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Thermal Cyclodehydrogenations To Form 6-Membered Rings: Cyclizations of [5]Helicenes

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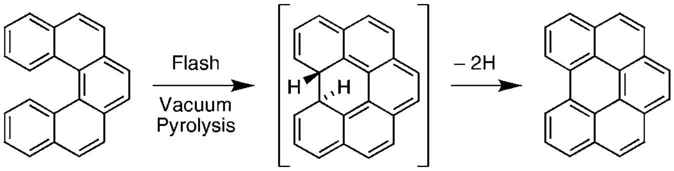
ABSTRACT

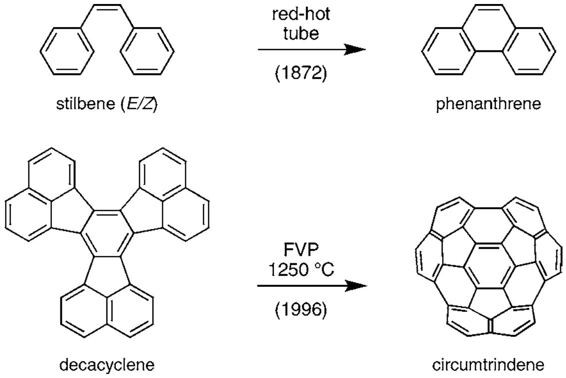


Flash vacuum pyrolysis (FVP) of [5]helicene induces a thermal cyclodehydrogenation to form benzo[*ghi*]perylene. Evidence is presented that supports an electrocyclization–rearomatization mechanism and is inconsistent with mechanistic alternatives involving the intermediacy of aryl radicals or carbenes in the helicene fjord region.

Thermal cyclodehydrogenation reactions have been investigated since as long ago as 1872, when Graebe reported that phenanthrene is formed by passing stilbene through a red-hot tube (Scheme 1).[1] Since that time, innumerable examples of such transformations have been found.[2] A resurgence of interest in this class of reactions was sparked in the late 1990s by the demonstration that circumtrindene can be prepared by thermal cyclodehydrogenation of decacyclene (Scheme 1),[3] and other geodesic polyarenes have subsequently been obtained by using the same strategy.[4] In 2002, thermal cyclodehydrogenations played a key role in the first chemical synthesis of C_{60} in isolable quantities.[5]

Most thermal cyclodehydrogenations require rather harsh conditions, but some have been observed to proceed quite readily even at relatively low temperatures in solution.[6] Surprisingly little is known about the mechanism(s) of these transformations, however, and this gap in our understanding has stimulated us to initiate a program aimed at probing the mechanisms of thermal cyclodehydrogenations of polycyclic aromatic hydrocarbons (PAHs).

Scheme 1. Gas-Phase Thermal Cyclodehydrogenations



At the outset, it seemed unlikely to us that a single universal mechanism would explain all thermal cyclodehy-

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(1) (a) Graebe, C. *Ber. Dtsch. Chem. Ges.* **1874**, *7*, 48. (b) Graebe, C. *Liebigs Ann. Chem.* **1879**, *167*, 161. (c) Graebe, C. *Ber. Dtsch. Chem. Ges.* **1904**, *37*, 4145.

(2) Clar, E. *Polycyclic Hydrocarbons*; Academic Press: New York, 1964.

(3) Scott, L. T.; Bratcher, M. S.; Hagen, S. *J. Am. Chem. Soc.* **1996**, *118*, 8743.

(4) Tsefrikas, V. M.; Scott, L. T. *Chem. Rev.* **2006**, *106*, 4868.

(5) (a) Scott, L. T.; Boorum, M. M.; McMahon, B. J.; Hagen, S.; Mack, J.; Blank, J.; Wegner, H.; de Meijere, A. *Science* **2002**, *295*, 1500. (b) Scott, L. T. *Angew. Chem., Int. Ed.* **2004**, *43*, 4994.

(6) Bodwell, G. J.; Bridson, J. N.; Cyranski, M. K.; Kennedy, J. W. J.; Krygowski, T. M.; Mannion, M. R.; Miller, D. O. *J. Org. Chem.* **2003**, *68*, 2089 and references cited therein.

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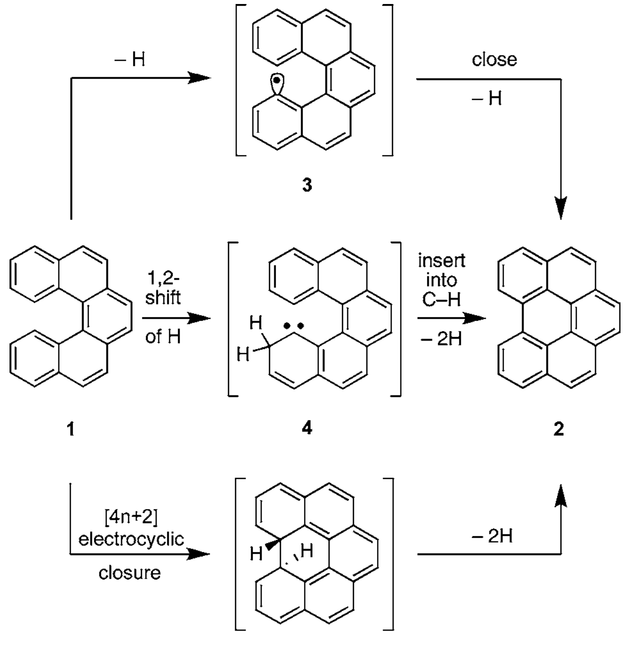
drogenations. Therefore, several specific cases that could give clean results were sought for study. In this regard, the closure of [5]helicene[7] (**1**) to benzo[*ghi*]perylene (**2**) appealed to us as one of the simplest imaginable cyclodehydrogenations that forms a new 6-membered ring. No competing side reactions were anticipated.

A search of the chemical literature revealed that cyclodehydrogenation of [5]helicene (**1**) to benzo[*ghi*]perylene (**2**) had previously been induced both photochemically[8] and by reduction with alkali metals,[9] but there seems to be no prior report of thermal cyclodehydrogenation of **1**. We therefore synthesized a sample of [5]helicene (**1**) by the new olefin metathesis route of Collins,[10] subjected it to FVP, and confirmed that it does indeed undergo a very clean and complete conversion to benzo[*ghi*]perylene (**2**) at 1000 °C (0.7−1.0 mmHg).

A priori, we can conceive of three plausible mechanisms for the conversion of **1** to **2** at high temperatures in the gas phase (Scheme 2). Aryl radical and carbene mechanisms analogous to the first two pathways have been studied computationally for cyclodehydrogenations that form 5-membered rings,[11] but for the formation of 6-membered rings, the electrocyclization−rearomatization pathway must also be considered.

Scheme 2. Plausible Mechanisms for the Thermal Cyclodehydrogenation of [5]Helicene (**1**)



Despite the complete loss of all aromatic stabilization energy in intermediate **5**, molecular orbital calculations at the B3LYP/6-31G(d) level of theory suggest that the electrocyclization−rearomatization shown here will be energetically favored over the aryl radical and carbene mechanisms for the thermal cyclodehydrogenation of **1**.[12] Intermediate **5** is calculated to lie 48.2 kcal/mol above **1** in energy. Energetic tradeoffs that partially compensate for disruption of the π-systems in all five benzene rings of **1** include the formation of a new σ-bond at the expense of a π-bond and an almost complete relief of strain energy in **5**.

Superficially, the least-motions isomerization of **1** to **5** represents a conrotatory electrocyclization of a fully benzannulated hexatriene and appears to violate the Woodward−Hoffmann rules of orbital symmetry conservation.[13] Inspection of the highest occupied molecular orbital (HOMO) of **1**, however, reveals an in-phase overlap of the orbital lobes at the site of bond formation (Figure 1), which makes this pathway symmetry-allowed.

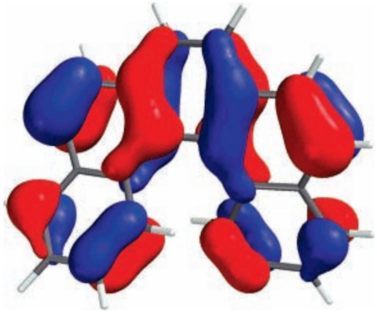


Figure 1. HOMO of [5]helicene (**1**): B3LYP/6-31G(d).

To test whether or not this thermal cyclodehydrogenation follows the electrocyclization−rearomatization pathway, we decided to compare the behavior of **1** to that of the benzo[5]helicene[14] **6**. There is no obvious reason why a remote benzannulation should affect the strain energy of the helicene, or the rate of the aryl radical pathway, or the rate of the carbene pathway, and B3LYP/6-31G(d) calculations support these intuitive conclusions.[12] Thus, [5]helicenes **1** and **6** should suffer thermal cyclodehydrogenation at essentially the same rate, if the reactions follow either the aryl radical or the carbene mechanistic pathway.

By contrast, the rate of thermal cyclodehydrogenation by the electrocyclization−rearomatization pathway should be retarded significantly by the additional benzene ring, because *the aromatic stabilization energy would now be lost in six benzene rings* instead of only in five (Scheme 3, contrast polyenes **7** and **5**). Intermediate **7** is calculated to lie 53.1 kcal/mol above **6** in energy,[12] which leads to the prediction that electrocyclization of **6** should be approximately 5 kcal/mol more difficult than electrocyclization of **1**.[15]

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[7] IUPAC name for [5]helicene (**1**): dibenzo[*c*,*g*]phenanthrene.

[8] (a) Tinnemans, A. H. A.; Laarhoven, W. H.; Sharafi-Ozeri, S.; Muszkat, K. A. *Recl. Trav. Chim. Pays-Bas* **1975**, *94*, 239. (b) Grellmann, K. H.; Hentzschel, P.; Wismontski-Knittel, T.; Fischer, E. *J. Photochem.* **1979**, *11*, 197.

[9] Ayalon, A.; Rabinovitz, M. *Tetrahedron Lett.* **1992**, *33*, 2395.

[10] Collins, S. K.; Grandbois, A.; Vachon, M. P.; Cote, J. *Angew. Chem., Int. Ed.* **2006**, *45*, 2923.

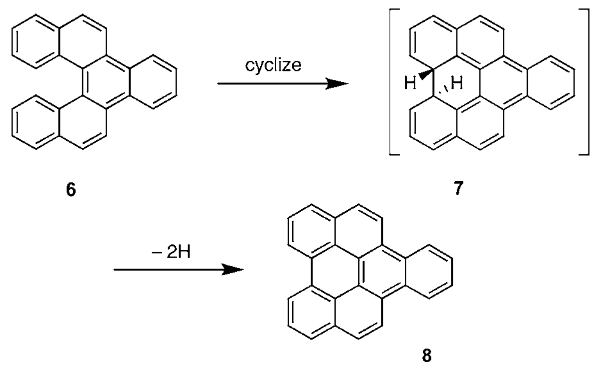
[11] Violi, A. *J. Phys. Chem. A* **2005**, *109*, 7781.

[12] See the Supporting Information for computational details.

[13] Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Academic: New York, 1970.

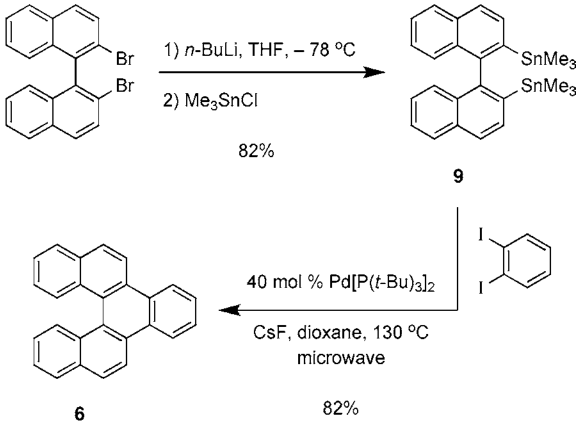
[14] IUPAC name for benzo[5]helicene **6**: naphtho[1,2-*g*]chrysene.

Scheme 3



Unfortunately, no practical synthesis has been reported for the benzannulated[5]helicene needed to conduct our experiments (**6**).[8a,16] We found it necessary, therefore, first to develop a synthesis that could provide usable quantities of **6**. Scheme 4 illustrates the route we devised. Thus, a double Stille coupling between 1,2-diiodobenzene and the functionalized 1,1′-binaphthyl **9**[17] gives helicene **6** in good yield in two steps from commercially available starting materials.

Scheme 4. Synthetic Route to Benzo[5]helicene **6**



With ample supplies of the two helicenes available, we then subjected both to FVP under the same conditions. As predicted, the thermal cyclodehydrogenation of **6** was found to be more difficult than that of **1**.[18] At 1000 °C, a temperature at which the conversion of **1** to **5** is complete, a significant portion of **6** survives FVP unchanged. Only by lowering the temperature could we prevent the parent[5]helicene from cyclodehydrogenating completely. At 850 °C, the contrast between the two helicenes is even more pronounced; 3–4 times more of the parent[5]helicene cyclizes than does the benzannulated derivative under these conditions (Figure 2 and Table 1).

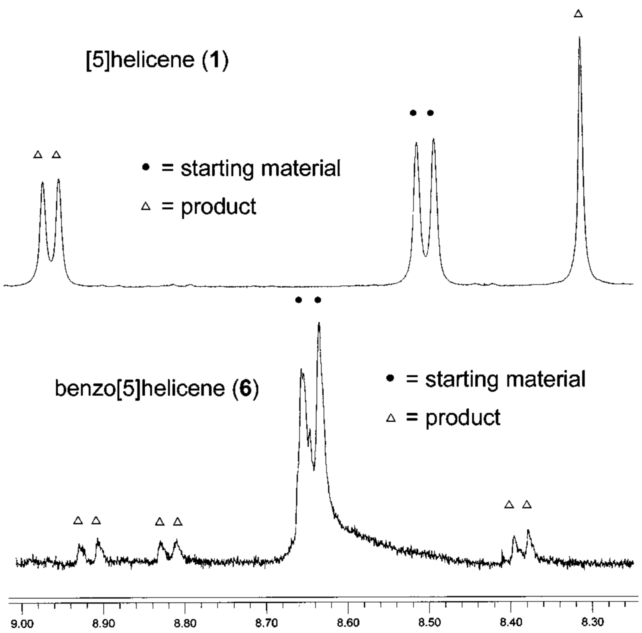


Figure 2. ^{1}H NMR spectra of the product mixtures obtained from FVP at 850 °C of **1** (top) and **6** (bottom).

Our results are consistent with the electrocyclization–rearomatization pathway for thermal cyclodehydrogenation of these [5]helicenes, and they are not readily explained by either the aryl radical pathway or the carbene pathway outlined in Scheme 1.

One unanticipated complication was encountered in the experiment summarized in Scheme 3, but fortunately, it does not weaken the evidence in support of the electrocyclization–rearomatization pathway for these thermal cyclodehydrogenations. In contrast to FVP of the parent[5]helicene (**1**), which gives cleanly only a single product (**2**), FVP of the benzannulated[5]helicene (**6**) gives a second, minor product in addition to the expected hydrocarbon (**8**). Repeated attempts to separate the minor product from **8** by a variety

Table 1. Ratios of Unchanged Helicenes: Cyclodehydrogenation Products Following Flash Vacuum Pyrolysis (0.5–1.0 mmHg)[a]

	850 °C	1000 °C
[5]helicene (**1**)	58:42	0:100
benzo[5]helicene (**6**)	88:12	12:88

[a] Determined by integration of the ^{1}H NMR spectra of the crude pyrolysis mixtures; error limits estimated at approximately ±5%.

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[15] Rate differences will be determined by the relative energies of the two transition states, but for such exceedingly endothermic processes, the relative energies of the high-energy intermediates (**5** and **7**) should provide an approximate measure of the transition state energy differences (Hammond's postulate).

[16] A tetrafluoro-derivative of **6** has been reported: Morrison, D. J.; Trefz, T. K.; Piers, W. E.; McDonald, R.; Parvez, M. *J. Org. Chem.* **2005**, *70*, 5309.

[17] Hoshi, T.; Shionoiri, H.; Katano, M.; Suzuki, T.; Ando, M.; Hagiwara, H. *Chem. Lett.* **2002**, 600.

[18] For the ^{1}H NMR spectrum of **8**, see: Bunte, R.; Gundermann, K. D.; Leitich, J.; Polansky, O. E.; Zander, M. *Chem. Ber.* **1986**, *119*, 3521.

of chromatographic methods, regrettably, all failed. In the ^{1}H NMR spectra of the hydrocarbon mixtures, both before and after chromatography, a number of signals arising from hydrogens of the minor product are clearly identifiable, including several doublets in the chemical shift range normally associated with bay region hydrogen atoms (8.8−9.2 ppm).[19] The mass spectrum of the mixture shows a large peak at m/z 326 ($C_{26}H_{14}$) and no evidence for a significant quantity of $C_{26}H_{16}$, beyond the small amount corresponding to residual starting material.

On the basis of the similarity of the minor product's chromatographic behavior to that of **8**, the similarity of its ^{1}H NMR signals to those of **8**, and the mass spectrum of the mixture, we tentatively concluded that the minor product was most likely an isomer of **8** and not an isomer of **6**. Following a hunch that the minor product might have structure **10**, we synthesized an authentic sample of **10**[20] and were gratified to see that the peaks in its ^{1}H NMR spectrum match well with the peaks of the minor product that are visible in the spectrum of the pyrolysis product mixture.

It is not difficult to formulate a plausible mechanism leading quite naturally to **10** from intermediate **7**.[21] Such a gross skeletal isomerization would be difficult to explain, however, without invoking intermediate **7**, so we chose to treat **10** as a second cyclodehydrogenation product. Accordingly, the ratios of unchanged helicenes:cyclodehydrogenation products reported in Table 1 were determined by adding together the integration data for both **8** and **10** and then comparing that sum to the integration data for unchanged helicene **6**. If **10** were treated as the result of a competing side reaction that had nothing to do with the thermal cyclodehydrogenation of **6**, then the rate retardation seen for **6** relative to **1** would look even *greater* than it does in Table 1. We have chosen a conservative treatment and still find the data to be compelling. In fact, the formation of **10** as a second product from FVP of **6** actually strengthens the evidence in favor of the electrocyclization−rearomatization mechanism involving intermediate **7**, as illustrated in Scheme 3.

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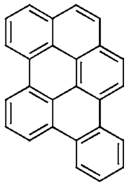

In sum, the thermal cyclodehydrogenation of **1** has been found to proceed significantly faster than the corresponding thermal cyclodehydrogenation of **6** under the same high-temperature conditions in the gas phase. Of the three plausible mechanisms outlined in Scheme 2, only the electrocyclization−rearomatization mechanistic pathway readily accounts for the experimental results, and those are in good accord with DFT calculations. One must recognize, of course, that no mechanism is ever "proven"; we have simply eliminated two plausible alternatives to the electrocyclization−rearomatization pathway. In principle, other alternatives that are consistent with our data might materialize in the future.

Finally, any extrapolation of conclusions from these experiments to systems other than [5]helicenes should be made with caution, especially if the electrocyclization reaction introduces significantly more strain. The mechanism operating here is *not universal for all thermal cyclodehydrogenations that form 6-membered rings*. FVP experiments currently under investigation in our laboratory point to the operation of a different pathway in at least one other aromatic hydrocarbon system, and these results will be published in due course.

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Supporting Information Available: Experimental procedures and ^{1}H NMR spectra of the crude product mixtures from FVP of **1** and **6** at 1000 °C, *XYZ* coordinates and energies calculated at the UB3LYP/6-31G* level of theory on **1**, **3**−**7**, and the benzannulated derivatives of **3** and **4**, and proposed mechanistic pathway from **7** to **10**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[19] See the Supporting Information for copies of the ^{1}H NMR spectra.

[20] Tinnemans, A. H. A.; Laarhoven, W. H. *J. Am. Chem. Soc.* **1974**, *96*, 4617.

[21] A mechanistic pathway from **7** to **10** that involves well-precedented steps is proposed in the Supporting Information.