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Aromatic Transition States in Nonpericyclic Reactions: Anionic 5-Endo Cyclizations Are Aborted Sigmatropic Shifts

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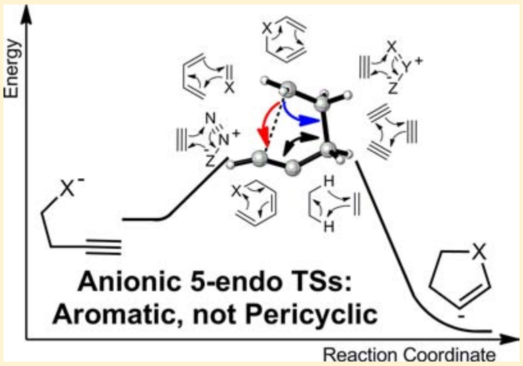
Supporting Information

ABSTRACT: The transition states (TSs) of 5-endo-dig and 5-endo-trig anionic ring closures are the first unambiguous examples of *nonpericyclic* reactions with TSs stabilized by aromaticity. Their five-center, six-electron in-plane aromaticity is revealed by the diatropic dissected nucleus-independent chemical shifts, −24.1 and −13.7 ppm, respectively, resulting from the delocalization of the lone pair at the nucleophilic center, a σ CC bond, and an in-plane alkyne (or alkene) π bond. Other seemingly analogous exo and endo cyclization TSs do not have these features. A symmetry-enhanced combination of through-space and through-bond interactions explains the anomalous geometric, energetic, and electronic features of the 5-endo ring closure transition state. Anionic 5-endo cyclizations can be considered to be "aborted" [2,3]-sigmatropic shifts. The connection between anionic cyclizations and sigmatropic shifts offers new possibilities for the design and electronic control of anionic isomerizations.



INTRODUCTION

Electronic effects that stabilize transition states[1] (TSs) selectively are conceptually important for predicting and interpreting the outcome of chemical processes. Such effects are exemplified by the aromaticity of transition states, a key element of "concerted" pericyclic reactions involving cyclic arrays of orbitals involved in bond forming and bond breaking.[2] Importantly, the relationship between the cyclic Hückel or Möbius topologies[3−5] of these orbitals and the special thermochemical stability (as well as geometric and magnetic[4] manifestations) of aromatic TSs provides a theoretical basis[6,7] for understanding the prevalence of a myriad of pericyclic reactions, e.g., Diels−Alder,[8] 1,3-dipolar cycloaddition,[9] and Cope rearrangements.[10]

Recently, we re-examined the stereoelectronic Baldwin[11] rules for the formation of cyclic structures.[12,13] Contrary to the Baldwin rules, our study revealed that nucleophilic cyclizations of alkynes favor exo-dig, rather than endo-dig, ring closure. The *obtuse*, rather than *acute*, nucleophilic attack trajectory in the exo-dig TS[14] leads to better orbital overlap and lowers the activation barrier (see Figure 1 for the description of three factors on which the Baldwin classification is based). Such stereoelectronic preferences are opposite the earlier assumptions on which the Baldwin ring closure rules for alkynes were based. Thus, the competing 3-exo/4-endo and 5-exo/6-endo ring closure reactions involving the parent C, N, and O centered anions all favor the "exo" rather than the "endo" pathway.[12] In sharp contrast, the 4-exo/5-endo-dig competition is much closer and, in some cases, may favor 5-endo-dig closure (Figure 1, right panel).

Since strain in the four-membered ring 4-exo product[16] could overwhelm the stereoelectronic advantages of its TS, we investigated the differences of the 4-exo vs. 5-endo potential energy profiles more closely, comparing them to the smaller (3-exo/4-endo) and larger (5-exo/6-endo) analogues. Surprisingly, unlike the other ring cyclization TSs, the 5-endo-dig transition state displayed anomalous structural and energetic features. The latter are apparent from the intrinsic barriers, evaluated by Marcus theory,[17,18] which effectively filters out the thermodynamic preferences unique to the system and reveals the inherent stereoelectronics of each transition state more accurately.[19] The contrasting intrinsic barrier[20] trends for the exo-dig (3-exo < 4-exo < 5-exo) versus endo-dig (4-endo≫ 5-endo ≤ 6-endo) series in Figure 1 suggest an unexpectedly low intrinsic barrier for the 5-endo-dig closure. Although the accuracy of Marcus theory depends on the geometric features for the key regions of the reaction potential energy surfaces,[21] the intrinsic and activation barriers of 5-endo- vs. 6-endo-dig reactions for the parent carbon case, as well as for the nitrogen and oxygen analogues, favor the 5-endo-dig pathway consistently.

Structural features of the 5-endo-dig TS also are unusual. Notably, the greater incipient C⋯C bond distance for the 5-endo TS versus the 6-endo TS (Figure 2) implies an earlier TS

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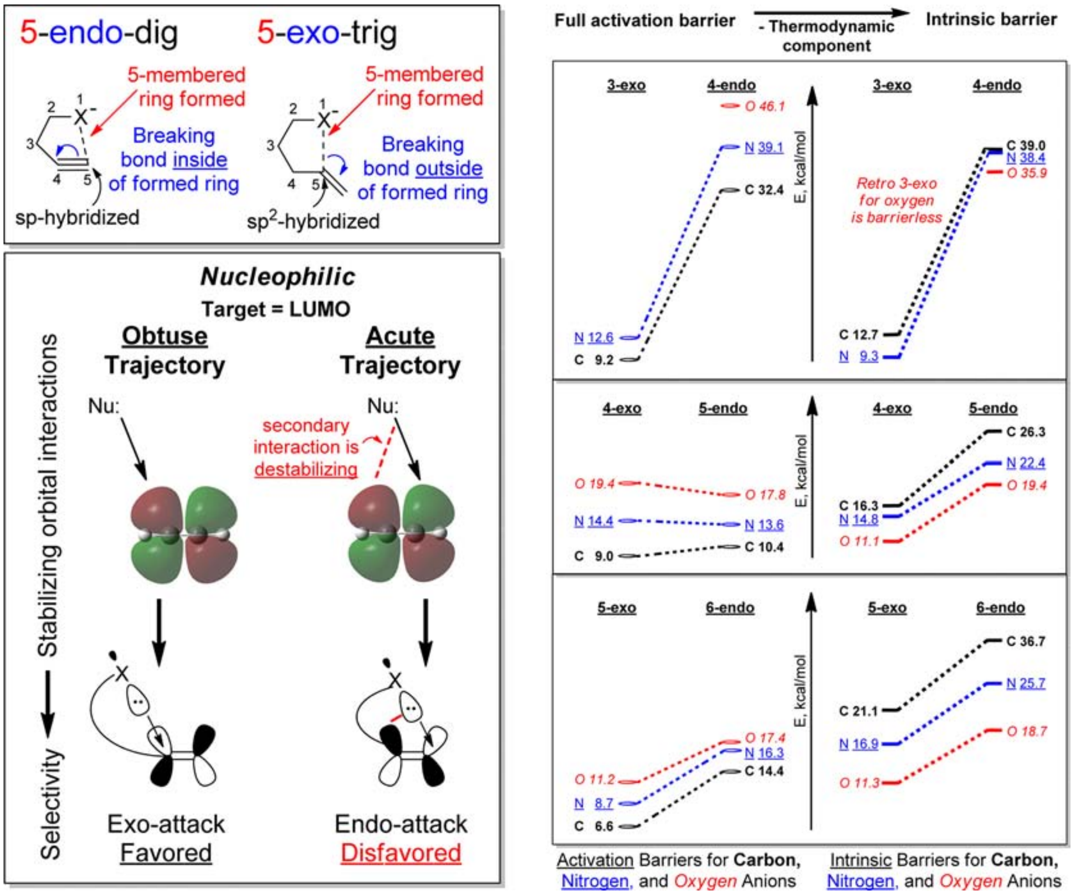


Figure 1. (Left top) Three Baldwin rule features used to classify cyclizations: ring size, location of the breaking bond [within (endo) or external (exo) to the ring], and hybridization of the atom being attacked (sp^3 = tet, sp^2 = trig, sp = dig). (Left bottom) Comparison of orbital interactions for the exo and endo selectivity in nucleophilic alkyne cyclizations. Straight arrows designate the dominant stabilizing interactions; dashed lines depict secondary interactions. (Right) Activation barriers and intrinsic barriers for the cyclization of carbon (black, bold), nitrogen (blue, underlined), and oxygen (red, italics) anions with terminal alkynes (M05-2X/6-31+G(d,p) level).[15] (Right middle) Note that while the 4-exo vs. 5-endo activation barriers are similar, their intrinsic barriers are distinctly different.

for the less exothermic 5-endo-dig closure, in contrast to the Hammond−Leffler postulate.[22]

As seen in Figure 2, the E_o of the 5-endo-dig TS is "lower" than expected (negative ΔE), but the incipient bond is "longer" than expected (positive Δd) when compared to those of the other endo-dig reactions (see the dashed lines). On the other hand, the E_o and Nu···C distances for the 3/4/5-exo-dig closures increase linearly (see the solid lines). But why is the 5-endo-dig ring closure transition state stabilized more than the TSs of the other endo-dig cyclizations? Our computational analysis shows that the favorable continuous orbital interactions in the *nonpericyclic* 5-endo-dig ring closure TS result in aromatic stabilization. This is the first unambiguous example of a nonpericyclic reaction with an aromatic transition state.

■ COMPUTATIONAL METHODS

Stationary point geometries in both radical and anionic cyclizations were computed at the M05-2X/6-31+G(d,p) level reported to give accurate thermochemistry for organic systems[23] using Gaussian 03.[24] Harmonic vibrational frequency computations confirmed that equilibrium geometries were minima or transition structures with all positive values or one imaginary value, respectively. All barriers are given relative to the gauche conformations, which are closer to the "near attack" geometry than the more stable anti conformations (see the Supporting Information). The continuous set of gauge transformation (CSGT) procedure was used to compute the magnetic susceptibility exaltations (MSEs)[25] at the B3LYP/6-311+G(d,p)//M05-2X level.[46] Dissected localized molecular orbital (LMO)−nucleus-independent chemical shifts (NICS) and isotropic NICS values for the 4-, 5-, and 6-endo-dig TSs were computed with the individual gauge for localized orbitals (IGLO) method as implemented in the DeMon-Master program[26] (at the PW91/IGLOIII level) employing the Pipek−Mezey localization procedure.[27] Isotropic NICS(0)[28] are the negative values of the computed magnetic shielding at the heavy atom center of the forming TS rings. However, isotropic NICSs are contaminated by contributions from in-plane (*xx* and *yy*) tensor components and from molecular orbitals (MOs) that are not relevant to aromaticity.[29,30] The refined dissected $\mathrm{NICS}(0)_{\mathrm{MO}zz}$ values,[29c,30] computed at the same position, provide a superior index, based on the out-of-plane (*zz*) tensor components contributed by only the MOs relevant for probing the "in-plane aromaticity" of the TSs (vide infra, Figure 5). These MOs are (1) the in-plane C_1 (or N_1/O_1 for the nitrogen/oxygen analogues) lone pair (LP), (2) the in-plane ethynyl (or ethenyl) π orbital, and (3) the C−C σ bond orbital vicinal to the ethynyl (or ethenyl) moiety. As none of the TSs have a planar geometry, a model plane was selected. This was defined by the C_1 atom (or N_1/O_1 for the nitrogen/oxygen analogues) and the two ethynyl (for endo-dig TSs) or ethyl (for endo-trig TSs) carbon atoms. For example, the 5-endo-dig TS "plane" for $C_5H_7^-$ (defined by C_1, C_4, and C_5) was selected to identify the in-plane (*xx*, *yy*) and out-of-plane (*zz*) tensor component contributions. Large negative/positive $\mathrm{NICS}_{\mathrm{MO}zz}$ values at the heavy atom "forming ring" centers indicate the presence of induced diatropic (aromatic)/paratropic (antiar-

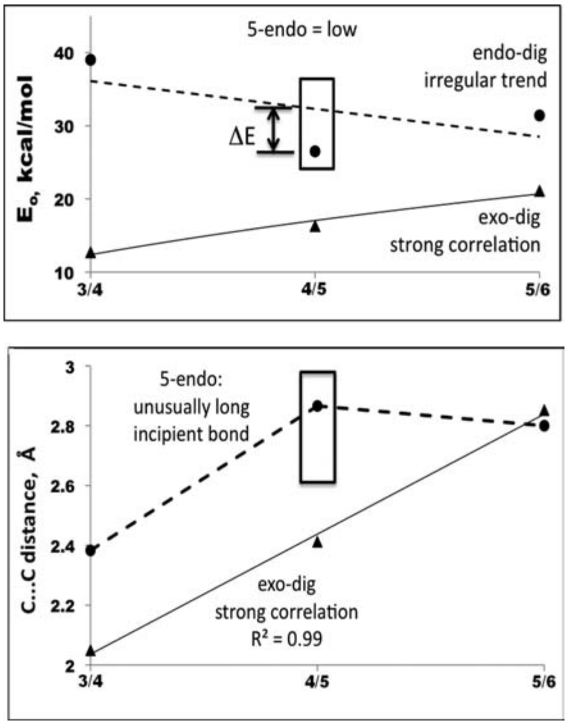


Figure 2. (Top) Intrinsic barriers for the nucleophilic primary carbanion−terminal alkyne closures for the competing ring sizes: 3-exo vs. 4-endo (3/4), 4-exo vs. 5-endo (4/5), 5-exo vs. 6-endo (5/6). (Bottom) Lengths of the bond being formed in the TS. Dashed lines refer to the 4/5/6-endo-dig trends, while the solid lines indicate the 3/4/5-exo-dig trends. ΔE_o is the deviation of the computed 5-endo-dig E_o from its expected value based on an extrapolation of the E_o of the 4-endo- and 6-endo-dig closures. This figure emphasizes the unexpectedly low intrinsic barrier (ΔE_o, top) and the large incipient bond distance (box, bottom) of 5-endo-dig closure at the M05-2X/6-31+G(d,p) level. Similar trends are observed for oxygen and nitrogen nucleophiles (see the Supporting Information).

omatic) ring currents. Nonaromatic species have NICS values close to zero.

Marcus theory[17] was applied to understand how the reaction exothermicity alters cyclization barriers. In this description, the energy of activation (ΔE_a) of a nondegenerate reaction is the sum of the intrinsic barrier (ΔE_o) and the thermodynamic contribution (ΔE_r, or reaction energy) as given by

$$\Delta E_a = \Delta E_o + {}^{1}\!/_{2}(\Delta E_r) + (\Delta E_r)^2/16(\Delta E_o) \qquad (1)$$

The intrinsic barrier in eq 1 represents the barrier of a thermoneutral process (e.g., a degenerate transformation) in the absence of thermodynamic bias. Intrinsic barriers can be used to compare intrinsic stereoelectronic requirements of different reactions. If the reaction barrier and reaction energy are known, the intrinsic activation energy ΔE_o is estimated by

$$\Delta E_o = \frac{\Delta E_a - {}^{1}\!/_{2}(\Delta E_r) + \sqrt{(\Delta E_a)^2 - \Delta E_a \Delta E_r}}{2} \qquad (2)$$

RESULTS/DISCUSSION

Geometries. The computed angle of attack at the triple bond corresponds to the stereoelectronically unfavorable acute trajectory only in the 5-endo TS. Note that the incipient C···C bond is longer for the 5-endo-dig closure than for the other three cyclizations in Figure 3. The computed C_2-C_3 bond length (1.610 Å) in the 5-endo-dig ring closure TS geometry is considerably longer than those in the competing 4-exo-dig (1.529 Å), 5-exo-dig (1.540 Å), and 6-endo-dig (1.549 Å) alternatives (see Figure 3).

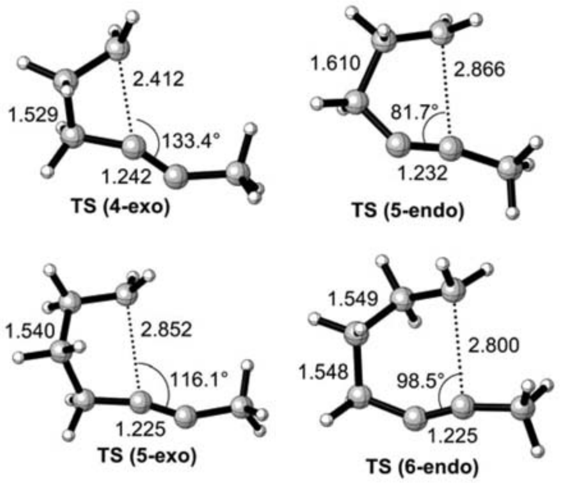


Figure 3. Transition-state geometries for 4-exo-, 5-endo-, 5-exo-, and 6-endo-dig carbanionic cyclizations for methyl-substituted alkynes computed at M05-2X/6-31+G**. Distances are in Ångstrømes. Angles correspond to the trajectory of attack at the π bond. For exo closures, this angle is external to the forming ring. For endocyclic closures, the angle is within the forming cycle. Note that only the 5-endo-dig TS has an acute (≤90°) angle of attack at the triple bond.

On the basis of natural bond orbital (NBO) analysis, the long C_2-C_3 distance in the 5-endo-dig ring closure TS can be attributed to hyperconjugative donation of the anionic LP into the σ^* C_2-C_3 orbital (see Figure 4). The greater elongation of the C_2-C_3 bond indicates an increased importance of delocalizing interactions which involve this bridge bond in the 5-endo TS relative to the other systems in Figure 3. The long C_2-C_3 distances (1.62 Å) and LP → C_2-C_3 σ^* interaction energies in the 4-pentynyl carbanion reactant indicate similar hyperconjugation, suggesting that this effect is due to through-bond (TB) interaction with the C_4-C_5 π system (vide infra).[31] In the transition state, there also is the direct through-space interaction between the lone pair and alkyne π^*, which accounts for the significant population increase (0.22 e^-) of the in-plane alkyne π^* orbital. Although a relatively strong (albeit slightly weaker) n → $\sigma^*_{C_2-C_3}$ interaction is observed in the 5-hexynyl anion reactant, this interaction is lost in the 6-endo TS where the C_2-C_3 bond and the anionic orbital become misaligned (Figure 4, bottom).

Magnetic Properties. Magnetic properties are the most direct approach for identifying cyclic electron delocalization in unusual aromatic systems.[4,32] In particular, the NICS method[28,29] is a reliable and versatile approach.[30] The most sophisticated dissected $\mathrm{NICS}_{\mathrm{MO}zz}$ index[33] isolates the aromaticity-related out-of-plane (zz) tensor components of specific MO contributions and has many interpretive advantages (see the Computational Methods).

Dissected NICS values illustrate the different natures of the in-plane delocalization of the methylated 4-, 5-, and 6-endo-dig TSs. The in-plane-aromaticity of the methylated 5-endo-dig TS is supported by its large (−20.5 ppm) negative $\mathrm{NICS(0)}_{\mathrm{MO}zz}$ value (which includes contributions from the CH_2^- lone pair, the in-plane ethynyl π electrons, and the C_2-C_3 σ bond, Figure 5b) and documents the existence of an induced diatropic ring current. Notably, this value is more than half the $\mathrm{NICS(0)}_{\pi zz}$

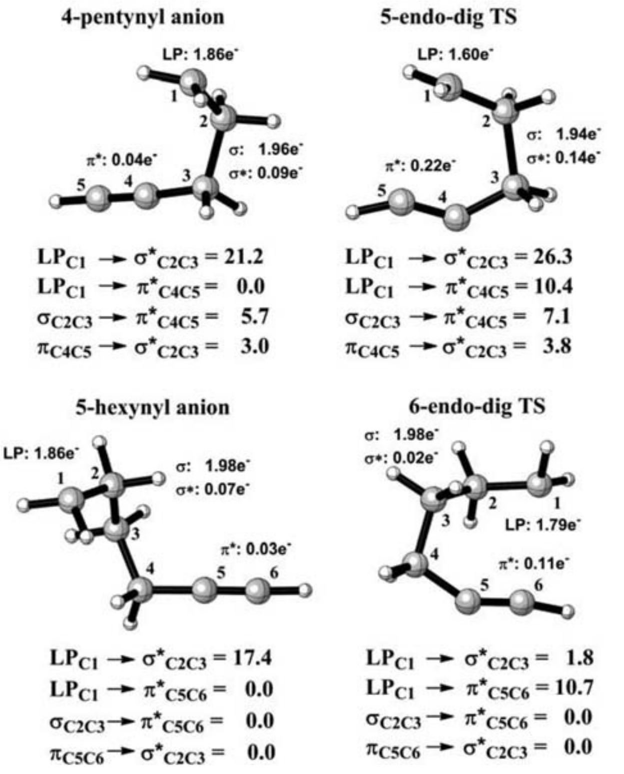


Figure 4. NBO evaluated hyperconjugative interactions (kcal/mol, at M05-2X/6-31G+(d,p) level) involving the carbanion, σ bond, and π bond of the acyclic 4-pentynyl/5-hexynyl anions and the 5-endo/6-endo-dig TSs. Occupancies of the interacting filled and virtual orbitals are indicated. LP = lone pair.

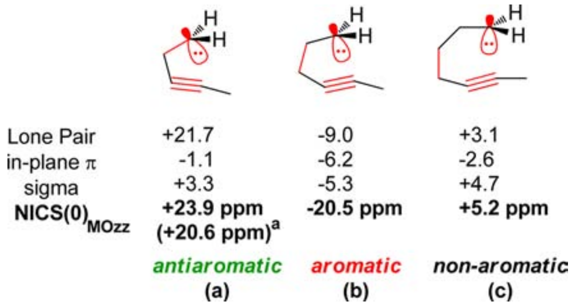
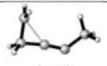
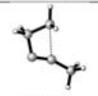
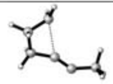
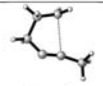
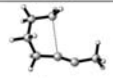
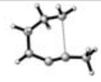


Figure 5. Dissected NICS(0)$_{MOzz}$ data (ppm, computed at PW91/IGLOIII) for the methylated (a) 4-endo-dig, (b) 5-endo-dig, and (c) 6-endo-dig TSs, based on NICS(0)$_{zz}$ contributions from the CH_2^- lone pair orbital, the ethynyl in-plane π orbital, and the σ bond orbital vicinal to the ethynyl group (see the red highlights). Note *a*: The value in parentheses only includes the contributions from the anion lone pair and the ethynyl in-plane π orbitals.[35]

Table 1. Computed NICS(0)$_{MOzz}$ and NICS(0) (ppm, at the PW91/IGLOIII Level) and Magnetic Susceptibility Exaltation (Λ(TS) (ppm cgs, at the B3LYP/6-311+G(d,p)//M05-2X/6-31+G(d,p) Level) for the TSs of 3-Exo/4-Endo-Dig, 4-Exo/5-Endo-Dig, and 5-Exo/6-Endo-Dig Ring Closures of the Methyl-Substituted Anions[a]

Ring closure TS's for the methyl substituted anions	NICS(0)$_{MOzz}$	NICS(0)	Λ (TS)
 3-exo	-1.6	−19.3	-2.27
 4-endo	+23.9 (+20.6)^a	+1.8	+8.34
 4-exo	N/D	−4.0	+2.1
 5-endo	−20.5	−15.2	−8.2
 5-exo	N/D	−8.8	−0.3
 6-endo	+5.2	−0.9	+7.03

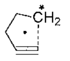
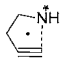
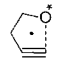
[a] The NICS values are computed at the heavy atom center of the forming ring. [b] The value in parentheses only includes NICS(0)$_{zz}$ contributions from the anion lone pair orbital and the ethynyl in-plane π orbital. N/D = not determined.

value of benzene (−36.9 ppm, computed at the same level). In sharp contrast, the methylated 4-endo-dig and 6-endo-dig TSs have positive NICS(0)$_{MOzz}$ values, +23.9 ppm (or +20.6 ppm if only the in-plane π and lone pair orbitals are considered, Figure 5) and +5.2 ppm. These values indicate antiaromaticity[12] and nonaromaticity, respectively; see Figure 5a,c.

The computed isotropic NICS and magnetic susceptibility exaltation (Λ) of the methylated 5-endo-dig TS (NICS(0) = −15.2 ppm, Λ(TS) = −8.2 ppm cgs) are also more negative than the analogous endo- and exo-dig TS values (see Table 1) and are similar in magnitude to the isotropic NICS(0) values reported for other aromatic transition states, e.g., for the 1,3-dipolar cycloaddition of fulminic acid and acetylene (−17.8)/ethylene (−20.1).[34] However, both the NICS(0) and Λ methods are marred by the inclusion of contaminating magnetic effects not related to aromaticity, and cautious interpretations are required to avoid misleading conclusions. Thus, the suspiciously large negative isotropic NICS(0) value (−19.3 ppm) of the 3-exo-dig TS illustrates the danger of probing aromaticity with outmoded isotropic NICS. Dissected NICS reveals that the irrelevant in-plane tensor components, *xx* (−16.3 ppm) and *yy* (−40.0 ppm), dominate the isotropic NICS value (which is the average of the *xx*, *yy*, and *zz* components). In contrast, the small value of the more relevant out-of-plane (*zz*) tensor component (−1.6 ppm) indicates the nonaromaticity of the 3-exo-dig TS.

Interestingly, the large negative NICS(0)$_{MOzz}$, NICS(0), and Λ values of the 5-endo-dig cyclization TSs for CH_2, NH, and O 4-pentyn-1-yl anions, indicative of special in-plane aromaticity, involve the CH_2^-, NH^-, and O^- lone pair, the in-plane ethynyl π bond, and the “long” σ bond (vicinal to the ethynyl group). However, the dissected NICS(0)$_{MOzz}$ for the CH_2^- (−24.1 ppm), the NH^- (−18.0 ppm), and the O^- (−11.0 ppm) analogues become less negative for the more electronegative nucleophilic centers (Table 2), as expected by their reduced ability to participate in σ electron delocalization. The computed isotropic NICS and Λ values reveal the same trend (Table 2). Expectedly, when one electron is removed, smaller negative NICS(0)$_{MOzz}$ values (ranging from −5.3 to −6.7 ppm, Table 2) are obtained for the CH_2, NH, and O 4-pentyn-1-yl radicals.

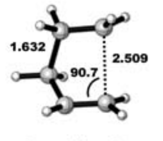
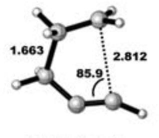
Table 2. Computed NICS(0)$_{MOzz}$ and NICS(0) (ppm, at the PW91/IGLOIII Level) and Magnetic Susceptibility Exaltation (Λ(TS) (ppm cgs, at the B3LYP/6-311+G(d,p)//M05-2X/6-31+G(d,p) Level)) for the 5-Endo-Dig 4-Pentyn-1-yl Carbanion and Radical TSs, as Well as for the O and NH Analogues

5-endo TS	NICS(0) Anion	NICS(0)$_{MOzz}$ Anion	NICS(0) Radical	NICS(0)$_{MOzz}$ Radical	Λ (TS) Anion
	−17.2	−24.1	−13.1	−6.7	−10.3
	−14.1	−18.0	−11.2	−5.3	−7.2
	−13.1	−11.0	−11.6	−6.6	−5.7

The reduced degree of aromaticity for the radicals compared to their parent anions confirms the advantages of having six electrons in the interacting cyclic orbital arrays.

Our NICS analysis of the stereoelectronically unfavorable 5-endo-trig cyclization TS (nucleophilic attack at a *double* bond) also shows a moderately negative NICS(0)$_{MOzz}$ value (−13.7 ppm, Table 3). Notably, the activation barrier, as well as the reaction energy (E_r), of 5-endo-trig closure is lower than that of 5-endo-dig closure (Table 3). The TS of 5-endo-trig closure also is later than that of the respective digonal closure, as expected from its lower exothermicity and marginally obtuse attack trajectory (91°, Table 3). Our findings explain the unexpected experimental prevalence of 5-endo-trig closure reactions[36] and provide another example of a nonpericyclic aromatic TS.

Table 3. Calculated E_a and E_r for the 4-Penten-1-yl and the 4-Pentyn-1-yl[12] Carbanion Reactions at the M05-2X/6-31+G(d,p) Level (kcal/mol)[a]

5-endo TS	E_a	E_r	NICS(0)	NICS(0)$_{MOzz}$
 5-endo-trig	+9.5	−7.0	−13.2 ppm	−13.7 ppm
 5-endo-dig	+10.4	−39.1	−17.2 ppm	−24.1 ppm

[a] Dissected NICS(0)$_{MOzz}$ and isotropic NICS(0) values for the respective ring closure TSs were computed at the PW91/IGLOIII level (ppm). Distances are in Ångstrømes and angles in degrees for the TS geometries (M05-2X/6-31+G** level).

Molecular Orbital Analysis. Both through-space and through-bond orbital interactions can stabilize molecules.[37−40] The energy inversions of the symmetric and antisymmetric nonbonding MOs in diazobicyclooctane (Figure 6)[41] and in pyrazine[42] are illustrative. The ca. 3−5 kcal/mol stabilization of the cyclic 1,4-diradical (*p*-benzyne) intermediate of the Bergman cyclization by through-bond orbital interactions decreases its reactivity relative to that of a phenyl radical.[43] In *p*-benzyne, mixing of the 1,4-diradicals with the two σ bonds (Figure 7) creates a cyclic six-electron system, topologically similar to the σ aromatic Cope rearrangement transition state. Direct through-space interactions, e.g., the two-electron, three-center, doubly aromatic C_6H_3 cation (see Figure 7, bottom right),[44] also can lead to σ aromaticity. The neutral 3,5-disubstituted heterocyclohexanes[45] (Figure 7, bottom left) show signs of σ aromaticity involving homohyperconjugative interactions.[46]

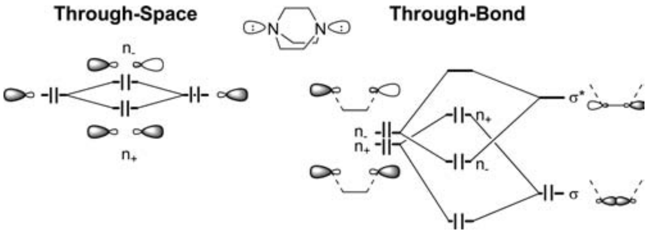


Figure 6. Through-space and through-bond interactions of the nonbonding (n_+ and n_-) orbitals with the C−C σ and σ* orbitals in diazobicyclooctane. Note that each of the group orbitals n_+ and n_- can participate in only one of the two coupling mechanisms but not in both at the same time.

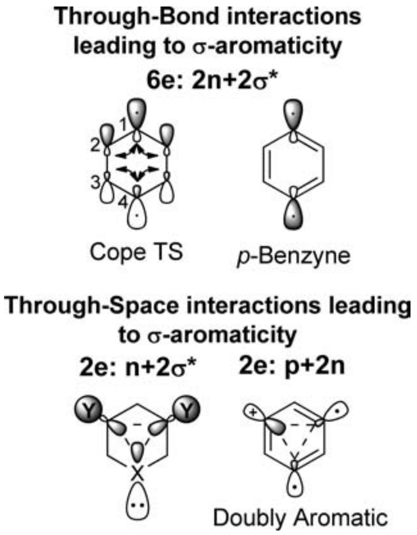


Figure 7. Both through-bond and through-space interactions can lead to σ aromaticity.

As illustrated in Figure 8, the five-center, six-electron 5-endo-dig (and -trig) TS aromaticity involves both "through-space" and "through-bond" interactions between the anionic lone pair and in-plane π bond. In contrast to the interaction of nonbonding orbitals in Figure 6 where these two interaction mechanisms cannot stabilize the same MO due to the symmetry restrictions, the involvement of a π* orbital instead of a lone pair changes the interaction symmetry and allows the through-space and through-bond interactions to be combined in a symmetry-enforced cyclic interaction.

Unlike the situation in pericyclic reactions, the intervening C_2−C_3 σ bond is elongated but is not broken. Topologically, the aromatic nonpericyclic 5-endo-dig transition state resembles other known aromatic transition states involving σ orbitals, π orbitals, or both (see Figure 9). While classic π aromatic TSs, e.g., those in the Diels−Alder[47] or ethyne trimerization[48] reactions, are due to the delocalization of three π bonds, other

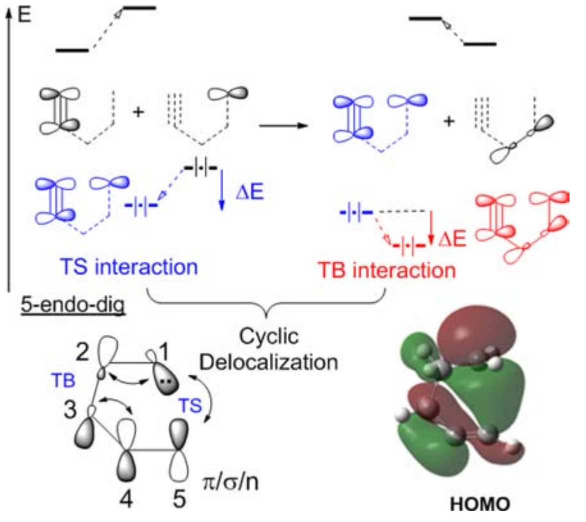


Figure 8. (Top) Symmetry-enforced combination of orbital interactions among the anionic lone pair, in-plane π bond, and long $C_2{-}C_3$ σ bond of the aromatic 5-endo-dig transition state. Note that, unlike the two nonbonding orbitals in Figure 6, the π^* and nonbonding orbitals can participate in through-space (TS) and through-bond (TB) interactions *simultaneously*. The detailed MO correlation diagram is given in the Supporting Information. (Bottom) Schematic representation of the cyclic delocalization and HOMO of the carbanionic 5-endo-dig transition state.

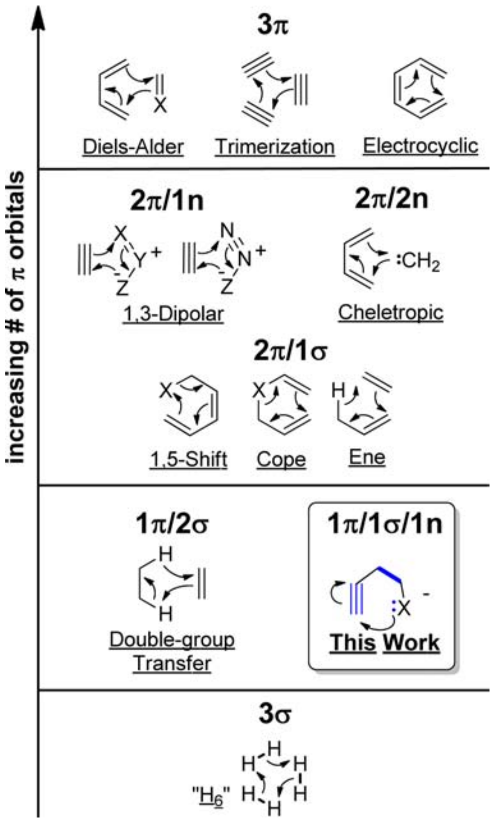


Figure 9. Different combinations of π and σ orbitals in cyclic aromatic six-electron transition states.[58] Note that cyclic redistribution of electron density for all pericyclic reactions in the figure leads to the formation and/or breaking of new bonds at *each* atom in the cyclic array.[59] In contrast, only three atoms are directly involved in the bond-forming/bond-breaking processes in the 5-endo ring closure: the bridge C−C bond participates in cyclic delocalization but does not break.

transient six-electron aromatic systems, e.g., in pericyclic reactions,[3,6,49] can involve a mix of two π bonds and one σ bond (1,5-shifts,[50] Cope rearrangement[51]) or two σ and π bonds (double group transfer[52]) or include lone pairs (e.g., the $\pi/\pi/n$ system in dipolar cycloadditions[53] of alkenes[54] and alkynes[9f,55]). Aromatic systems comprised of σ bonds exclusively are also known.[56,57]

Extended Classification of Pericyclic Reactions: "Aborted" Pericyclic Reactions. Although the 5-endo closures are not pericyclic, the combination of energetic and magnetic criteria indicates the presence of cyclic aromatic delocalization. We consider the formally *nonpericyclic* 5-endo ring closures to be an *aborted* anionic [2,3]-sigmatropic shift (see Figure 10). The cyclic 5-endo-trig product is positioned midway at the potential energy surface which connects two identical 4-penten-1-yl anions in the same way as the TS for a degenerate concerted sigmatropic shift. However, in the 5-endo closure, this geometry, instead of a TS, corresponds to a global minimum at the pericyclic potential energy surface due the greater stability of the cyclic structure relative to the two acyclic precursors. The potential energy surface for the 5-endo-dig process is similar but nondegenerate since it connects 4-pentyn-1-yl and 3,4-pentadien-1-yl anions.[60] In both 5-endo-dig and 5-endo-trig reactions, the replacement of a weaker π bond by a stronger σ bond stabilizes the cyclic intermediates. In the dig-cyclization, the sp^3 anion in the acyclic species also converts into a more favorable sp^2 (vinylic) anion.

The possibility of stabilizing pericyclic transition states by additional electronic effects has been considered before. Doering noted that the ability of conjugated aromatic groups to stabilize biradicaloid TSs can lead to a flattened "caldera" at the TS region of the potential energy surface.[61−63] Likewise, Schreiner et al. considered the Bergman cyclization as an *interrupted* Cope rearrangement (a [3,3]-sigmatropic shift) and pointed out that "nonconcerted (Cope rearrangement) reactions take place when biradical intermediates are stabilized either by allyl or aromatic resonance".[64] The ability to intercept the high-energy intermediate via a hydrogen atom transfer[65] or C−C bond formation[19e,66] leads to a variety of important applications, including the design of DNA-damaging anticancer agents.[67] Johnson applied similar concepts to Diels−Alder reactions.[68] Houk and co-workers had shown that allylic stabilization of diradical intermediates interrupts allowed [5,5]-sigmatropic shifts.[69] Siebert and Tantillo reported that a combination of transition-state complexation and benzylic resonance can convert a Cope TS into a cyclic zwitterionic intermediate in palladium-promoted [3,3]-sigmatropic shifts.[70]

The anionic 5-endo cyclizations presented in our work are unusual because the cyclic product formed by the *exothermic* anionic 5-endo-dig ring closure has no energetically favorable escape route and cannot continue along the pericyclic reaction path.[71]

We propose the following nomenclature for degenerate-type reactions (automerizations or their close relatives) for pathways between a reactant and its degenerate product: "concerted" with only one TS between the two species, "interrupted" where one or more intermediates exists higher in energy than the reactant/product, and "aborted" with an intermediate that is lower in energy than the reactant and becomes the new product (Figure 10).

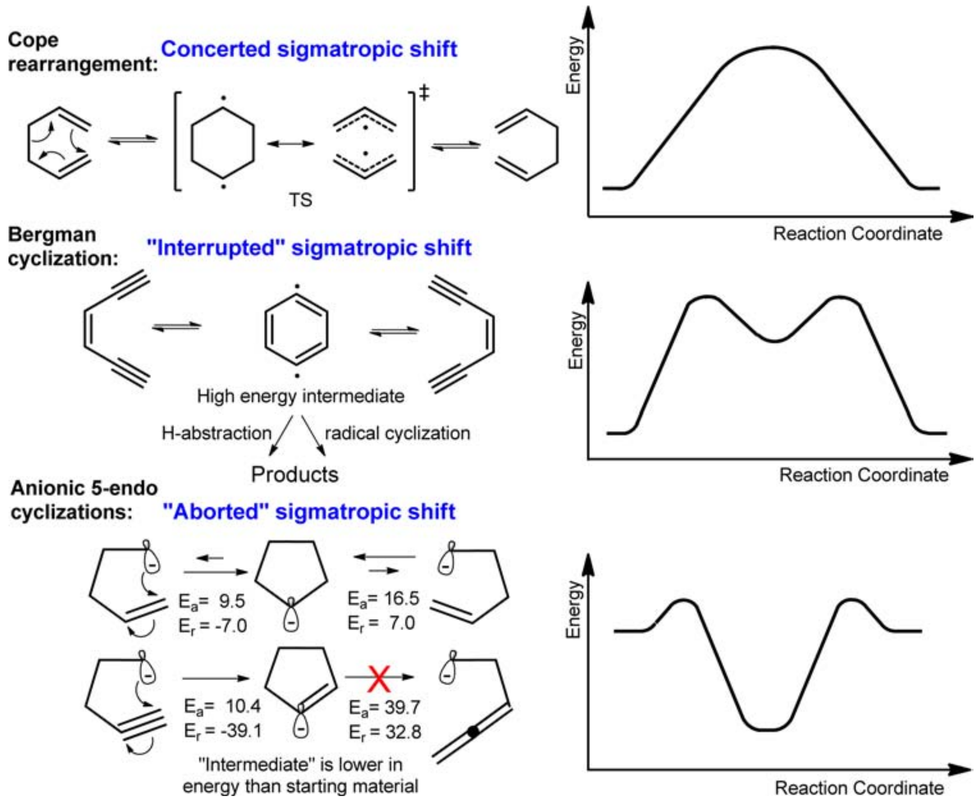


Figure 10. "Concerted", "interrupted", and "aborted" sigmatropic shifts, distinguished by the presence and stability of the intermediate cyclic species. MO5-2X/6-31+G(d,p) barriers and reaction energies are given for the anionic ring closures as well as the cyclic anion ring-opening.

Competition between Anionic 5-Endo Closures and [2,3]-Sigmatropic Shifts. Selectivity between competing sigmatropic shifts,[72,73] concerted (e.g., the Wittig and aza-Wittig rearrangements) and aborted (e.g., the anionic 5-endo ring closure),[74] can be controlled by structural alterations (see Figure 11). Thus, the intervening cyclic species (the TSs for concerted or the intermediates for aborted reactions) can be stabilized electronically (e.g., via hyperconjugation, conjugation, or translocation of the anion to a more electronegative atom).[75−77] Electron-withdrawing substituents, e.g. amide,[78] sulfonyl,[79] or nitro[80] groups, and electronegative atoms[81] at the Y_4 position (see Figure 11) promote 5-endo-trig (and -dig) products (due to enhanced conjugation with the anionic center at Y_4^-). However, σ acceptors geminal to atom Y (i.e., $\sigma^*_{C_5-Z}$ in Figure 11) favor [2,3]-shift products. Negative hyperconjugation[82] involving the anionic Y center (atom 4 in Figure 11) with endocyclic (σ^*_{C-X} and σ^*_{C-Nu}) and with exocyclic (σ^*_{C-Z}) acceptors facilitates [2,3]-shifts[83] and 5-endo-trig/dig cyclizations, respectively. Endocyclic n → σ^*_{C-X} hyperconjugation promotes C−X bond scission and enables the formation of [2,3]-shift products (see Figure 12). Exocyclic n → σ^*_{C-Z} hyperconjugation leads to the elongation or scission[84,85] of C−Z bonds and favors 5-endo-trig cyclization products. Experimental examples of alkyne cyclizations governed by similar

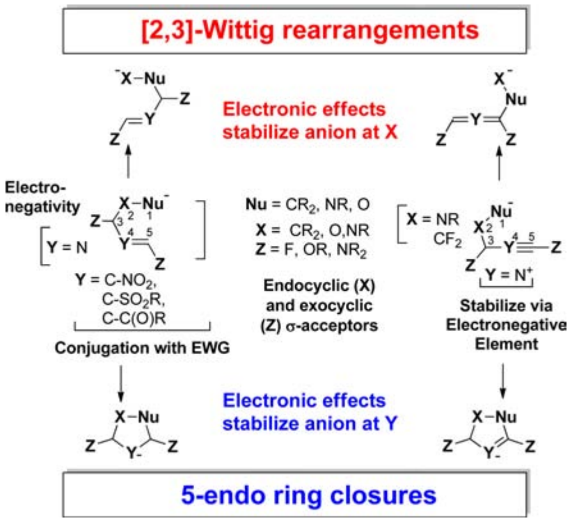


Figure 11. Electronic effects controlling the competition between 5-endo-trig/dig closure and [2,3]-sigmatropic shifts.

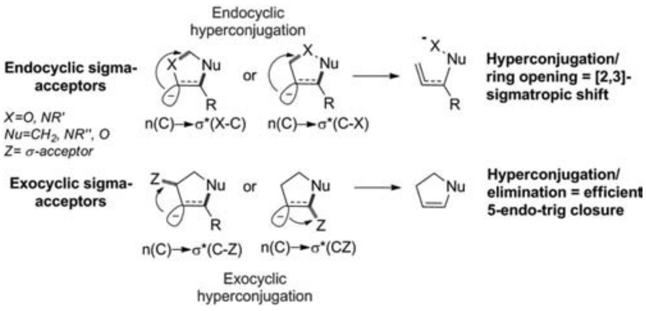


Figure 12. Selected patterns of hyperconjugative stabilization of the anionic center in the products of 5-endo-dig and 5-endo-trig cyclizations and two possible reactions of 5-endo-trig products facilitated by the transfer of electron density into the σ^*_{C-X} and σ^*_{C-Z} orbitals.

exocyclic n → $\sigma^*_{\mathrm{C-X}}$ stabilization are also known. For example, the 5-endo-dig cyclization of 3,3-difluoro nitrogen anions[86] is facilitated by negative hyperconjugation between the incipient anionic center and exocyclic $\sigma^*_{\mathrm{C-F}}$ bond.[87] High 5-endo-dig cyclization yields (>80%) also result when carbonyl groups are present at the internal propargylic carbon.[88]

■ CONCLUSIONS

Remarkably, aromatic TSs can facilitate nonpericyclic 5-endo (-dig and -trig) nucleophilic ring closure reactions just as they do for pericyclic reactions. The five-center, six-electron aromaticity of the 5-endo-dig (and -trig) nucleophilic ring closure TSs arises from favorable symmetry-enforced continuous orbital interactions involving a lone pair, a π bond, and a σ bond.[89] Our finding expands the class of aromatic motifs by disclosing a significant, but previously unrecognized, connection between anionic cyclizations and pericyclic sigmatropic reactions. This work identified the first example of an aborted pericyclic reaction where the cyclic structure topologically identical to the TS of a classic pericyclic reaction is *more stable* than the acyclic reactants. Competition among concerted, interrupted, and aborted sigmatropic shift reactions can be controlled electronically, by stabilizing various positions of the intervening cyclic (TS or intermediate) structures selectively. The new connection between different classes of organic reactions should open a new avenue for the design of selective molecular rearrangements.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Geometries and energies of all transition states and complete ref 24. 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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