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# Cycloaromatization of 1,4-Pentadiynes: A Viable Possibility?

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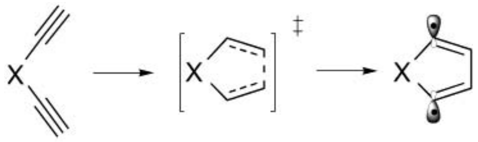
## ABSTRACT

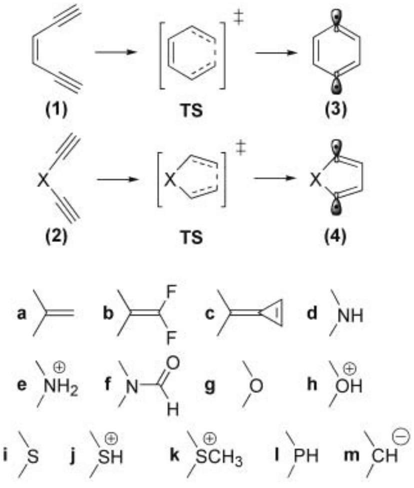


**The effects of several mostly $\sigma$-withdrawing, $\pi$-donating substituents X on the hitherto unknown Bergman-like cyclizations of 3-substituted 1,4-pentadiynes were studied at the BLYP/6-311+G*//BLYP/6-31G* level of theory. As the cyclization with X = OH$^+$ has the lowest barrier and is about thermoneutral, we predict that the title reaction is viable, for instance, through activation of derivatives with X = O with Lewis acids.**

While there is extensive work[1,2] on the cyclization reactions of (*Z*)-hex-3-ene-1,5-diyne (**1**) and its derivatives (mostly Bergman cyclization), 1,4-diynes (**2**) have, to the best of our knowledge, not been studied with respect to their ability to cycloaromatize in a fashion similar to **1** (Scheme 1). This analogy derives from the fact that formation of an aromatic product drives the reaction of **1**.[3] Merely two extra electrons in addition to the four already available from the out-of-plane triple-bond $\pi$-orbitals are required to provide the aromatic electron sextet. These two electrons may in principle come from a double bond, as in the case of **1**, or from a substituent X having an electron lone pair in conjugation with the $\pi$-system (Scheme 1). In other words, not only benzene rings but also furan, thiophene, pyrrole, and perhaps a list of other derivatives may be accessible through a Bergman-like cyclization of appropriate pentadiyne derivatives.

The heteroatom effect is not very well understood for the Bergman and related cyclizations but comes into play much more so for the cyclization reactions of **2**.[4] Our findings[2d] for the substituent effects on the Bergman cyclization indicate that $\sigma$-acceptors lower the barriers of these reactions significantly by removing some of the high electron density

**Scheme 1**



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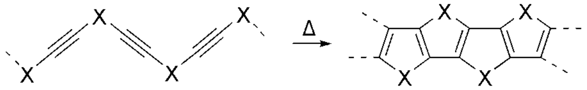
from the in-plane diyne system. A nice confirmation of this theoretical finding is brought out by the experimentally found *exergonicity* of the cyclization of 1,3,4,6-tetrafluorohex-3-ene-1,5-diyne.[5] This analysis is also supported by the notion that the Bergman cyclization may be considered a forbidden 2 + 2 addition in the initial stages: electron removal lowers the otherwise rather large activation barrier.[6] Note that this is a mixed $\sigma/\pi$ effect because the in-plane $\pi$-orbitals are transformed into the new bonding $\sigma$-orbitals in the product.[2d,3,7] The perpendicular $\pi$-system, however, should be electron-rich, as it is responsible for the aromatic stabilization energy that may partially compensate for the high barrier. Ideal substituents X should therefore be $\sigma$-withdrawing and $\pi$-electron donating. As conjugated six $\pi$-electron five-membered rings are less aromatic than their six-membered ring counterparts,[8] we expect that the barriers for the cycloaromatization of **2** will generally be higher than for **1**. Consequently, the choice of X will be crucial.

The reactions presented here may provide novel access to heteroaromatic five-membered rings via well-known acetylene chemistry.[9] This is important for the construction of carbon-rich compounds such as (hetero)fullerenes, where five-membered rings are responsible for the curvature. Analogues such as **5** could also undergo cycloaromatization to give **6** (Scheme 2), which is a molecular wire for X = S.[10]

**Scheme 2**



**(5)** **(6)**

In this paper, we present an exploratory computational study on the cycloaromatizations of a series of 1,4-pentadiyenes. We aim at identifying an experimentally accessible system with a low enough cyclization barrier amenable to experimental conditions.

All computations were performed with Gaussian 94,[11] using Becke's pure gradient corrected exchange functional[12] and the Lee−Yang−Parr nonlocal correlation functional[13] (BLYP) with a 6-31G* basis set.[14] A restricted approach was used for geometry optimizations, energy evaluations, and frequency analyses of the reactants, while transition structures and biradical products were computed with an unrestricted broken-spin approach (BS-UBLYP). All stationary structures were identified as minima or transition structures by computing analytic vibrational frequencies, which were also used to compute zero-point vibrational energies (ZPVE) and thermal corrections. Although DFT is a single-reference method in the formal sense, the applicability of DFT to these types of molecules has been demonstrated amply.[4a,15−17]

Relative Gibbs free activation and reaction energies as a function of X are presented in Figure 1. The energetic relations between the reactants (**2**), transition structures (**TS$_{24}$**), and products (**4**) and the expectation values of the Slater determinants ($\langle S^2 \rangle$) for transition structures and products are summarized in Table 1; additional materials are collected in the Supporting Information.

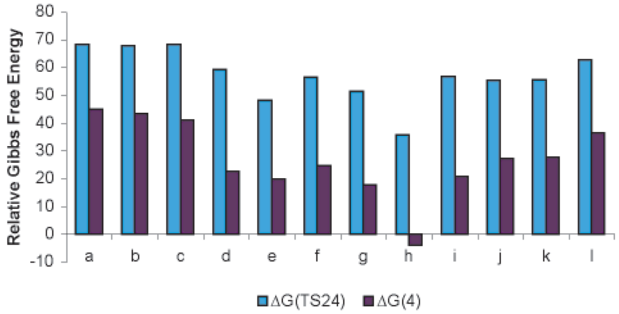


**Figure 1.** Relative Gibbs free activation (blue) and reaction energies (purple, in kcal mol$^{-1}$, at UBLYP/6-31G*) for the thermal cyclization of 1,4-pentadiynes (**2**) as a function of X.

Similar to the Bergman cyclization, these reactions involve the transformation of two doubly occupied in-plane triple bond $\pi$-orbitals of **2** into one doubly occupied $\sigma$-bonding orbital as well as two singly occupied sp$^2$-orbitals with mostly uncoupled electrons (open-shell singlets). The degree of coupling may be (with some restriction for DFT[17]) judged

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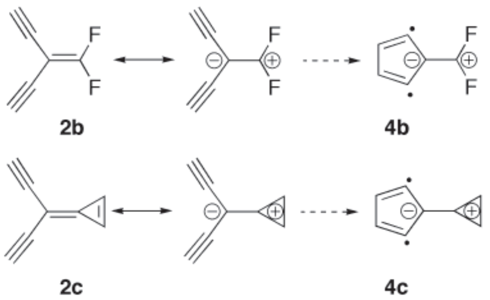
**Table 1.** Slater Determinant Expectation Values of ($<S^2>$), Relative Energies, Enthalpies, Gibbs Free Energies (kcal mol$^{-1}$) at BLYP/6-31G*, Relative Single Point Energies (kcal mol$^{-1}$), and NICS Values (in the Five-Membered Ring Centers) at BLYP/6-311+G* for the Transition Structures and Products for the Thermal Cyclization of 1,4-Pentadiynes (**2**)

| | | BLYP/6-31G* | | | BLYP/6-311+G* | |
|---|---|---|---|---|---|---|
| X | $<S^2>$ | $\Delta E$ | $\Delta H°$ (298 K) | $\Delta G$ (298 K) | $\Delta E$ | NICS |
| | | | Transition Structures (**TS$_{24}$**) | | | |
| **a** | 0.88 | 68.2 | 67.4 | 68.2 | 71.3 | 32.0 |
| **b** | 0.85 | 67.8 | 67.1 | 67.9 | 70.9 | 28.7 |
| **c** | 0.85 | 68.3 | 67.6 | 68.4 | 71.3 | 30.7 |
| **d** | 0.67 | 57.5 | 58.1 | 59.5 | 61.1 | 20.2 |
| **e** | 0.82 | 47.8 | 47.2 | 48.3 | 51.6 | 25.5 |
| **f** | 0.75 | 57.0 | 56.1 | 56.7 | 64.8 | 61.7 |
| **g** | 0.74 | 51.4 | 50.7 | 51.5 | 55.0 | 15.9 |
| **h** | 0.77 | 34.9 | 34.4 | 35.8 | 39.0 | 18.8 |
| **i** | 0.79 | 56.7 | 55.8 | 56.8 | 59.2 | 34.7 |
| **j** | 0.84 | 55.1 | 54.2 | 55.4 | 57.6 | 34.7 |
| **k** | 0.84 | 55.4 | 54.6 | 55.7 | 57.7 | 34.9 |
| **l** | 0.81 | 62.6 | 61.6 | 62.7 | 65.2 | 37.7 |
| **m** | 0.27 | 68.8 | 67.8 | 68.4 | 65.9 | 24.4 |
| | | | Products (**4**) | | | |
| **a** | 0.65 | 42.6 | 44.1 | 45.0 | 47.9 | 5.1 |
| **b** | 0.67 | 40.6 | 42.4 | 43.4 | 46.4 | 0.1 |
| **c** | 0.57 | 38.2 | 40.1 | 41.1 | 46.3 | 3.1 |
| **d** | 0.33 | 18.0 | 20.9 | 22.6 | 25.1 | −8.3 |
| **e** | 0.85 | 16.6 | 18.2 | 19.8 | 23.1 | −3.2 |
| **f** | 0.71 | 21.6 | 23.5 | 24.6 | 28.2 | −13.4 |
| **g** | 1.01 | 15.8 | 16.8 | 17.8 | 21.0 | −8.7 |
| **h** | 1.05 | −5.2 | −4.7 | −3.8 | 0.9 | −5.6 |
| **i** | 0.54 | 16.9 | 19.3 | 20.7 | 21.9 | −10.7 |
| **j** | 0.72 | 24.2 | 25.7 | 27.2 | 28.4 | −0.9 |
| **k** | 0.66 | 24.8 | 27.3 | 27.8 | 28.7 | −0.7 |
| **l** | 0.37 | 33.5 | 35.2 | 36.5 | 38.0 | 0.9 |
| **m** | 0.0 | 32.6 | 34.1 | 34.9 | 34.8 | −13.7 |

by the $<S^2>$ values, which identify all transition structures and products as singlet−triplet mixtures (i.e., largely open-shell biradicals).

The barriers for the computed reactions vary considerably but are, as expected, generally quite high (36−68 kcal mol$^{-1}$); the reaction energies are more acceptable in terms of experimental viability (−4 to 45 kcal mol$^{-1}$). The rather electron-rich "parent" system with X = CH$^-$ (**2m**) also displays an unrealistically large activation barrier (68.4 kcal mol$^{-1}$) and is therefore not a realistic experimental target. Starting materials with protonated amino (X = $NH_2^+$, **2e**) and oxygen (X = OH$^+$, **2h**) functions display the lowest barriers (48.3 and 35.8 kcal mol$^{-1}$, respectively); the reaction of **2h** is the only *exergonic* one in this series ($\Delta G_{298K}$ = −3.8 kcal mol$^{-1}$). Hence, diethynyl ethers should in the presence of Lewis acids (of which the proton used here is the simplest model) give furan derivatives. The Lewis acid dependent cyclization of these substrates may also be used to design catalyst as well as trigger-systems for these types of reactions, e.g., in the polymerization of **5** (X = O).

But why are the barriers and reaction energies generally so high despite the formal formation of an aromatic sextet? We had hoped that the $\sigma$-accepting, $\pi$-donating ability of the difluoro vinyl substituent (**2b**) would make the ring moiety of the product more cyclopentadienyl-like by means of resonance and the ability of fluorine to stabilize carbocations through of $\pi$-conjugation. However, this effect seems too small to provide significant stabilization, and it is only effective in the products. Similarly, the cyclopropenyl substituent (**2c**) was expected to stabilize the product via formation of a doubly aromatic system (cyclopropenyl ($2\pi$) and cyclopentadienyl ($6\pi$)). The effect, however, is marginal, and the TSs do not seem to benefit very much from the developing aromaticity.



The computed NICS values[18] at BLYP/6-311+G* indicate, with the exception of **4a−c** as well as **4l**, that all products are aromatic. Products **4d**, **4f**, **4i**, and **4m** display NICS values that are even larger than that of benzene (−7.6) at the same level. The most favorable product **4h**, however, has a modest NICS value of −5.6 (furan has a NICS value of −11.8). Hence, the NICS values only very modestly qualitatively correlate with the reaction energies for the cyclization of pentadiynes to six $\pi$-electron, aromatic five-membered biradical ring systems (note that **3** is also significantly aromatic).[3,7] All transition structures are antiaromatic, that is, they experience only part of the aromatic stabilization energy of some of the products. This is, as also found for the Bergman cyclization, an example of nonperfect synchronization whereby the electronic stabilization (aromaticity) lags behind the geometrical changes.[7,19,20]

The active molecular orbitals of the transition structures **TS$_{24}$** are comparable to those of the Bergman system (**TS$_{13}$**); they consist of $\pi$ and $\sigma$ contributors (Scheme 3). As the developing aromaticity of the $\pi$-space perpendicular to the molecular plane is not very important (vide supra), the in-plane $\pi$-system, which is transformed into the new $\sigma$-system in the course of the bond formation, determines the barrier heights. Hence, the rather high barriers result from the formally forbidden $[2 + 2]\pi$ character of this interaction in the initial stages of the ring closure.

As a consequence, the $\sigma$-accepting abilities of certain substituents in the acetylenic positions dominate both the barriers of substituted enediynes[2d] and of the pentadiyne derivatives presented here. Highly electronegative substitu-

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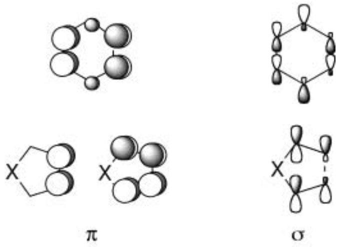
**Scheme 3.** $\pi$- and $\sigma$-HOMOs for the Bergman (Top Two) and Pentadiyne Cyclizations



ents withdraw in-plane electron density and reduce the antibonding character of the $\sigma$-HOMO. This is also evident from the relatively low barrier for the cyclization of **2e** that formally is a 4$\pi$-(antiaromatic) system: the electron-withdrawing ability of the substituent outweighs the anti-aromatic character of the overall process. As protonation amplifies the electron-withdrawing ability of oxygen and nitrogen, the barriers for protonated amino and oxygen functions are the lowest.

The title question can, in principle, be answered with "yes": the cyclizations of 3-substituted-1,4-pentadiynes are viable. With respect to the experimental realization of these reactions, starting materials with protonated amino ($X = NH_2^+$, **2e**) and oxygen ($X = OH^+$, **2h**) functions are most promising as they have the lowest cyclization barriers. Lewis acids may be practical for the activation of diethynyl ethers or amides (**2f**). These possibilities are currently under investigation.

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**Supporting Information Available:** Tables of all the energies and *xyz* coordinates of all the optimized species. This information is available free of charge via the Internet at http://pubs.acs.org.

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