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Biscyclization Reactions in Butadiyne- and Ethyne-Linked Triazenes and Diazenes: Concerted versus Stepwise Coarctate Cyclizations

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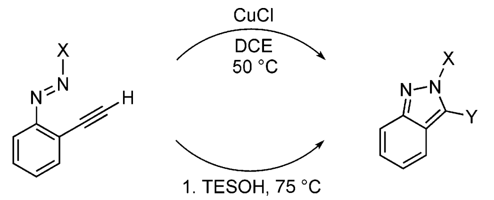
Abstract: A series of alkyne-linked bis-*2H*-indazoles has been prepared by the double cyclization of ethyne- or butadiyne-linked phenyltriazene or phenyldiazene moieties. Even though there are two five-membered ring cyclizations and several triple bond shifts involved, the reactions proceed rapidly under neutral conditions with mild heating, affording the heterocycles in excellent yields. DFT calculations, in agreement with experimental observations, indicate that the reactions: (1) occur via a very short-lived carbene intermediate, (2) are concerted via an asymmetrical transition state, or (3) are even synchronous, with as many as 16 bonds that are made or broken simultaneously. The biscyclizations presented herein strikingly illustrate the concept of coarctate reactions, the stabilization of transition states by coarctate Möbius aromaticity, the ethynologation principle, and the stereochemical rules.

Introduction

There has been growing interest in recent years in reactions involving ene-yne-ketones,[1] ene-yne-diketones,[2] ene-yne-imino ethers,[3] imine-yne-ketones,[4] ene-yne-hydrazones,[5] diene-ynes,[6] and ene-yne-heteroallenes.[7] These structurally related functionalities, when reacted thermally, photochemically, or in the presence of a transition metal, generally undergo cyclization reactions and consequently form an external carbene or metal carbenoid.[8,9] The carbene/carbenoid can then be trapped inter- or intramolecularly. These reactions are not only interesting because of their uncommon mechanisms, but also provide access to novel classes of heterocycles or to known heterocycles with substitution patterns that are otherwise difficult to obtain.

Scheme 1



1 (X = NEt$_2$)
3 (X = Ph)

2 (X = NEt$_2$, Y = CHO)
4 (X = Ph, Y = CH$_2$OH)

Our interest in hetero-dieneyne reactions stems from our recent synthetic and mechanistic investigations of the cyclization of ene-yne-azo compounds (Scheme 1). Specifically, Cu(I)-promoted reaction of (2-alkynylphenyl)triazenes[10,11] (e.g., **1**) led to formation of a carbene intermediate that could be trapped either by molecular oxygen to yield an aldehyde (e.g., **2**) or by an external alkene to yield a cyclopropane. (2-Alkynylphenyl)-phenyldiazenes[12] (e.g., **3**) also underwent thermal cyclization but without the requirement of the Cu(I) salt. Optimal product formation was achieved by trapping of the carbene with a silyl

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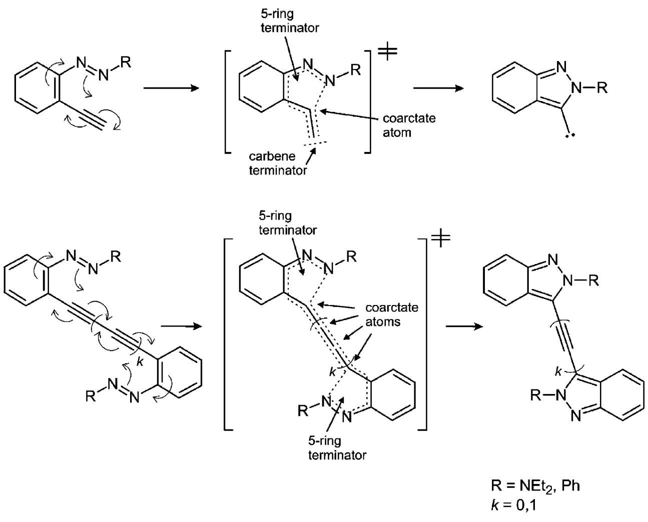
Scheme 2

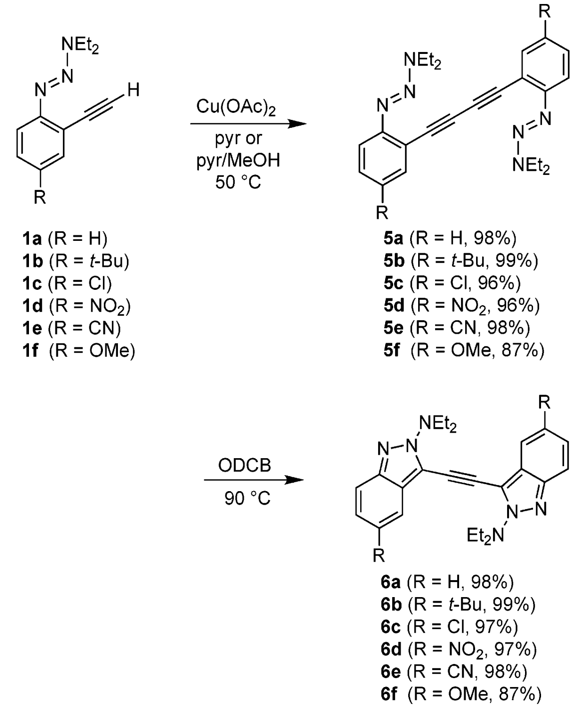


alcohol followed by desilylation to afford **4**. Theoretical and experimental mechanistic investigations revealed that both of these five-membered ring cyclizations were concerted reactions with "coarctate" transition states.[11,12]

Reactions are defined as "coarctate" if there is at least one atom at which two bonds are made or broken.[13] The coarctate atom, or linear succession of coarctate atoms, is terminated by two loops in such a way that the array of electron arrow-pushing forms a compressed ("coarctate") closed cycle, as opposed to pericyclic reactions where the sequence of bond making and bond breaking forms a normal (i.e., uncompressed) cycle. The two loops (terminators) in coarctate reactions are either carbenes or odd-membered rings. In the cyclizations of alkynylphenyltriazenes and -diazenes (Scheme 1, Scheme 2, top), there is one coarctate atom and a five-membered ring (or nine-membered ring if the fused benzene ring is included) and a carbene terminator. Although experimental conditions were determined that permitted efficient trapping of the carbenes,[10b,12] we sought to avoid the intermediacy of these highly reactive species. By combining the five-membered ring cyclization with another symmetrical five-ring cyclization, we designed coarctate reactions with two ring terminators, systems that in principle should cyclize at mild temperatures and without the need of metal catalysis (Scheme 2, bottom).

We have previously shown that similar to pericyclic reactions there is a homologation principle to coarctate reactions termed "ethynylogation".[14] The succession of coarctate atoms can be extended by introducing an even number of additional sp hybridized carbon atoms; therefore, we designed a series of triazenes and diazenes linked with either an ethyne or a butadiyne unit ($k = 0$ or 1). Moreover, the proposed biscyclizations provide an opportunity to confirm the stereochemical rules that have been predicted for coarctate reactions. Coarctate reactions with $[4n + 2]$ π-electrons (which can be formally written with an odd number of electron pushing arrows) exhibit a compressed (coarctate) Hückel aromatic transition state with two coplanar terminators. Those with $[4n]$ π-electrons (an even number of electron pushing arrows, see Scheme 2) have a coarctate Möbius aromatic transition state with two orthogonal terminators.[15] Hence, in the anticipated biscyclizations with 12 ($k = 0$) or 16 π-electrons ($k = 1$), both cyclizations should be orthogonal with respect to each other in the transition state.

Scheme 3



1a (R = H)
1b (R = *t*-Bu)
1c (R = Cl)
1d (R = NO$_2$)
1e (R = CN)
1f (R = OMe)

5a (R = H, 98%)
5b (R = *t*-Bu, 99%)
5c (R = Cl, 96%)
5d (R = NO$_2$, 96%)
5e (R = CN, 98%)
5f (R = OMe, 87%)

6a (R = H, 98%)
6b (R = *t*-Bu, 99%)
6c (R = Cl, 97%)
6d (R = NO$_2$, 97%)
6e (R = CN, 98%)
6f (R = OMe, 87%)

Coarctate reactions exhibit characteristics similar to those of pericyclic reactions. Even if the bond making and breaking is concerted, the system of delocalized electrons might not resemble a closed cycle (pericyclic) or a compressed cycle (coarctate), but in a number of cases exhibits a "disconnection". The so-called pseudopericyclic reactions[16] therefore do not necessarily follow Woodward−Hoffmann rules, and the pseudocoarctate reactions do not obey the stereochemical rules established by us. The ACID method[17] distinguishes between true and pseudopericyclic as well as true and pseudocoarctate reactions. We herein apply the ACID method to characterize these new biscyclizations and use the so-called "critical isosurface value" (CIV) defined within ACID to quantify the degree of "pseudo" character of the corresponding transition states.

Results and Discussion

Triazene Biscyclization. Synthesis of the substituted (2-ethynylphenyl)triazenes (**1a**−**f**) was carried out as reported previously.[10b] The butadiynes were prepared (Scheme 3) using Eglinton homocoupling conditions[18] (Cu(OAc)$_2$ in pyr (**5a**−**e**) or 1:1 pyr/MeOH (**5f**)), affording the desired dimers in excellent

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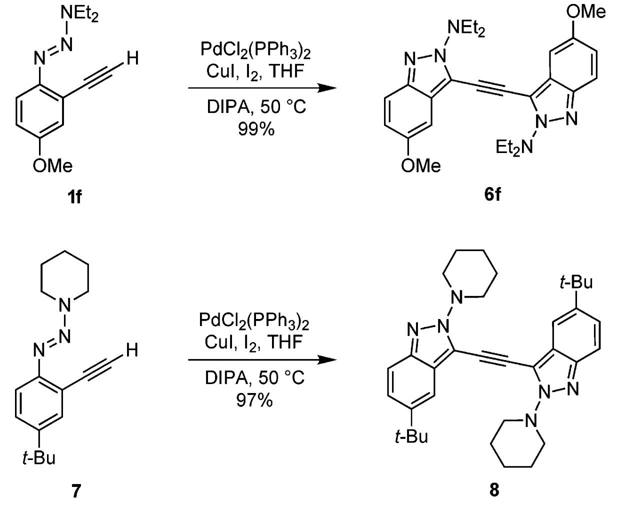
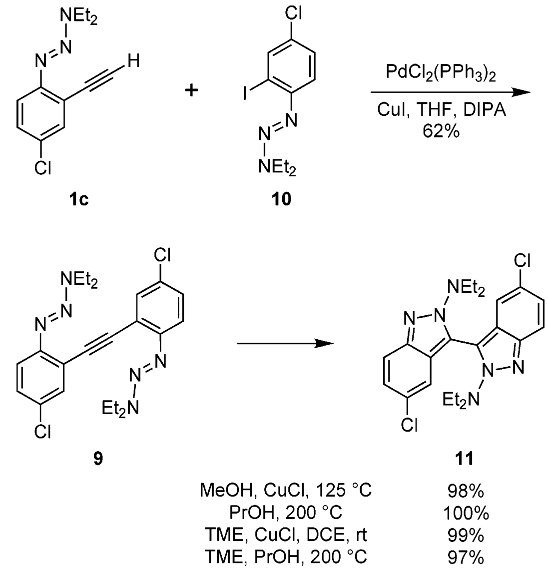
Scheme 4



Scheme 5



yield for all functional groups attempted. The mixed solvent system (and decreased reaction time) was essential for obtaining a high yield of **5f**, which bears an electron-donating methoxy. In pyridine only, diyne **5f** (43%) was accompanied by the formation of a major byproduct, the biscyclized isoindazole **6f**, in 23% yield. Similar heightened reactivity was observed in the Cu-mediated cyclization of **1f**, where the electron-donating group helped stabilize the carbene intermediate; thus, facile formation of **6f** is not wholly unexpected.

Although initial attempts focused on heating **5** in 1,2-dichloroethane (DCE) with excess CuCl, conditions that previously had given excellent results for cyclization of the monomers, the high propensity of the dimers to undergo biscyclization showed that a carbene stabilizer was not required. Instead, heating the triazene dimers **5a**−**f** in *o*-dichlorobenzene (ODCB) at 90 °C for 2−8 h furnished the respective bisisoindazoles **6a**−**f** in excellent yields. The cyclization also proceeded in a variety of lower boiling solvents such as EtOH and toluene in similar excellent yields. The dimers also underwent cyclization even upon refrigeration for several months in the solid state. As compared to many other ring forming reactions involving carbenes, this biscyclization reaction is uncommon because the temperatures (energetics) required are relatively low and a carbene stabilizer is not necessary. Worthy of note is the total absence of any biscinnoline formation, which would have resulted from a dual six-membered ring cyclization.[11] In all trials, under all conditions, five-membered cyclization products were the only species encountered.

As an alternative to the Eglinton reaction, and thus hopefully to minimize the formation of biscyclized side products such as **6f**, we attempted the homocoupling of **1f** utilizing recently developed oxidative “Sonogashira”-type conditions (Scheme 4).[19,20] Interestingly, in the presence of the coordinatively unsaturated Pd with I_2 as the oxidant, the homodimer **5f** was never detected; instead, the dimerized/cyclized product **6f** was synthesized in 99% isolated yield. Similarly, treatment of piperidyl-triazene **7**[10b,21] to the Pd/Cu-catalyzed dimerization/biscyclization conditions afforded bisisoindazole **8** in 82% overall yield from *p*-*tert*-butylaniline. In general, we are able to prepare the isoindazole dimers from the commercially available anilines in 75−85% overall yield for the four or five synthetic steps.

Initial mechanistic experiments focused on whether the reactions were indeed concerted. If stepwise, the carbene intermediate generated by the initial cyclization reaction should rapidly induce a second, tandem cyclization at the remaining triazene moiety. Alternatively, the resultant carbene might be sufficiently stable to be intercepted by a carbene trap. Saito et al. have demonstrated the latter two possibilities with their ene-yne-linked ketone systems, in that photoinduced cyclization is accompanied by tandem carbene-promoted cyclization to yield substituted bisfurans.[3] To test these mechanistic possibilities, monoyne **9** was synthesized by cross-coupling triazene **1c** to iodide **10**[10b] using standard Sonogashira conditions (Scheme 5). Whereas heating **9** to 125 °C in MeOH overnight resulted in no reaction, switching to PrOH and heating to 200 °C gave bisisoindazole **11** in quantitative conversion. Double cyclization could also be induced by heating to 125 °C in MeOH in the presence of CuCl with near quantitative formation of **11**. Despite the ready availability of protic solvents as carbene traps, no products resulting from O−H insertion were detected. Alternatively, stirring **9** in DCE at room temperature for 3−4 d in the presence of CuCl and tetramethylethylene (TME), or in PrOH at 200 °C with excess TME, also afforded only the biscyclized product **11** in exemplary yield; [2 + 1] cycloaddition products were never observed.

Extension of these experiments with external carbene traps to the biscyclization of diyne **5c** provided similar results. Heating **5c** in the presence of excess TME or in a variety of protic solvents generally afforded **6c** in excellent yield; again, no evidence of carbene-trapped molecules was obtained. Although the results for **5c** and **9** do not address whether the reactions

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Scheme 6

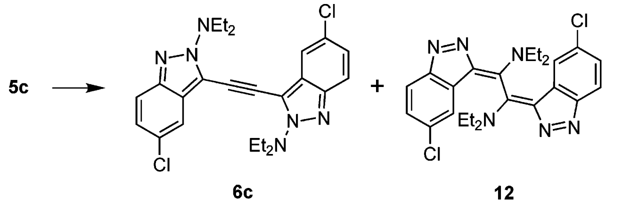


Table 1. Yield of Isoindazole **6c** and Indazole **12** via Scheme 6

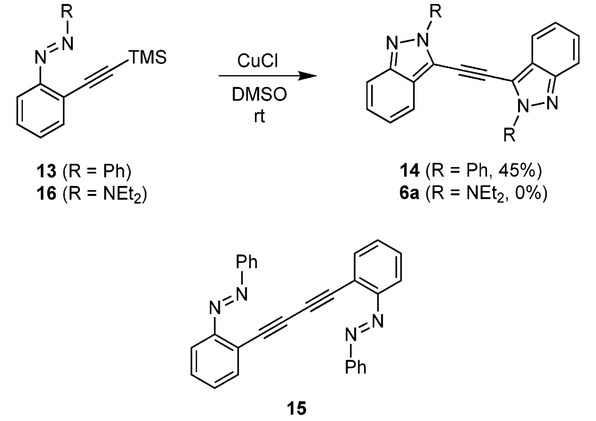
solvent (0.005 M)	temp (°C)	**6c**	**12**
EtOH	125	94%	0%
MeOH	125	75%	21%
MeOH	190	96%	0%
DMSO	125	98%	0%
DMSO/H_2O/MeOH (1:1:1)	125	69%	29%
DMSO/H_2O (1:1)	125	95%	0%
CF_3CH_2OH	125	65%	33%
CF_3CH_2OH/MeOH (1:1)	100	42%	55%

proceed in a concerted or stepwise fashion, they do suggest that, in the biscyclizations, any carbene intermediate that might be formed is short-lived and undergoes rapid migration/tandem cyclization.

Some of the protic solvent trapping experiments, however, rendered a peculiar result. For example, exchanging MeOH for EtOH and heating to 125 °C furnished, in addition to the expected bisisoindazole **6c** in 75% yield, a 21% yield of an unknown second product. Recrystallization from MeCN afforded material suitable for X-ray diffraction (see Supporting Information), which identified the compound as structurally isomeric bisindazole **12**, and not an O−H insertion product (Scheme 6). Although 1,5-aromatization driven proton shifts are known,[22] aromatization to an indazole or amine migration has thus far never been encountered in any of our prior research with isoindazoles or (2-alkynylphenyl)triazenes. The MeOH was checked for purity and the reaction repeated several times for verification of reproducibility. This result is perplexing as the physical properties of MeOH and EtOH are essentially identical, with only slight differences in polarity and pK_a. The molecules, therefore, should not have significantly different solvating properties. Heating **5c** in a wide range of polar or protic solvents at varying temperatures (Table 1) gave unsatisfying and intuitively contradictory results, yielding only **6c** and **12** as products and thus providing little insight into their mechanism of formation. At best, we were able to obtain a ca. 1:1 mixture of isoindazole to indazole. Attempts were also made to convert **12** into **6c** and vice versa using heat, PPh_3, or AIBN; the respective starting material was always recovered quantitatively.

Diazene Biscyclization. Unlike their triazene analogues, *o*-(ethynylphenyl)diazenes are highly reactive compounds upon removal of the silyl protecting group as the free alkynes degrade rapidly.[12] This facet of the diazenes necessitated a different synthetic route to the corresponding dimer. Diazene **13** was synthesized as previously described[12] and subjected to different permutations of Mori's homocoupling method (Scheme 7).[23]

Scheme 7



This procedure entails in situ trans-metalation of the alkynylsilane to the alkynylcopper species, which is then oxidatively homocoupled to yield the diyne. Although numerous reaction conditions were examined, use of CuCl as the copper source, DMSO as solvent, and ambient temperature provided the highest yield of **14**, although only in a modest 45%. It should be noted that uncyclized dimer **15** was not detected in any synthetic trials due to its propensity to form **14**. For comparison, attempted dimerization of the triazene analogue **16** using the conditions that worked best for **13** resulted in no reaction at room temperature after several days or upon heating for several hours.

Computational Studies. Our failure to experimentally trap intermediates prompted us to utilize density functional theory (DFT) calculations to determine the probable mechanism(s) of the biscyclization reactions. The B3LYP/6-31G* level of theory previously proved to be a good compromise between accuracy and computational cost in determining the mechanistic pathway for the cyclization of the triazene and diazene monomers[11,12] and was used throughout this study. To reduce the number of conformational degrees of freedom, we replaced the two ethyl substituents in the triazene units by H atoms and used parent **17a** instead of **1a** as a model for our computations. The ACID (anisotropy of the induced current density) method[17] was used to determine the extent of conjugation in the transition states and has been utilized successfully by our groups[11,12,24] and others for this purpose.[25,26] The ACID scalar field can be interpreted as the density of delocalized electrons. By definition, bond making and bond breaking in a coarctate reaction follow the path of a hairpin-like pinched cycle. The topology of the delocalized system as visualized by the ACID plot and the current density induced by an external magnetic field in coarctate transition states corresponds to a compressed or "coarctate" cycle (hence the name). If the transition state has a perfect D_{2d} or D_{2h} structure and if there is a clear disconnection in the ACID plot, the term pseudocoarctate must be employed in analogy to pericyclic/pseudopericyclic nomenclature. This disconnection

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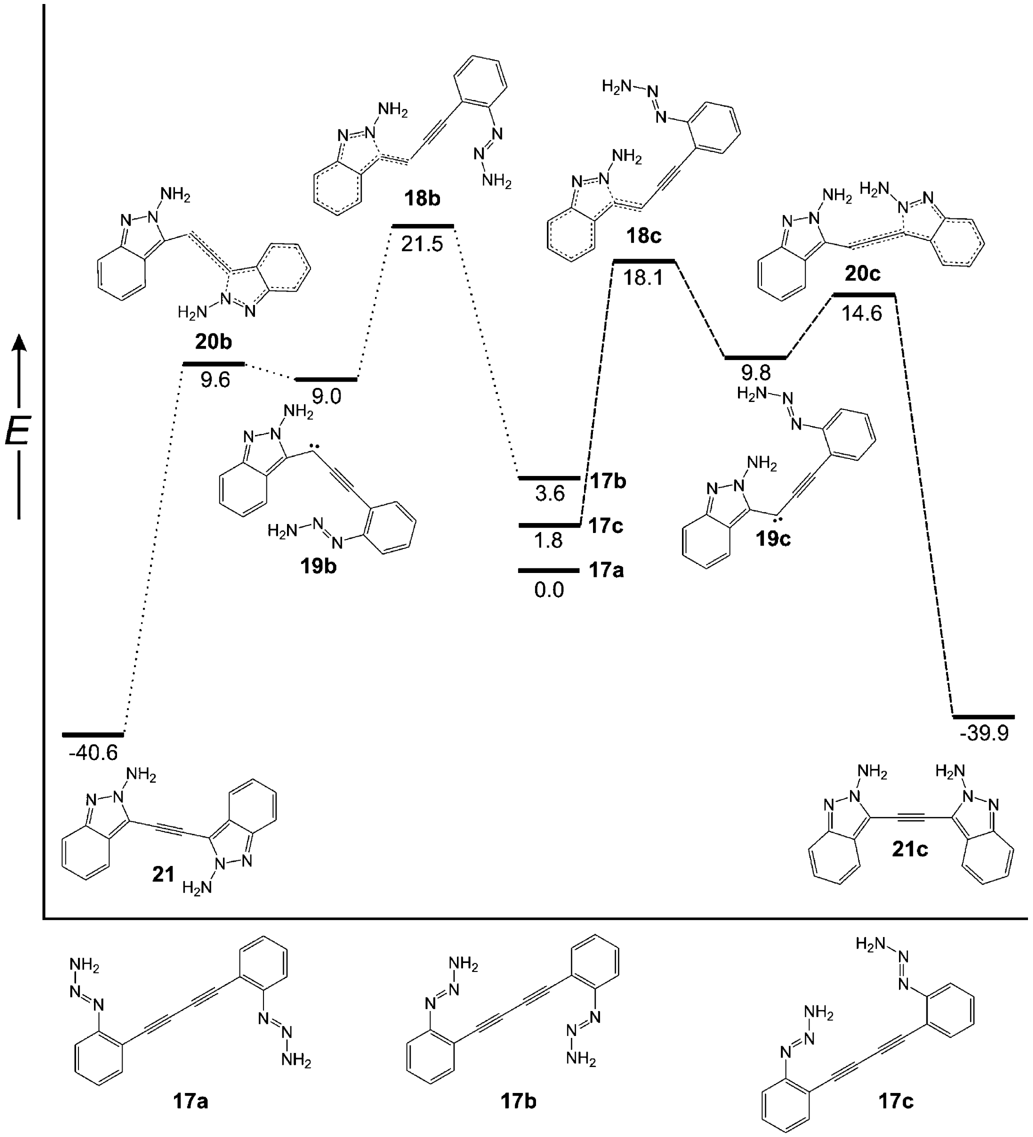

Figure 1. DFT (B3LYP/6-31G* + ZPE) calculated relative energies (kcal mol^{-1}) of reactants, transition states, intermediates, and products of the butadiyne-linked triazene dimer cyclization.

is due to the orthogonality of the interacting orbitals and is most often encountered in systems containing heteroatoms. There is no unambiguous dividing line between a coarctate and a pseudocoarctate mechanism, but there is a continuum from one to the other. The degree of “pseudo” character can be quantified using the CIV (critical isosurface value) in ACID. The CIV is defined as the ACID value at the point at which the gradient of the ACID scalar field is zero and the Laplacian has two negative and one positive eigenvalue. The higher the CIV is, the greater the extent of conjugation in the transition state and the more fully coarctate a reaction is. The lower the CIV is, the lower the extent of conjugation in the transition state and the more the reaction is pseudocoarctate in nature. Several conditions have been outlined in the literature as to when a reaction should be termed pericyclic versus pseudopericyclic.[16,27,28] These stipulations are virtually identical to those placed on coarctate versus pseudocoarctate reactions. We propose the following CIV values to quantify the “pseudo” nature of pericyclic and coarctate reactions: CIV < 0.02, pseudo; 0.02 < CIV < 0.03, borderline case; CIV > 0.03, genuine pericyclic or coarctate.

On the potential energy hypersurface of the triazenediyne biscyclization of **17** to **21**, we identified two different pathways (Figure 1). The most stable conformation of **17** is **17a** with both triazene groups anti with respect to each other and the triazene units rotated in such a way that the reacting (middle) nitrogen atom is pointing away from the diethynyl unit. To initiate the reaction, at least one of the triazene groups has to rotate by 180° around the C−N bond. The lower energy mechanism starts from **17c** passing the transition state **18c** forming intermediate **19c** with a barrier of only 18.1 kcal mol^{-1}. The carbene-like species **19c** can be expected to be short-lived because it would undergo the second ring closure with a relative barrier of only 4.8 kcal mol^{-1} forming product **21c**. The imaginary frequency

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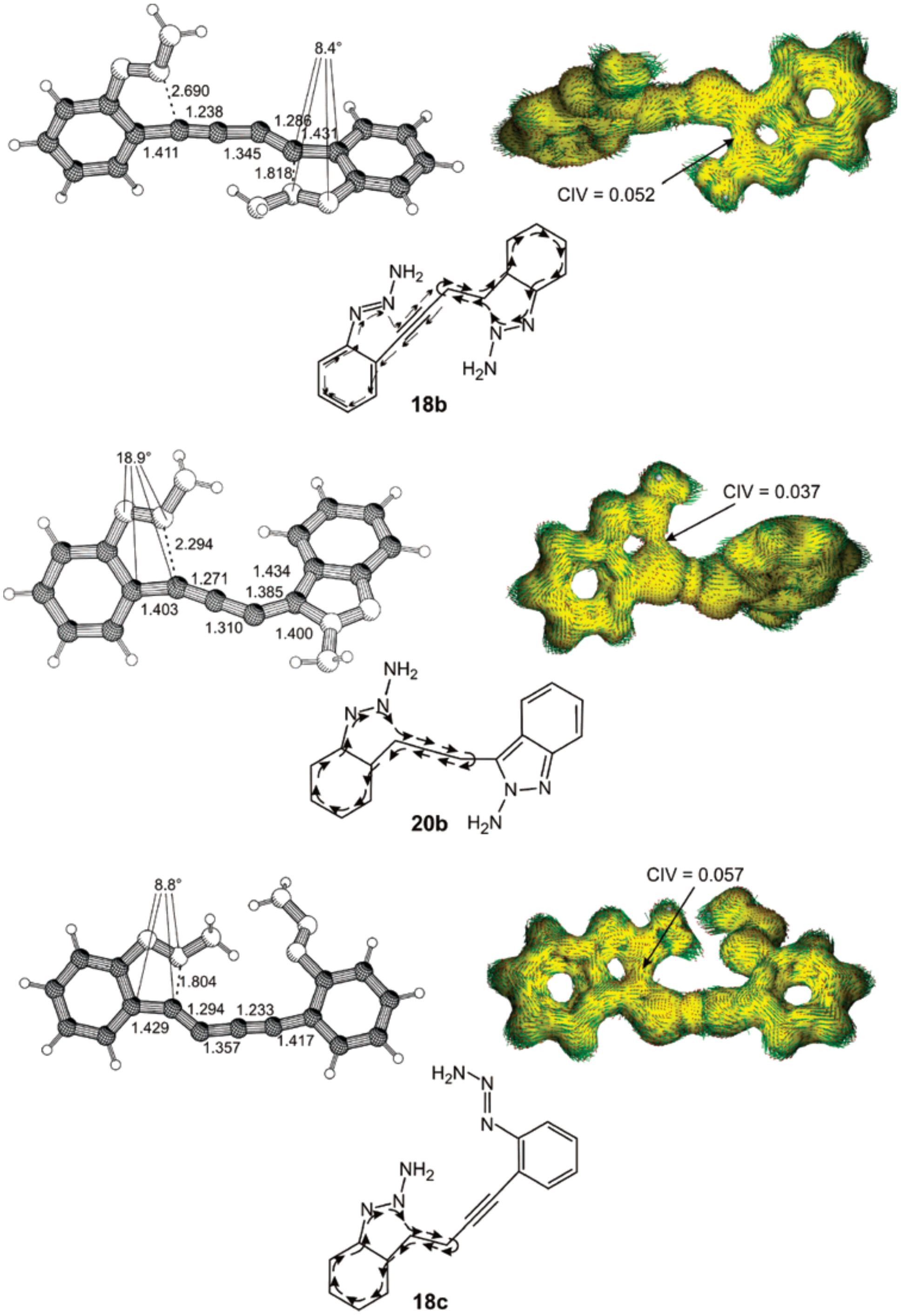

Figure 2. DFT optimized structures (bond lengths in angstroms) and ACID plots (yellow isosurfaces) of transition states **18b**, **18c**, and **20b** of the biscyclization of triazene diyne **17** (Figure 1). Current density vectors are plotted onto the ACID isosurface (isosurface value 0.025, magnetic field orthogonal to the forming isoindazole unit and pointing toward the viewer). The CIV values are given at the forming C−N bonds. The topology of the ring current is qualitatively depicted (below optimized structure and ACID plot). Bold arrows indicate strong currents.

in transition state **20c** mainly describes a rotation of the triazene unit around the C−N bond, leading to a favorable geometry for ring closure. However, carbene **19c** probably is only a "shoulder" and not a minimum on the energy hypersurface. After rotation of the triazene unit, the ring closure proceeds with no or a very small barrier. All attempts to locate a carbene intermediate analogous to **19b**, where the terminal NH_2 group is syn to the carbene center, failed. A second, alternative pathway with a somewhat higher activation barrier (21.5 kcal mol^{-1}) starts from **17b**. Intermediate **19b** is only a very shallow minimum on the potential energy hypersurface. Thus, both mechanisms are two-step processes with low activation barriers, passing through very unstable, short-lived carbene-like intermediates.[29] This is in good agreement with our experimental results. The cyclization proceeds at a moderately low temperature and without the requirement of a metal carbene stabilizer. In addition, our lack of success in attempts to synthesize alkene cycloaddition or O−H insertion products is clarified by the

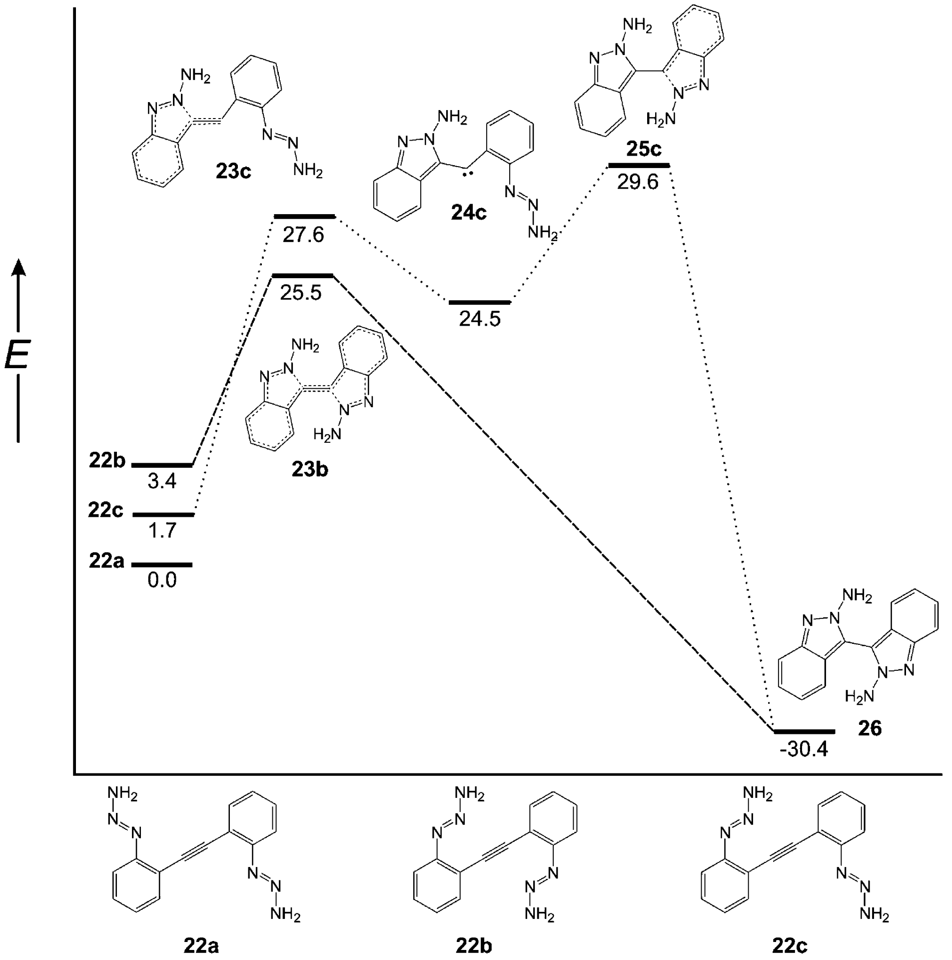

Figure 3. DFT (B3LYP/6-31G* + ZPE) calculated relative energies (kcal mol^{-1}) of reactants, transition states, intermediates, and product of the ethyne-linked triazene dimer cyclization, synchronous versus two-step reaction.

diagram. Trapping the short-lived carbenes **19b** and **19c** with an external carbene trap is experimentally unrealistic. Correspondingly, stationary points indicative of a 1,3-carbene migration along the alkyne chain[30] were also not observed.

According to the ACID analysis of transition states **18b**, **18c**, and **20b** (Figure 2), the mechanism is best described as a back-to-back sequence of two cyclizations. The CIV values of the forming C−N bonds (0.052 in **18b**, 0.057 in **18c**, and 0.037 in **20b**) and the nonplanar geometry of the forming indazole ring (N−N−C−C = 8.4° in **18b**, 8.8° in **18c**, and 18.9° in **20b**) in transition states **18b**, **18c**, and **20b** indicate that the cyclizations are coarctate. A close look at the current density vectors on the C atom in **18b** that becomes the carbene shows them looping back upon themselves, and there is only a minor continuous flow of electron density along the alkyne chain connecting both ring systems. It is noteworthy that in the transition states the isoindazole rings are not planar with respect to each other (e.g., ~95° in **18b** and 40° in **20b**) even though the reactant and the product are planar molecules (0.00° in **17b** and **21b**). The orthogonal arrangement of the terminators has been predicted for reactions with [4*n*] electrons delocalized in a Möbius coarctate transition state.[15]

The calculated energy diagram corresponding to the cyclization of triazene monoyne **22** is shown in Figure 3. Cyclization of the triazene units proceeds with a relative barrier of 25.5 kcal mol^{-1}. The alternative two-step mechanism, involving carbene intermediate **24c**, has a higher barrier of activation (27.6 kcal mol^{-1}). Carbene **24c** is a very shallow minimum only if the triazene moiety has the anti conformation (the terminal NH_2 group pointing away from the carbene center, as depicted in Figure 3). This is obviously unfavorable for the second cyclization. The barrier for the second ring closure is 2.0 kcal mol^{-1} higher than the ring opening leading back to the reactant. The interpretation is simple: the biscyclization is a one-step, but two-stage concerted coarctate reaction, in that both of the cyclizations are not occurring symmetrically.

The ACID plot of the transition state **23b** (Figure 4) corroborates the unsymmetrical but concerted nature of the biscyclization of **22b** → **26**. The delocalized system extends over the entire molecule; however, the CIV values of 0.045 and 0.025 at the forming C−N bonds indicate that both cyclizations

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(29) One of the referees suggested that the reaction could also be viewed as a concerted nucleophilic attack of the nitrogen lone pairs on the ethynyl units. This would imply, however, an accumulation of negative charge in the center of the system, which is energetically unfavourable. From calculations on the corresponding monocyclizations,[11,12] the activation barrier decreases with increasing nucleophilicity of the heteroatom X forming the new C−X bond; therefore, some nucleophilic contribution is probably involved in the biscyclizations, similar to the polar contributions involved in most pericyclic reactions.

(30) Herges, R.; Mebel, A. *J. Am. Chem. Soc.* **1994**, *116*, 8229−8237.

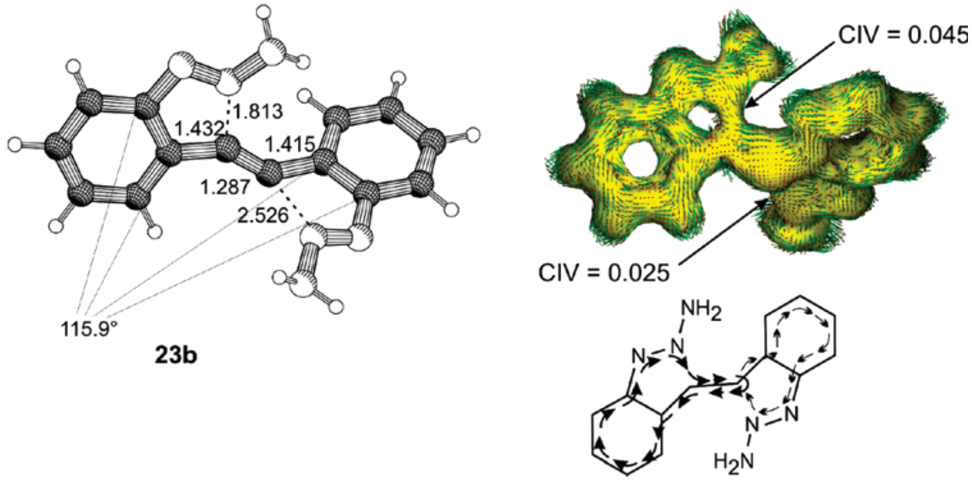

Figure 4. DFT optimized structure (left, bond lengths in angstroms, dihedral angle in deg) and ACID plot (right) of the transition state **23b** of the biscyclization of triazene monoyne **22b** (Figure 3). Current density vectors are plotted onto the ACID isosurface (isosurface value 0.025, magnetic field parallel to the approximate C_2 axis and pointing toward the viewer). The CIV values are given at the two forming C−N bonds. The topology of the ring current is qualitatively depicted (bottom). Bold arrows represent strong currents.

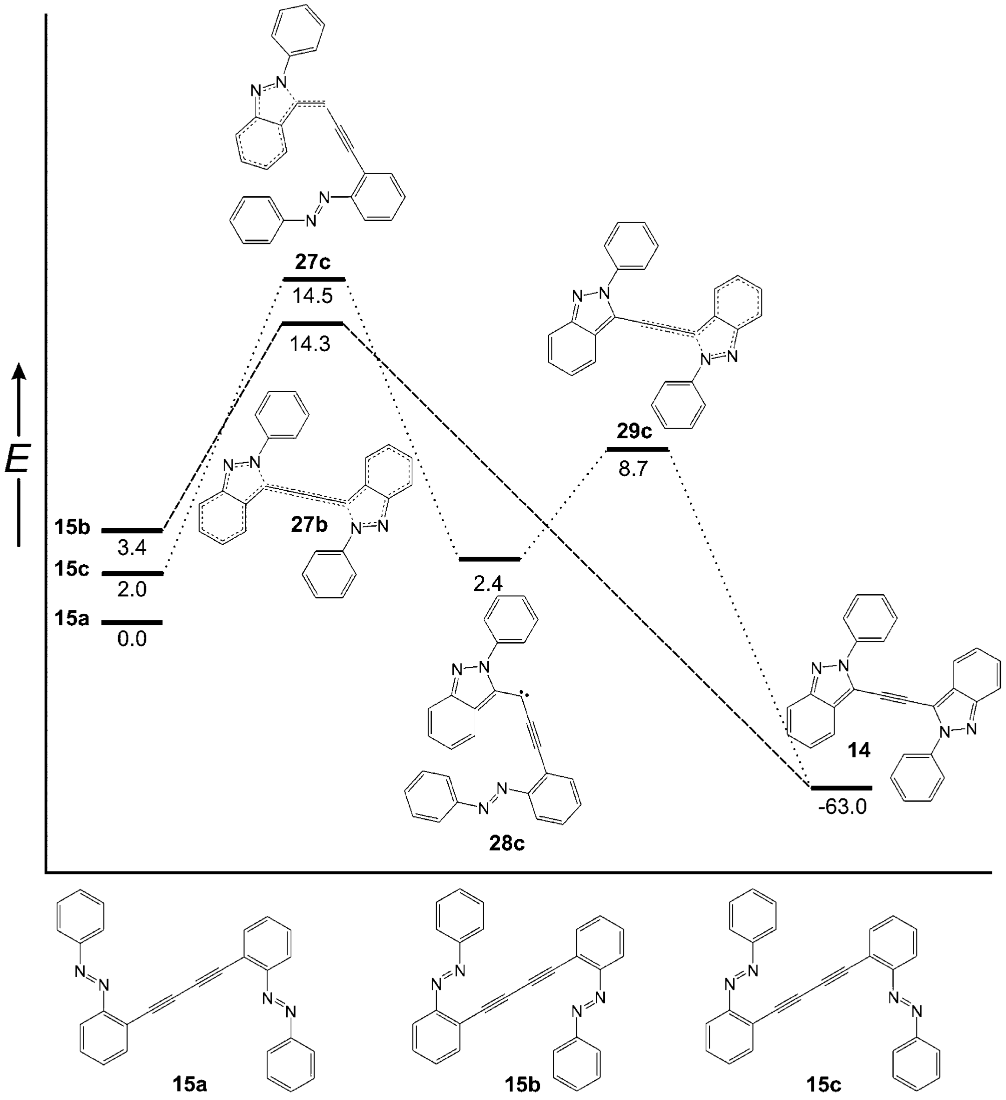

Figure 5. DFT (B3LYP/6-31G* + ZPE) calculated relative energies (kcal mol^{-1}) of reactants, transition states, intermediates, and product of the butadiyne-linked diazene dimer cyclization, synchronous versus two-step reaction.

are not equally advanced in the transition state. Similar to the diyne system, both reactant and product are almost planar, and in the transition state the forming isoindazole rings are twisted by 115.9° with respect to each other.

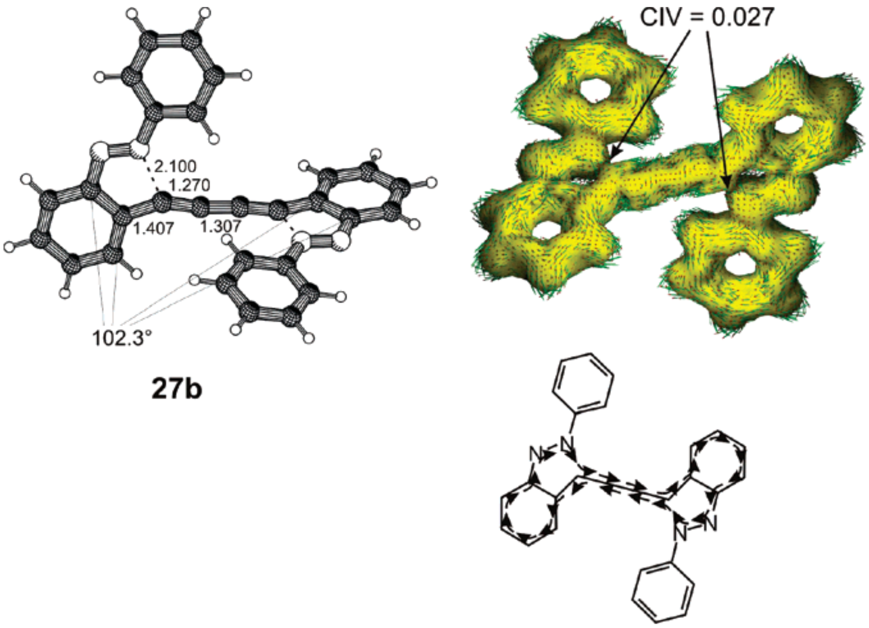

Figure 6. DFT optimized structure (left, bond lengths in angstroms, dihedral angle in deg) and ACID plot (right) of the transition state **27b** of the biscyclization of diazene monoyne **15** (Figure 5). Current density vectors are plotted onto the ACID isosurface (isosurface value 0.025, magnetic field parallel to the C_2 axis and pointing toward the viewer). The CIV values are given at the two forming C−N bonds. The topology of the ring current is qualitatively depicted (bottom).

The diazene diyne analogue **15**, according to our experiments, exhibits a higher reactivity in comparison to the triazene compounds that were studied. Again, there are two mechanistic pathways for the biscyclization: a synchronous pathway and a two-step mechanism involving a carbene intermediate (Figure 5). The synchronous reaction has a slightly lower barrier of activation (14.3 vs 14.5 kcal mol^{-1}, respectively). As in the previous triazene cases, the carbene **28c** is a very shallow minimum on the energy hypersurface with a low barrier (6.3 kcal mol^{-1}) for the second ring closure. Transition state **27b** is unique as it corresponds to the perfectly symmetrical cyclization of both diazene moieties. These data agree with the fact that **15** spontaneously cyclizes upon formation and that no intermediates could be detected or trapped.

The extent of conjugation (aromaticity) in the ACID plot of TS **27b** reveals a Möbius coarctate topology of delocalized electrons, which is aromatic with 16 π-electrons, and requires the two forming isoindazole rings to be orthogonal with respect to each other (Figure 6).[13,15] At 0.027, the CIV values of the forming C−N bonds indicate borderline coarctate/pseudocoarctate conjugation. Both reactant **15** and product **14** are perfectly planar molecules (with a rotation barrier of 0.6 and 1.0 kcal mol^{-1}, respectively; Figure S1 in Supporting Information) because all atoms are sp or sp^2 hybridized and all bonds are conjugated. The fact that the two forming isoindazole rings are almost perpendicular (102.3°) with respect to each other in transition state **27b** indicates that there is a completely different topology of conjugation, which is absent in reactant and product. Whereas in the planar reactant and product structure only one set of p orbitals of the sp hybridized acetylene carbon atoms is in conjugation with the remaining sp^2 hybridized atoms, in the coarctate transition state both p orbitals at each sp hybridized carbon atom are involved. The analysis of the current density vectors plotted onto the ACID isosurface (Figure 6, bottom) reveals that the ring current forms a hairpin loop including both orthogonal π orbitals in the acetylene unit with the current flowing in opposite directions in this linear part of the transition state. The two isoindazole "loops" complement the electron flow to form a cycle. It is easy to show (e.g., with a simple paper model) that a Möbius cycle that is aromatic with [4*n*] π-electrons can only be realized with both "loops" being approximately orthogonal.

The corresponding diazene monoyne reaction was not attempted experimentally but investigated computationally (Figure 7). With a predicted barrier of only 15.5 kcal mol^{-1} for TS **31b**, there is probably little chance to isolate starting material **30a**. Because of steric hindrance, the phenyl substituents are slightly twisted out of conjugation (11°) in the reacting conformation **30b**. The steric problems are even more pronounced in product **34** where the isoindazole units are twisted by 161° with respect to each other. As in the previous cases, there is a competing two-step mechanism via carbene **32** that, however, exhibits a higher barrier of activation.

In the transition state **31b** the twist angle is 129.7° (Figure 8), which is in agreement with the stereochemical rules for coarctate reactions with [4*n*] π-electrons. With CIV values of 0.037 at both forming C−N bonds in **31b**, the reaction is synchronous and clearly coarctate. As in the transition state **27b** of the diyne-linked diazene, there is a distinct "coarctate" ring current in **31b** involving all four p orbitals of the central acetylene unit (Figure 8, bottom).

Conclusions

Expanding upon our previous research by connecting triazene and diazene moieties through butadiyne and/or ethyne linkages, the synthetic practicability of coarctate cyclizations has been increased. Experimental and computational investigation of the

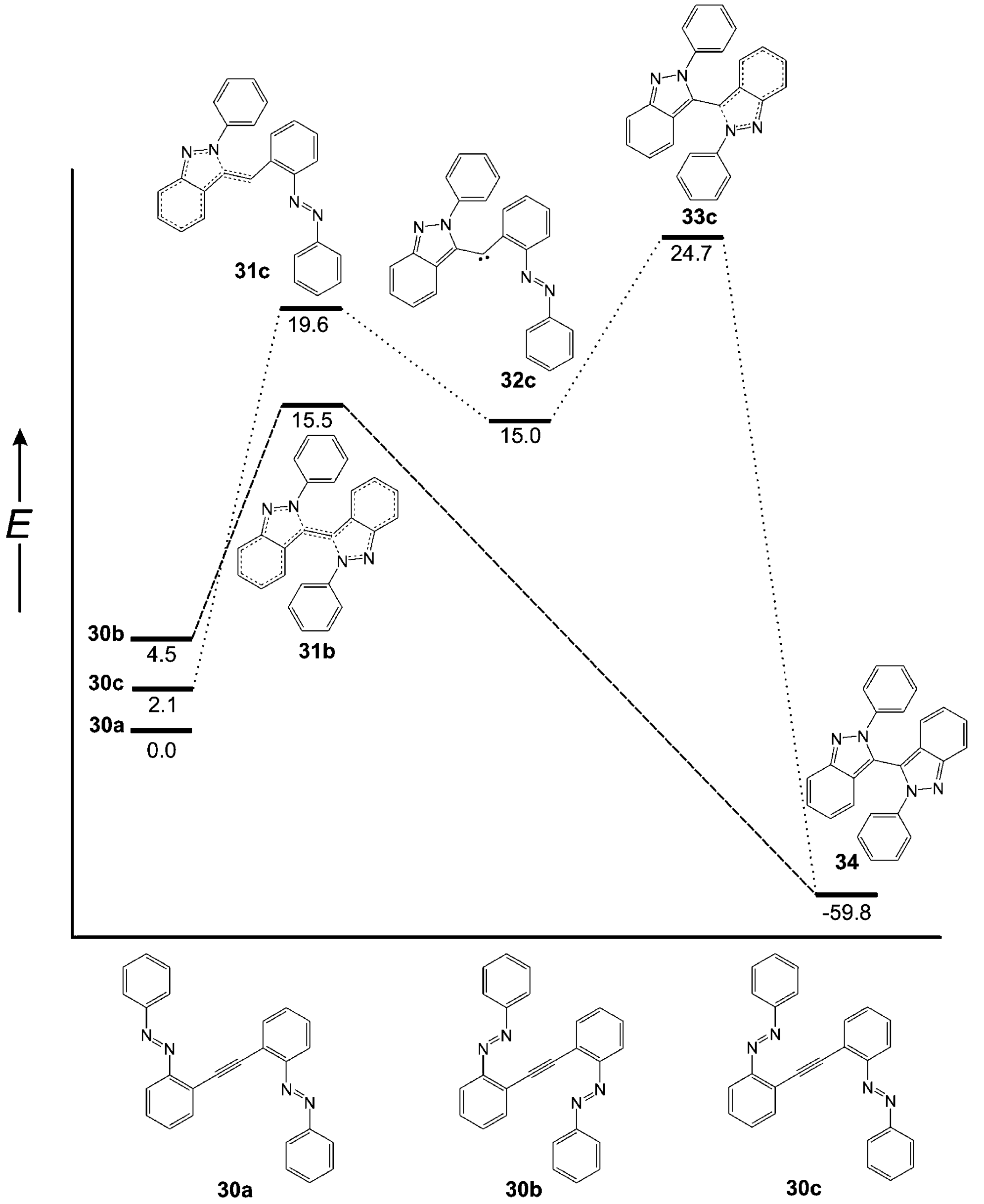

Figure 7. DFT (B3LYP/6-31G* + ZPE) calculated relative energies (kcal mol^{-1}) of reactants, transition states, intermediates, and product of the butadiyne-linked diazene dimer cyclization, synchronous versus two-step reaction.

triazene cyclizations revealed low barriers to cyclization that proceed through stepwise or nonsynchronous yet concerted reaction mechanisms, thus not permitting the viable trapping of carbene intermediates. In the diazene systems, both cyclizations are perfectly synchronous according to DFT calculations, and 12 (monoyne) or 16 (diyne) bonds are made and broken simultaneously. The synchronous bicyclization in **15** competes with a stepwise reaction involving a very short-lived carbene-like intermediate. The stereochemical rules for coarctate reactions with [4*n*] π-electrons predict a coarctate (compressed) transition state with Möbius topology and two loops (isoindazoles) that are approximately perpendicular with respect to each other (Figure 9).[31] These qualitative predictions that were made previously as well as the low activation barrier in the diyne system are confirmed by DFT calculations. Along with additional research into the generation and migratory aptitude of these types of transient carbenes, we continue to investigate other possible heteroatom variations of coarctate cyclizations in our laboratories.

Computational Methods

All theoretical calculations were performed with the Gaussian 98[32] suite of programs at the B3LYP/6-31G*[33] level of DFT. All stationary points were confirmed by harmonic frequency analysis and checked for stability toward triplet and SCF convergency. All transition states and carbene intermediates were additionally optimized at the UB3LYP/

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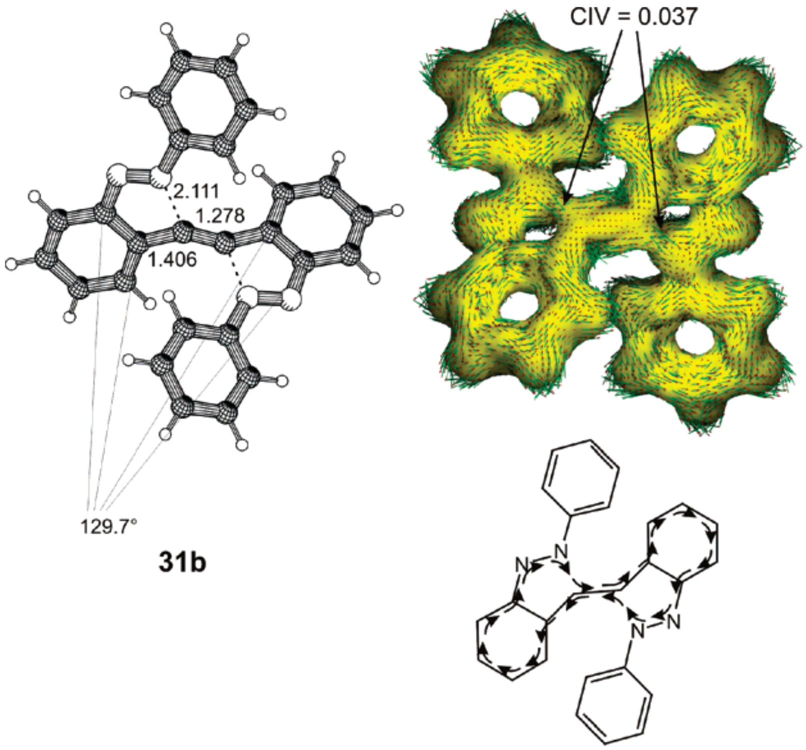
(31) The stereochemical rules of coarctate reactions, and the electronic structure of their transition states (such as the Möbius topology depicted in Figure 9), have recently been derived on the basis of group theory. This extensive theoretical treatment will be the subject of a forthcoming paper.

(32) Frisch, M. J.; et al. *Gaussian 98*, revision A.6; Gaussian, Inc.: Pittsburgh, PA, 1998.

(33) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648−5652.



31b

Figure 8. DFT optimized structure (left, bond lengths in angstroms, dihedral angle in deg) and ACID plot (right) of the transition state **31b** of the biscyclization of diazene monoyne **30** (Figure 7). Current density vectors are plotted onto the ACID isosurface (isosurface value 0.025, magnetic field parallel to the C_2 axis and pointing toward the viewer). The CIV values are given at the two forming C−N bonds. The topology of the ring current is qualitatively depicted (bottom).

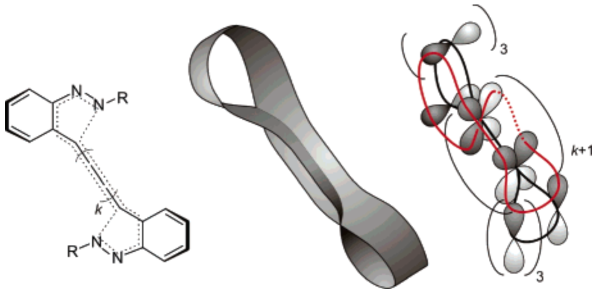


Figure 9. Coarctate Möbius topology of the diazene biscyclizations (R = Ph). There are 12 ($k = 0$) and 16 ($k = 1$) electrons (or 20 and 24 if the fused benzene rings are included) delocalized in the transition state. With $[4n]$ π-electrons, the transition state must have Möbius topology and because of the coarctation the loops (forming isoindazole rings) are orthogonal with respect to each other. This is reflected by the mutual overlap of the basis orbitals (right). There is a cyclic overlap (red line) and one sign inversion (dashed red line), indicating a Möbius topology. Note that the red line passing the origin of a p orbital is not a sign inversion (this is not an overlap of two different basis orbitals with opposite phase).

6-31G* level of DFT (guess=mix, nosym). In all cases, the unrestricted collapsed to the closed shell wave function. The energies of the stationary points were determined, including zero point energies at the same level of theory. ACID scalar fields were computed with our own program.[17] Current density vectors were calculated with the CSGT method of Keith and Bader.[34]

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Supporting Information Available: Experimental details and copies of ^{1}H or ^{13}C NMR spectra for **5a−f**, **6a−f**, **8**, **9**, **11**, and **12**; X-ray structural data for **12** (CIF file, structure refinement details, tables of atomic coordinates, thermal parameters, bond lengths, bond angles, etc.); calculated rotational barriers for **14** and **15**; Cartesian coordinates for all optimized structures in Figures 1, 3, 5, and 7; complete ref 32 citation. This material is available free of charge via the Internet at http://pubs.acs.org.

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(34) Keith, B. A.; Bader, R. F. W. *J. Chem. Phys.* **1993**, *99*, 3669−3682.