the furan structure liberates 17.4 kcal mol^{-1} at the MP2(f)-SP level, which is slightly less than for the formation of the oxane structure (19.2 kcal mol^{-1}) (Figure 8). Therefore we conclude that the cyclization of **1** is kinetically controlled by the activation energy.

A different control mechanism has to be assumed for the construction of the heterocycle starting from **2**, or, to be more precise, the seleniranium intermediate **2a**. Again, two transition

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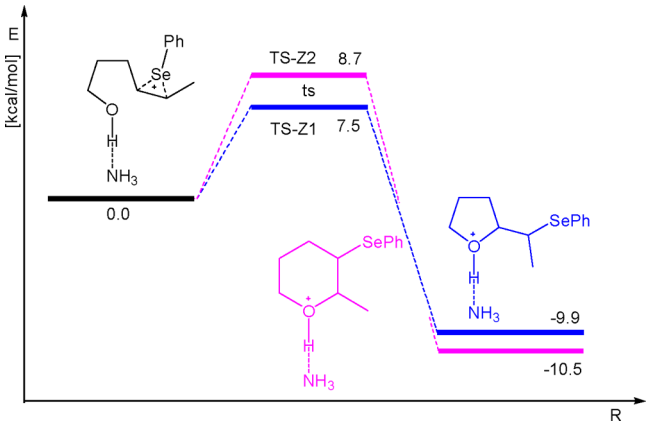

Figure 8. MP2(f)-SP-calculated reaction pathway for the cyclization of (*Z*)-hex-4-en-1-ol.

states could be passed, one leading to the tetrahydrofuranoid structure and the other to the tetrahydropyranoid structure. The transition state leading to the five-membered ring is associated with an activation barrier of 6.9 kcal mol^{-1} at the MP2(f)-SP level, while the alternative transition state linked to the pyranoid form has a barrier of 12.4 kcal mol^{-1}. The distance between the hydroxyl oxygen atom and the C4 carbon is 0.1 Å longer (2.91 Å) than the distance to the C5 carbon (2.80 Å). This structurally favors the six-membered ring. In the transition states, these distances are shortened to 2.08 Å for the formation of the five-membered-ring product (O−C5: 2.86 Å; Figure 9, TS-E1) and 2.15 Å for the six-membered-ring species (O−C4: 2.72 Å; Figure 9, TS-E2). The relatively short distance between the hydroxyl O atom and C4 in TS-E1 may cause some extra stabilization of the transition state. In addition, this transition state, associated with the product that is not experimentally observed, is more productlike than the transition state that is most probably passed.

The succeeding exothermic steps assemble the O−C bonds (Figure 10). Overall, the six-membered-ring system has over

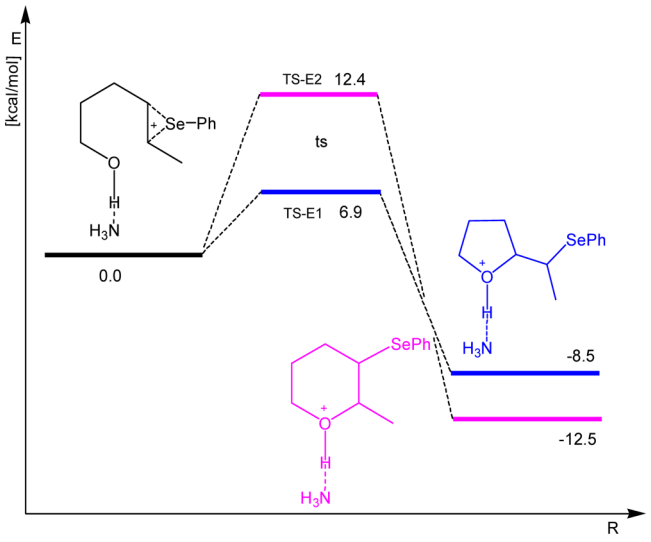

Figure 10. MP2(f)-SP-calculated reaction pathway for the cyclization of (*E*)-hex-4-en-1-ol.

50% more stability (−12.5 kcal mol^{-1}) than the five-membered-ring isomer (−8.5 kcal mol^{-1}) relative to the starting enol **2** at the MP2(f)-SP level. As the only product observed in the experiment is also the more stable pyranoid form, for which the reaction pathway has the higher activation energy, we conclude that in the case of **2** the reaction is thermodynamically controlled.

CONCLUSION

Two geometric isomeric alcohols, (*Z*)-hex-4-en-1-ol (**1**) and (*E*)-hex-4-en-1-ol (**2**), demonstrated very interesting behavior in terms of stereo- and regioselectivity, influenced by the

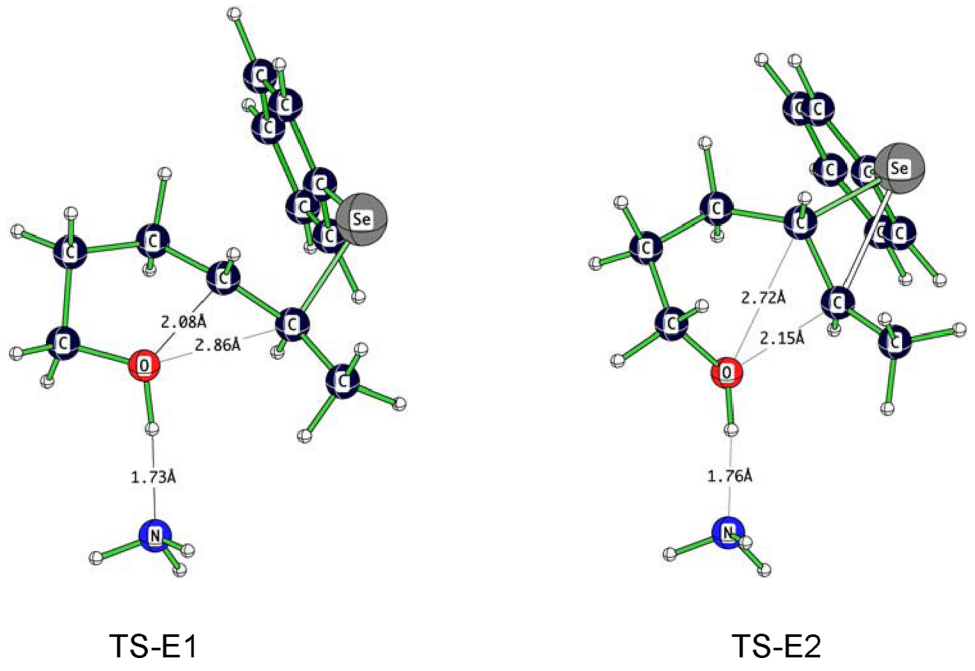

Figure 9. B3LYP/6-311+G**-calculated transition state structures for the cyclization of (*E*)-hex-4-en-1-ol.

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different orientations of the methyl group in these two isomers. Careful selection of an appropriate additive (Lewis acid or base) leads to the appearance of high stereo- and regioselectivity in these reactions. It has been demonstrated that the intramolecular cyclization is facilitated in the presence of a base as a result of the formation of a hydrogen bond between the base and alkenol's OH group. The rate constants in the base-catalyzed reactions are remarkably influenced by the bulkiness and basicity of the base used and the nature of the considered nitrogen donor. The values obtained for the rate constants have shown that the reaction with triethylamine is the fastest one. THF, with higher polarity and higher basic character, is a better solvent than CCl_4. The quantum-chemical calculations have shown that the cyclization of **1** is kinetically controlled by the activation energy, while the ring-closing reaction of **2** is thermodynamically controlled. These results are in agreement with our previous work.[7a] When the THF-type ether is formed from alkenol **1**, it can rather easily undergo an isomerization process to give the more stable product, while, once formed, the six-membered cyclic ether derived from alkenol **2** does not undergo isomerization because of its stability.

■ ASSOCIATED CONTENT

Supporting Information

(1) Data for all pseudo-first-order rate constants, k_{obs} (Tables S.1−S.5); (2) UV−vis spectra for (*Z*)-hex-4-en-1-ol (*C* = 1.5 mM) and PhSeBr (*C* = 0.1 mM) in THF as a solvent; (3) plots of k_{obs} versus alkenol concentration at 288 K for the reactions between PhSeCl and (*Z*)- and (*E*)-hex-4-en-1-ol in THF in the presence of various bases; (4) plots of k_{obs} versus alkenol concentration at 288 K for the reactions between PhSeX (X = Cl, Br) and (*Z*)- and (*E*)-hex-4-en-1-ol in CCl_4 in the presence and absence of pyridine; and (5) Gaussian 03 results for energies [MP2(fc)/6-311+G**] and molecular structures (B3LYP/6-311+G**). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Bartlett, P. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: London, 1984; Vol. 3, pp 411−445. (b) Boivin, T. L. B. *Tetrahedron* **1987**, *43*, 3309. (c) Cardillo, G.; Orena, M. *Tetrahedron* **1990**, *46*, 3321. (d) Orena, M. In *Houben-Weyl Methods in Organic Chemistry: Stereoselective Synthesis*, 4th ed.; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schumann, E., Eds.; Thieme: Stuttgart, Germany, 1995; Vol. *E21e*, pp 4760−4817. (e) Knight, D. W. *Prog. Heterocycl. Chem.* **2002**, *14*, 19.

(2) (a) Tiecco, M. *Top. Curr. Chem.* **2000**, *258*, 7. (b) Santi, C.; Santoro, S. In *Electrophilic Selenium Reagents in Organoselenium Chemistry*; Wirth, T., Ed.; Wiley-VCH: Weinheim, Germany, 2011; pp 1−51.

(3) Harring, S. R.; Edstrom, E. D.; Livinghouse, T. In *Advances in Heterocyclic Natural Product Synthesis*; Pearson, W. D., Ed.; JAI: Greenwich, CT, 1992; Vol. 2, pp 299−378.

(4) (a) Clive, D. L. J.; Chittattu, G.; Churtis, N. J.; Kiel, W. A.; Wong, C. K. *J. Chem. Soc., Chem. Commun.* **1977**, 725. (b) Nicolaou, K. C.; Lysenko, Z. *Tetrahedron Lett.* **1977**, *18*, 1257. (c) Tiecco, M.; Testaferri, L.; Tingoli, M.; Bagnoli, L.; Santi, C. *Tetrahedron* **1995**, *51*, 1277. (d) Tiecco, M.; Testaferri, L.; Bagnoli, L.; Purgatorio, V.; Temperini, A.; Marini, F.; Santi, C. *Tetrahedron: Asymmetry* **2001**, *12*, 3297. (e) Tiecco, M.; Testaferri, L.; Bagnoli, L.; Marini, F.; Santi, C. *ARKIVOC* **2006**, No. 7, 186.

(5) (a) Petragnani, N.; Stefani, H. A.; Valdugab, C. J. Recent Advances in Selenocyclofunctionalization Reactions. *Tetrahedron* **2001**, *57*, 1411. (b) Tiecco, M.; Testaferri, L.; Marini, F.; Bagnoli, L.; Santi, C.; Temperini, A.; Sternativo, S.; Tomassini, C. *Phosphorus, Sulfur Silicon Relat. Elem.* **2005**, *180*, 729. (c) Tiecco, M.; Testaferri, L.; Bagnoli, L.; Marini, F.; Temperini, A.; Tomassini, C.; Santi, C. *Tetrahedron Lett.* **2000**, *41*, 3241. (d) Paulimer, C. In *Selenium Reagents and Intermediates in Organic Synthesis*; Baldwinn, J. E., Ed.; Pergamon Press: New York, 1986; Vol. 4. (e) Paulimer, C. In *Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S., Ed.; Wiley: New York, 1987; Vol. 2. (f) Tiecco, M. Electrophilic Selenium, Selenocyclizations. *Top. Curr. Chem.* **2000**, *208*, 7.

(6) Konstantinović, S.; Bugarčić, Z.; Milosavljević, S.; Schroth, G.; Mihailović, M. Lj. *Liebigs Ann. Chem.* **1992**, 261.

(7) (a) Divac, V. M.; Bugarčić, Z. M. *Synthesis* **2009**, 3684. (b) Divac, V. M.; Rvović, M. D.; Bugarčić, Z. M. *Monatsh. Chem.* **2008**, *139*, 1373. (c) Bugarčić, Z. M.; Mojsilović, B. M.; Divac, V. M. *J. Mol. Catal. A: Chem.* **2007**, *272*, 288. (d) Bugarčić, Z. M.; Gavrilović, M. P.; Divac, V. M. *Monatsh. Chem.* **2007**, *138*, 149. (e) Bugarčić, Z. M.; Mojsilović, B. M. *Heteroat. Chem.* **2004**, *15*, 146.

(8) Espenson, J. H. *Chemical Kinetics and Reaction Mechanisms*, 2nd ed.; McGraw-Hill: New York, 1995; Chapters 2 and 6.

(9) (a) Stevens, P. J.; Devlin, F. J.; Chablowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623. (b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (c) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785. (d) Koch, W.; Holthausen, M. C. *A Chemist's Guide to Density Functional Theory*, 2nd ed.; Wiley-VCH: Weinheim, Germany, 2001; Chapter 13.

(10) (a) Wodrich, M. D.; Corminboeuf, C.; Schleyer, P. v. R. *Org. Lett.* **2006**, *8*, 3631. (b) Schreiner, P. R.; Fokin, A. A.; Pascal, R. A.; de Meijere, A. P. *Org. Lett.* **2006**, *8*, 3635. (c) Grimme, S.; Steinmetz, M.; Korth, M. *J. Org. Chem.* **2007**, *72*, 2118. (d) Wodrich, M. D.; Corminboeuf, C.; Schreiner, P.; Fokin, A. A.; Schleyer, P. v. R. *Org. Lett.* **2007**, *9*, 1851. (e) Schreiner, P. R. *Angew. Chem., Int. Ed.* **2007**, *46*, 4217.

(11) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986.

(12) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; et al. *Gaussian 03*, revision B.03; Gaussian, Inc.: Wallingford, CT, 2004.

(13) (a) Rvović, M. D.; Divac, V. M.; Puchta, R.; Bugarčić, Z. M. *J. Mol. Model.* **2011**, *17*, 1251. (b) Bugarčić, Z. M.; Petrović, B. V.; Rvović, M. D. *J. Mol. Catal. A: Chem.* **2008**, *287*, 171.

(14) Bugarčić, Z. M.; Rvović, M. D.; Divac, V. M. *ARKIVOC* **2009**, No. 14, 135.

(15) Espenson, J. H. *Chemical Kinetics and Reaction Mechanisms*, 2nd ed.; McGraw Hill: New York, 1995; Chapter 11.