

Nature of Bonding in the Cyclization Reactions of (2-Ethynylphenyl)triazene and 2-Ethynylstyrene

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The topological analysis of the electron localization function (ELF) has been applied to explore the nature of bonding in thermal cyclizations of (2-ethynylphenyl)triazene and 2-ethynylstyrene. These processes have been proposed to occur through both five- (i.e., coarctate) and six-membered (i.e., pericyclic) transition states. The analysis of *electron delocalization, as measured from an irreducible ELF f-localization domain reduction diagram*, allows us to characterize these cyclizations of 2-ethynylstyrene in terms of a more pronounced pericyclic or coarctate character than those associated with (2-ethynylphenyl)triazene. The latter evolve through pseudopericyclic and pseudocoarctate pathways. It is found that ELF results are also in good agreement with recent magnetic evidence data obtained from the anisotropy of induced current density (ACID) calculations.

I. Introduction

It has been shown recently by Haley et al.^{1–3} that the isoindazole (**4**) and cinnoline (**7**) heterocycles can be obtained in good proportions through thermal cyclization of (2-alkynylphenyl)triazenes (**1**) under neutral and soft conditions (see Scheme 1). This represents a novel and remarkable synthetic utility in the preparation of other unusual heterocyclic compounds from the relevant and essentially nonactivated triazenes.^{1–3}

It has also been emphasized that upon suitable different reaction conditions the cyclizations from compound **1** could favor either a five-membered (pseudo)coarctate or a six-membered (pseudo)pericyclic mechanistic pathway via carbene (**3**) or zwitterion (**6**) intermediates, respectively.^{1–3} These mechanistic proposals are based upon the probe of reaction products^{1–3} as well as upon recent theoretical^{2,4} density functional theory (DFT) potential energy surface explorations for the decomposition of 1-(2-ethynylphenyl)-3,3-dialkyltriazene (**1'**), used as a model system, as is depicted in Scheme 2.

Given the importance of these novel pathways toward heterocyclic compounds,^{1–4} the elucidation of the bonding details along the reaction pathways through transition structures TS2 and/or TS5 emerges as a very relevant subject of research.^{1–4} In particular, the elucidation between the pericyclic/pseudopericyclic and coarctate/pseudocoarctate nature of bonding occurring along these reactive pathways remains to be explored further.^{4–11} Pseudopericyclic/pseudocoarctate reactions, occurring through planar nonaromatic transition states, possess very different thermodynamic and selectivity patterns of reactivity, as compared to normal concerted processes.^{5–11} For instance, lower barriers along a pseudopericyclic/pseudocoarctate reaction pathway should be expected, providing a fundamental impact in the design of synthetic strategy and reaction pathway analysis.^{5,6} In this work, our goal is to further explore new

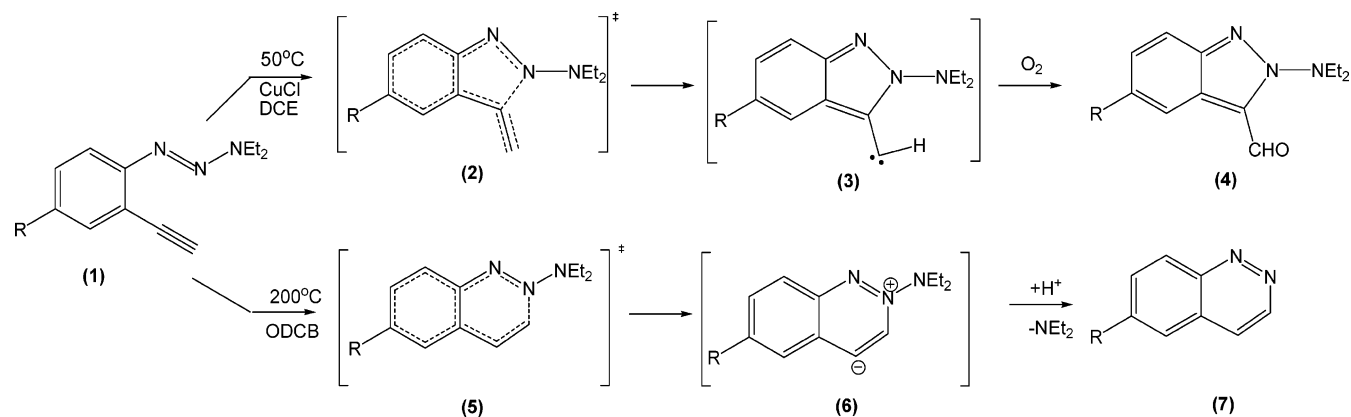
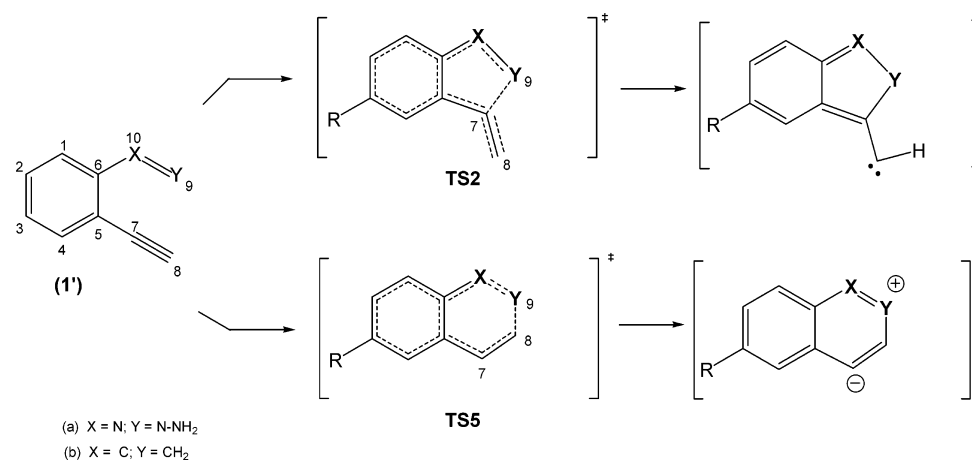
insight concerning the elucidation of bonding details that distinguish the electrocyclization pathways of 1-(2-ethynylphenyl)-3,3-dialkyltriazene (**1'**) through TS2 and TS5 transition structures.

As is well-known,¹² *pericyclic* is the term used for reactions that evolve via a cyclic, aromatic transition state of *delocalized* electrons where bond making and bond breaking occur simultaneously in a cyclic array. In contrast, in *pseudopericyclic* reactions, the cyclic delocalization of electrons in the transition state is broken (i.e., disconnected) because the orbitals involved in the delocalized system are orthogonal at some specific atomic center. Thus, pericyclic reactions involve no disconnection in the cyclic array of overlapping orbitals, whereas a pseudopericyclic reaction involves at least one such disconnection. Lemal was the first to describe a pseudopericyclic reaction for the tautomerization of sulfoxides,¹³ and, more recently because their advantageous characteristics, these processes have been the subject of renewed experimental and theoretical attention.^{5–11} However, in a *coarctate* reaction the bond making and bond breaking *do not follow a cyclic path*. That is, there is at least one center at which two bonds are made and two bonds are broken simultaneously. In analogy with the pseudopericyclic processes, when disconnections occur in coarctate reactions, they are termed as *pseudocoarctate* reactions. Henceforth, to gain further insight into the electronic structure of the corresponding transition states, theoretical tools should be employed.^{14–18} Quantities based upon nucleus-independent chemical shift (NICS) magnetic strategies,^{17,19} or anisotropy of induced current density (ACID) calculations,¹⁸ constitute relevant global descriptors in connection with the characterization of the aromatic character at concerted transition structures.²⁰ In this context, the ACID method has been proven to be a powerful tool to distinguish between pericyclic/pseudopericyclic and coarctate/pseudocoarctate topologies.^{2,21,22} This is because the ACID scalar field (i.e., a local quantity) can be interpreted straightforwardly as the density of *delocalized* electrons. The ACID boundary surface thus provides a continuous picture for the electron delocalization, which is cyclic and not cyclic for the

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SCHEME 1: Synthesis of the Isoindazole and Cinnoline Heterocycles: From Thermal Cyclization Reaction of Non-Activated Triazenes. ODCB \equiv O-dichlorobenzene

SCHEME 2: Cyclization Reaction Mechanisms for (2-Ethynylphenyl)triazene, 1'A, and 2-Ethynylstyrene, 1'B, via Pseudocoarctate and Pericyclic Pathways


pericyclic and coarctate topologies, respectively.^{18–20} Disconnections are present in this continuous pattern of delocalization if *pseudopericyclic* or *pseudocoarctate* reactions are implied. Furthermore, the current density vectors plotted onto the ACID isosurface provide an image of the diatropic ring current that can be associated with a pericyclic (if strong) or coarctate (if constricted) topology.^{18–20} The degree of conjugation, pericyclicity (or aromaticity), character then becomes associated directly with the so-called critical isosurface value (CIV).^{18–20}

Other tools, such as the topological analysis of the electron localization function (ELF),^{23–29} have been applied in some cases within this general goal.^{30,31} The advantage of using the ELF methodology, as will be noted briefly below, is that it provides a *direct local measure of the Pauli principle*, allowing a direct treatment of *electron delocalization* in several reacting and stationary systems.^{28,29} Some studies conducted in our group focusing on the [1,3]sigmatropic shifts of hydrogen, fluorine, and methyl in the allyl system,^{32a} the proton transfer in some thiooxalic acid derivatives,^{32b} some thermal chelotropic decarbonylations,^{32c} the structure of the N_5^+ cation,^{32d} and the thermal cyclization of (*Z*)-1,2,4,6-heptatetraene and its heterosubstituted derivatives,³¹ provide some examples in this framework. Several other applications have also been reported recently concerning the usefulness of the ELF analysis for electron delocalization.³³ It is also necessary to recall that topological-based (*de*)-localization indexes have been developed further upon the basis of the electron pair density³⁴ within an atoms-in-molecules (AIM)³⁵ framework. Several applications to bonding, aromaticity, and chemical reactivity have also been addressed

recently.^{36,37} A homomorphic relationship exists between the ELF picture of electron pairs and those derived from the scalar field of Laplacian of density within the AIM model. These relationships will therefore be manifest among the different delocalization indexes developed therein.³⁸

By returning to the characterization of the cyclization of triazene (1'), the ACID-based results from Haley et al.² indicate that in the case of the five-membered cyclization of (2-ethynylphenyl)triazene (1'a) to 2-amino-3-methylideneisoindazole the topology of delocalized electrons at TS2a exhibits a disconnection between the C7 and N9 atoms at which the new C–N bond is being formed. However, the current density vectors do not exhibit a closed circle in the five-membered ring, indicating that the TS should be considered essentially a pseudocoarctate one. In contrast, for the five-membered cyclization of 2-ethynylstyrene (1'b) to 1-methylidene-2*H*-indene, the current density vectors reveal a coarctate nature for the TS. It is clear that the ring current adopts an exocyclic loop involving carbon atom C8 that becomes the carbene center in the product. These authors have also studied the six-membered ring cyclizations.² Both cyclizations, from 1'a to the cinnolinium zwitterion, and from 1'b to isonaphthalene, exhibit a cyclic topology of delocalized electrons and thus they have been characterized as single pericyclic processes.² However, in the case of TS5a, the six-membered cyclization of (2-ethynylphenyl)triazene to cinnolinium zwitterion, the connection between the two bond-forming centers (C8–C9) is weak, and the calculated ACID critical isosurface value seems to indicate that the aromaticity degree in the transition state is rather weak and that the reaction

seems to be a borderline case between pericyclic and pseudo-pericyclic.² With the aim of searching for more insight concerning the nature of the electronic rearrangement in these systems, and to compare the results with the recent ACID predictions,² we have carried out a theoretical study of the above-mentioned cyclization reactions (Scheme 2) within the framework of topological analysis of ELF. We resort here to the analysis of ELF bifurcation diagrams that provide us with fundamental information about electron localization in a molecular system,^{24–32} that is, the highest isosurface value for a domain reduction (i.e., separation) into localization domains containing lower numbers of attractors, the highest delocalization between the associated regions.^{24–32}

II. Theoretical Approach and Computational Details

Transition states for the cyclizations of **1'a** and **1'b** have been optimized at the B3LYP/6-31G(d) level, following ref 2 for comparison purposes. This level is suitable enough to provide a good wave function for our topological approach to the problem at hand. Calculations were performed using the Gaussian 03 package of programs.³⁹ The topological analysis of ELF has been done using the TopMod program⁴⁰ and Vis5d visualization tools.⁴¹ With the aim of completeness, we briefly review here some of the more important concepts concerning the topological analysis of ELF. For more detailed discussions, the reader is referred to widely available reviews^{24–29} on this powerful descriptor of chemical bonding analysis.

Topological Analysis of the Electron Localization Function. The electron localization function (ELF), $\eta(\mathbf{r})$, has been proposed by Becke and Edgecombe within the framework of a natural Taylor expansion of the pair density probability³⁴ of electrons of identical spin (i.e., the Fermi hole)²³

$$\eta(\mathbf{r}) = \left[1 + \left(\frac{D_\sigma(\rho(\mathbf{r}))}{D_\sigma^0(\rho(\mathbf{r}))} \right)^2 \right]^{-1} \quad (1)$$

where D_σ and D_σ^0 represent the curvature of the Fermi holes for the system at hand and for a homogeneous electron gas with the same density, $\rho(\mathbf{r})$, respectively. For a close shell single determinantal wave function of Hartree–Fock or Kohn–Sham orbitals, ϕ_i , the D_σ term becomes

$$D_\sigma(\mathbf{r}) = \frac{1}{2} \sum_i |\nabla \phi_i(\mathbf{r})|^2 - \frac{1}{8} \frac{|\nabla \rho(\mathbf{r})|^2}{\rho(\mathbf{r})} = t_s(\rho(\mathbf{r})) - t_w(\rho(\mathbf{r})) \quad (2)$$

which can be interpreted straightforwardly^{24–29} as the difference between the positive definite local kinetic energy of a system of noninteracting fermions, $t_s(\rho)$ having the same density of the real system and the von Weizaecker kinetic energy density, $t_w(\rho)$. Therefore, this important term will stand for the *excess local kinetic energy density* due to the *Pauli repulsion*.^{24–29} Henceforth, it is expected that the gradient field of ELF provides us with the atomic or molecular space directly divided in regions of *pairing* electrons,^{24–29} that is, to define basins within which electron pairs can be found. Given the above definition in eq 1, the ELF function will be close to 1.0 in those regions with a high antiparallel spin-pair probability and close to zero within regions where it is low. In effect, the complete set of points on the gradient lines that end up on a local maxima, or *attractor* of the ELF gradient field, partitions the space of the system and defines the *basin* Ω of this attractor. Basins thoroughly fill the space, being expected to be proper open quantum subsystems.³⁴ Inner electrons will define *core* (C) *attractors*,

whereas the remaining maximums will be associated with *valence* (V) *attractors*. The corresponding basins will indeed be characterized by their *synaptic order*,²⁸ which will stand simply by the number of core basins sharing common separators.^{26,29} This convention provides a general framework for the treatment and description of the bonding by resorting to the synaptic order and associated topological concepts.²⁸ The basin populations, $\tilde{N}(\Omega_i)$, are calculated simply by integrating the entire density, $\rho(\mathbf{r})$, into these regions, Ω_i , and their respective *variances*, $\sigma^2(\tilde{N}; \Omega_i)$, which means the associated *quantum-mechanical uncertainty*, due to the *electron delocalization*, becomes obtained after the integration of the exchange-correlation hole weighted by density dependent terms over the corresponding domain basins. Of course, the variance can be also written in terms of *contributions arising from* all of the other basins (i.e., *covariance*)^{24–33}

$$\sigma^2(\tilde{N}_i; \Omega_i) = \int_{\Omega_i} d\mathbf{r}_1 \int_{\Omega_j} d\mathbf{r}_2 \pi(\mathbf{r}_1, \mathbf{r}_2) + \tilde{N}_i - [\tilde{N}_i]^2 = \sum_{j \neq i} \tilde{N}_i \tilde{N}_j - \tilde{N}_{ij} = - \sum_{j \neq i} \int_{\Omega_i} \int_{\Omega_j} \rho(\mathbf{r}_1) \rho(\mathbf{r}_2) h(\mathbf{r}_1, \mathbf{r}_2) d\mathbf{r}_1 d\mathbf{r}_2 \quad (3)$$

thus giving the degree of correlation between the population fluctuations of two given basins, i and j , that is the same to say, due to delocalization of the exchange-correlation hole, $h(\mathbf{r}_1, \mathbf{r}_2)$.^{24–33} Henceforth, it is clear that σ^2 will describe the excess of the number of pairs resulting from the interaction of a given pair region with other basins. It also becomes clear that an analysis of the covariance (i.e., fluctuation of electron populations among the basins) will represent a useful tool for the examination of the electron delocalization pattern involving pairs of basins.^{26–33}

However, the electron fluctuation between the ELF basins (i.e., eq 3) can also be analyzed straightforwardly in light of the *reduction of localization domains and bifurcation diagrams*^{24–33} without resorting directly to the covariance data, as was already exemplified for related systems.^{30–32} In such a type of diagrams, the complete valence *irreducible f-localization domain* picture is represented for the molecular system. Such irreducible f-localization domains simply constitute volumes bound by at least one isosurface $\eta(\mathbf{r}) = f$ that contains only one attractor.^{26,29–33} In this work, we resort to the direct examination of the value of bifurcation (i.e., reduction of the localization domain to contain a lower number of attractors) as a measure of the degree of fluctuation that is involved among different valence pair regions. Higher bifurcation values are associated with higher values of delocalization between the associated regions (i.e., σ^2 value). This fact follows from an interpretation of eq 3. A high value of bifurcation will be associated with a high value for the probability pair function for antiparallel spin electrons, $\pi^{\alpha\beta}(\mathbf{r}_1, \mathbf{r}_2)$, and therefore its contribution to the variance among these regions will be also high. This hypothesis has also been applied recently to the examination of the bonding nature of thermal cyclization of (Z)-1,2,4,6-heptatetraene and its heterosubstituted derivatives.³¹

III. Results and Discussion

Five-Membered Ring Cyclizations: (Pseudo)coarctate Pathways. The examination of the gradient field of ELF at the present level of theory reveals at first glance that a disynaptic basin associated directly with the C7 and C9 centers at TS2b exists, which is associated with the bond formation between these centers. There is no such type of basin for the case of TS2a. It is clear that a single disynaptic basin will be associated

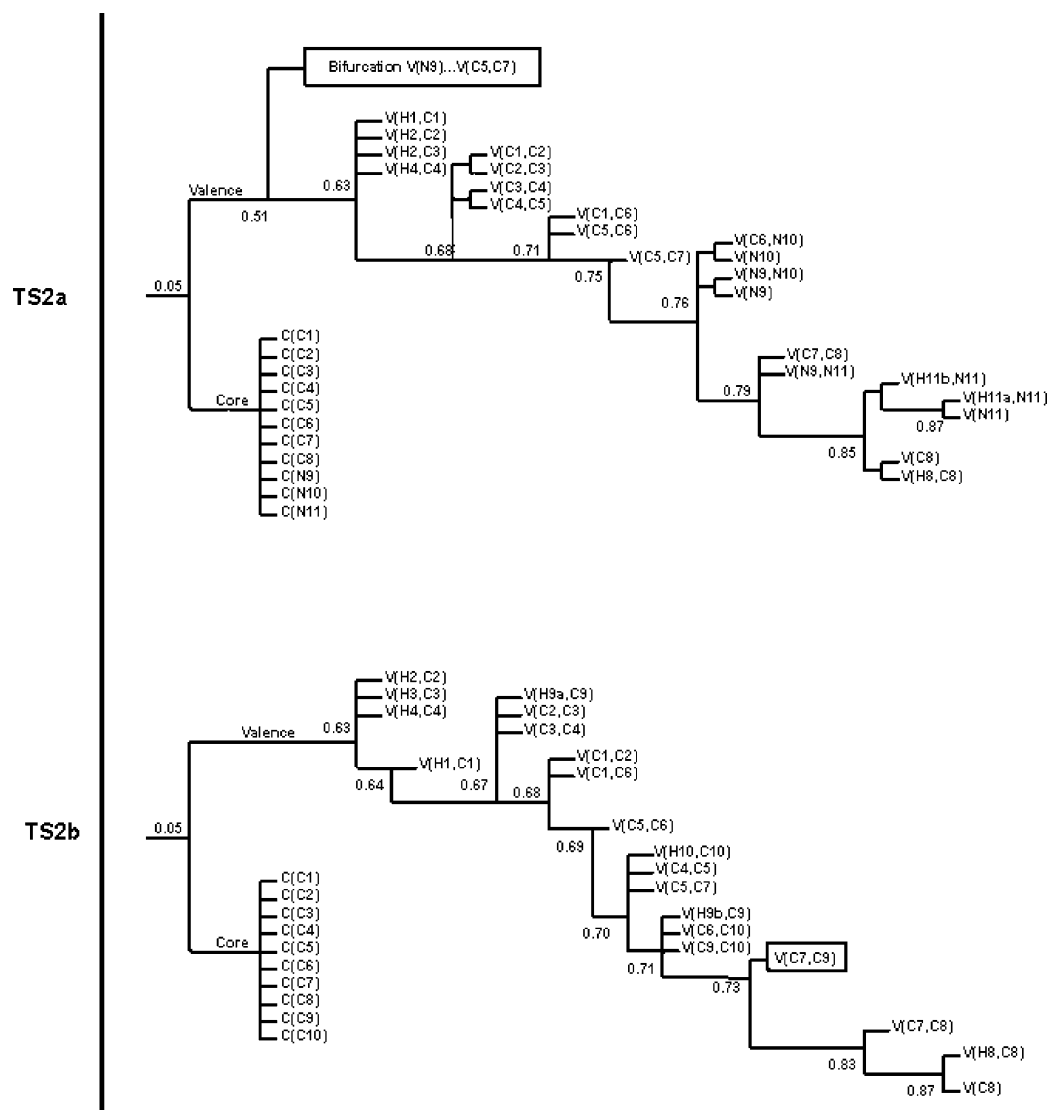


Figure 1. Localization-domain reduction tree diagrams based upon the electron localization function (ELF) analysis of TS2a and TS2b transition states from the optimized wave functions at the B3LYP/6-31G(d) level of theory.

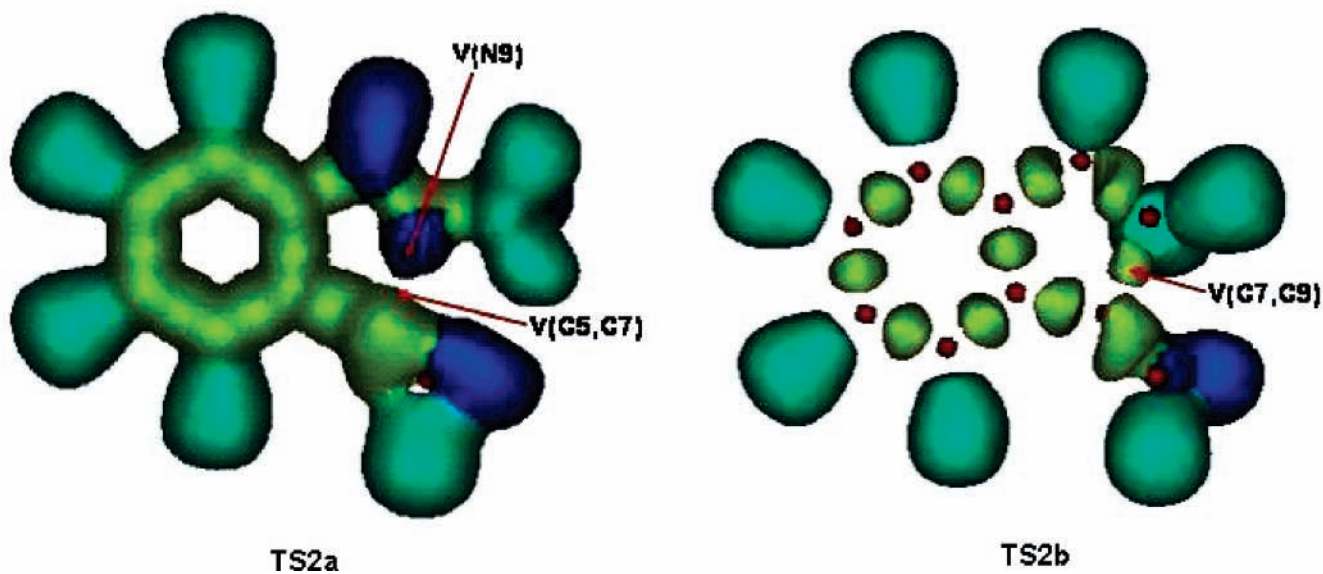


Figure 2. Localization domains of the electron localization function (ELF) at TS2a and TS2b transition states (as calculated at ELF = 0.51 and 0.73 isosurfaces, respectively) from the optimized wave functions at the B3LYP/6-31G(d) level of theory.

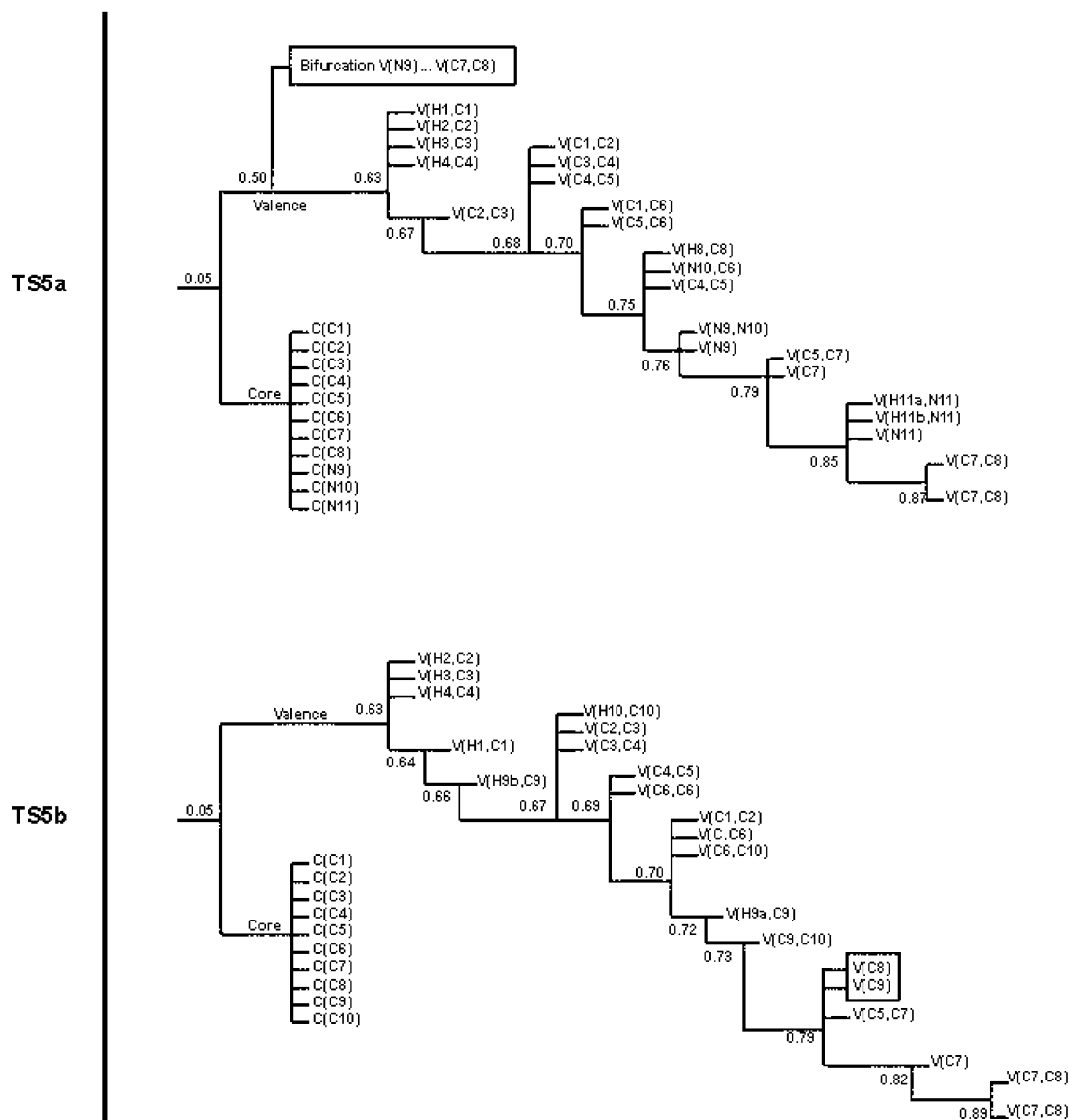


Figure 3. Localization-domain reduction tree diagrams based upon the electron localization function (ELF) analysis of TS5a and TS5b transition states from the optimized wave functions at the B3LYP/6-31G(d) level of theory.

with the new C7–C9 single bond in the products and such a basin will not exist at all in the reactants. Thus, in this case of TS2a, the CC bond formation is late along the reaction pathway. In the reactants, ELF predicts a disynaptic region for the C5–C7 single bond and two disynaptic basins associated with the triple bonding at C7–C8. In the products, via TS2, two disynaptic basins are associated with the C5–C7 double bond, whereas a disynaptic basin associated with the single bond between C7 and C8 exists and one monosynaptic region related to the carbene that is formed at the C8 center. Figure 1 depicts the localization domain reduction tree diagrams for TS2a and TS2b. The most important feature of the irreducible f-localization domain diagram for TS2b is that the localization domain reduction associated with the orbital disconnection occurring between C7 and C9 atoms, which corresponds to the V(C7, C9) basin, appears at a high value of ELF (0.73). A high value of ELF indicates a strong correlation between these populations. Conversely, for TS2a the corresponding domain reduction associated with this orbital disconnection between the C7 and N9 atoms occurs at a lower value of ELF equal to 0.51. Henceforth,^{24–33} it will be possible to associate these findings with a *pseudocoarctate* bonding character for TS2a. Recall that the homogeneous gas (i.e., ELF = 0.5) is taken as the comparing

reference in eq 1. It seems possible that the pericyclic and coarctate patterns of bonding are associated, whether the expected existence of disynaptic basins occurs, with high values of ELF along the entire reaction pathway. It has just been the case found for the TS2b topology. As has been discussed already, and above-mentioned following eq 3, higher values of bifurcation imply higher connection (i.e., fluctuations or variance) between corresponding basin populations.^{24–33} In Figure 2, the ELF isosurfaces for TS2a and TS2b are depicted for the disconnection ELF values. Note also from Figures 1 and 2 for TS2a and TS2b that it resembles the ACID plots obtained by Kimball et al.² from which they have concluded a *pseudocoarctate* nature of bonding for the TS2a transition state, being the TS2b characterized in terms of a *coarctate* one.^{2,42} Bond making and bond breaking in coarctate reactions do not follow a cyclic path. Indeed, it is noted that opposed to pericyclic reactions there is at least one atom at which two bonds are made and two bonds are broken simultaneously (i.e., the C7 center at TS2).² The analogy among the ACID and ELF results resides on the fact that both of these tools account for *electron (de)-localization*. However, in the first case, the delocalization (i.e., mobility) of the spin density is measured. In the other case, the electron localization function provides an interpretation in terms

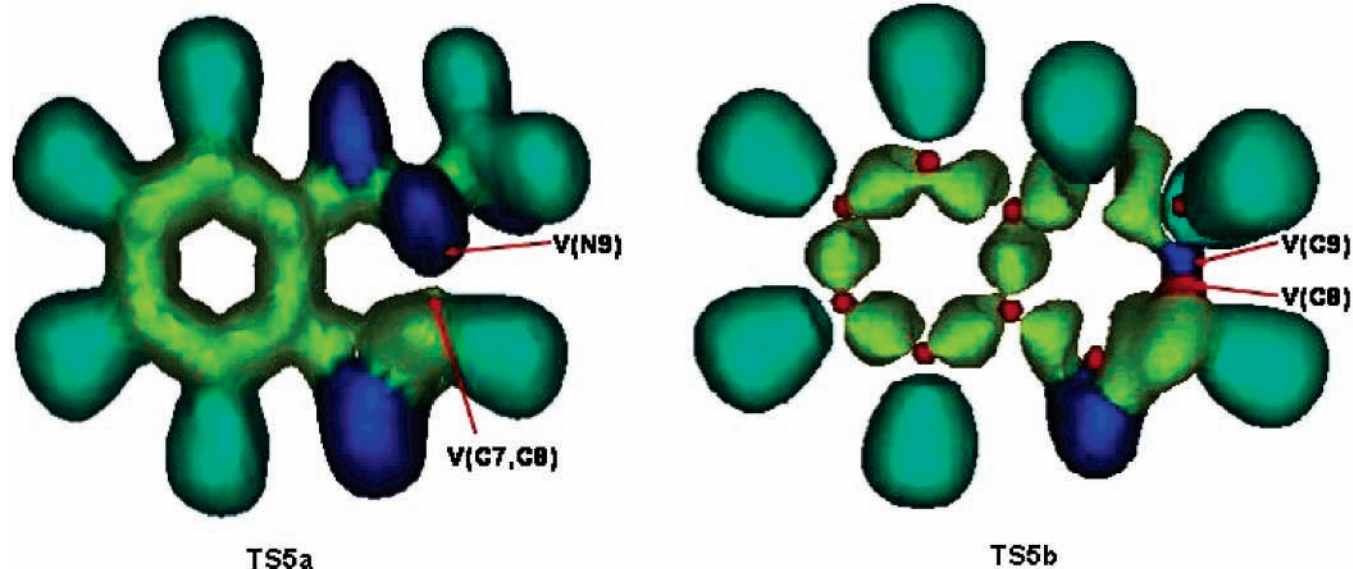


Figure 4. Localization domains of the electron localization function (ELF) at TS5a and TS5b transition states (as calculated at ELF = 0.50 and 0.68 isosurfaces, respectively) from the optimized wave functions at the B3LYP/6-31G(d) level of theory.

of the *local* excess of kinetic energy due to the Pauli repulsion. Henceforth, ELF provides us with a measure of the *local pairing for this mobile electron flow*. A clear analogy could also be expected between the ACID plots and the ELF- π analysis introduced recently.⁴³ However, a σ - π separation for the electron density is not always so clear, which precludes its application in the present case.

Six-Membered Ring Cyclizations: (Pseudo)pericyclic Pathways. Correspondingly with the five-membered cyclic case, the examination of the gradient field of the ELF also reveals in this case that there are not disynaptic basins associated directly with the C8 and X9 centers at TS5a and TS5b. In contrast to the five-membered case, the product via TS5 will reveal only a disynaptic region associated with the single bond between C5 and C7, and two disynaptic basins corresponding to the double bond C7-C8. As before, we concentrate the analysis in this case on the topology of the transition structures. Figure 3 depicts the localization domain reduction tree diagrams for TS5a and TS5b. In the first case, the reduction associated with the basin disconnection between the V(N9) and V(C7, C8) valence basins occurs at a low value of ELF equal to 0.50. Contrarily, for TS5b, the localization domain reduction associated with the disconnection between the V(C8) and V(C9) valence basins occurs at a higher ELF value of 0.79. These results might be associated with the weakly pericyclic and pericyclic characters of TS5a and TS5b, respectively, which were first described by Haley et al.² from the ACID analysis. In Figure 4, the ELF isosurfaces at the disconnection values for TS5a and TS5b have been depicted. A lower value for the reduction isosurface (ELF = 0.68) has been chosen for TS5b, to clearly show the basins that are disconnecting at the C8-X9 bonding region.

One final point should be remarked in this stage. The pericyclic (or coarctate) character of a transition state is indeed associated with high-energy barriers and nonplanar geometries, whereas the pseudopericyclic (or pseudocoarctate) character is associated with low barriers and planar geometries.^{5-11,44-47} The ELF value at which the disconnection between the basins associated with the reaction center occurs could be a measure of the "pericyclicity" (or "coarctaticity") of a transition state, but it is not possible to establish some value upper or lower from which a TS can be classified as pericyclic (or coarctate) or pseudopericyclic (or pseudocoarctate). Moreover, this com-

parison will only be meaningful among transition states with similar reaction centers, that is, as has been the case for the localization domain reduction values for TS2a with those for TS2b (five-membered cyclic transition states) or the corresponding values for TS5a with those for TS5b (six-membered cyclic transition states), but it is not possible to compare the TS2 values to those of TS5 directly because of the intrinsic differences of the topologies that exist between them. However, *electron localization* as measured here is, of course, a continuous variable, and the establishment of such a type of scales is open to more research.

IV. Concluding Remarks

In summary, the topological analysis of ELF, a measure of local Pauli repulsion and an orbital-independent technique for bonding analysis,²³⁻³³ has been used to explore the nature of bonding at the transition states of the five- and six-membered cyclizations of (2-ethynylphenyl)triazene and 2-ethynylstyrene (see Scheme 2). The five-membered cyclizations are processes in which the C7 atom neighboring the carbene center is a coarctate atom where two bonds are being made and two bonds are being broken. ELF results support the idea that the cyclization of 2-ethynylstyrene via TS2b has a more pronounced coarctate character than the cyclization of (2-ethynylphenyl)triazene via TS2a, which is a pseudocoarctate one. However, the six-membered cyclizations should be understood in terms of a pericyclic bonding character. ELF results have shown in this case that the cyclization of 2-ethynylstyrene via TS5b is a more pericyclic process than the cyclization of (2-ethynylphenyl)triazene via TS5a. By comparing the ELF values at which disconnection occurs between the basins associated with the reaction centers, we can classify TS2a and TS5a as pseudocoarctate and pseudopericyclic transition states, respectively. Both the ACID and ELF tools describe *electron (de)localization*. In the first case, it is a measure for the mobility of spin density at all. In the case of the electron localization function, it provides an interpretation in terms of the *local* excess of kinetic energy due to the Pauli repulsion. Thus, ELF will provide a characterization of the *local pairing* for this mobile electron flow. It could be expected that ELF analysis of the electron delocalization through bifurcation diagrams^{30-33,48} might also be

allocated effectively in the building of a general arbitrary scale of *pericyclicity*, as could be the case for aromaticity.⁴³ It is clear that this should imply a more complete analysis along some selected reaction pathway.

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