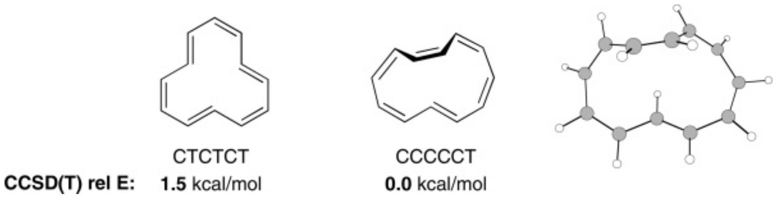
The [12]Annulene Global Minimum

Miles N. Braten,[†] Claire Castro,*[,†] Rainer Herges,*[,§] Felix Köhler,[§] and
William L. Karney*[,†,‡]

*Departments of Chemistry and Environmental Science, University of San Francisco, 2130 Fulton Street,
San Francisco, California 94117, and Otto-Diels Institut für Organische Chemie, Universität Kiel,
D-24118 Kiel, Germany*

castroc@usfca.edu; rherges@oc.uni-kiel.de; karney@usfca.edu

Received November 8, 2007



A new global minimum for [12]annulene has been computationally located. This mono-*trans* minimum **5** (CCCCCT) is computed to be 1.5 kcal/mol more stable (CCSD(T)/cc-pVDZ//BHHLYP/6-311+G**) than the known tri-*trans* isomer **1** (CTCTCT) and 2.4 kcal/mol lower than the di-*trans* isomer **4** (CCTCCT), for which there is indirect evidence. The barriers for several rearrangements of **5** were all computed to be above 15 kcal/mol, indicating that direct experimental characterization of **5** should be possible. The computed barriers for the dynamic processes (including conformational automerization) coupled with computed ^{1}H NMR shift values should aid in the future characterization of this [12]annulene isomer.

Introduction

For a variety of reasons, annulenes continue to excite interest in both experimentalists and theoreticians.[1] In the past several years, [12]annulene has been the focus of several investigations.[2,3] Unlike the case of [8]annulene or cyclooctatetraene (COT), in which the all-*cis* isomer is obviously the most stable, [12]annulene is the first [4*n*]annulene[4] in which there are several configurations within 5 kcal/mol of each other (Figure 1).[2a,b] The possibility of these competing structures, coupled with [12]annulene's instability, complicates the identification of any [12]annulene that is synthesized in the absence of reliable NMR data. In addition, the proclivity of [12]annulene[2a,b] and its substituted analogues[2d] to undergo facile dynamic processes further complicates its isolation and spectroscopic identification.

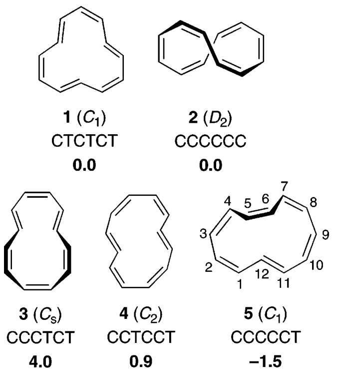


FIGURE 1. Five low-lying isomers of [12]annulene, showing *cis-trans* configurations and relative energies (kcal/mol) at the CCSD(T)/cc-pVDZ//BHHLYP/6-311+G** level. Energies are from refs 2a and 2b and the present work.

[†] Department of Chemistry, University of San Francisco.

[‡] Department of Environmental Science, University of San Francisco.

[§] Universität Kiel.

(1) For a recent review, see: Spitler, E. L.; Johnson, C. C., II; Haley, M. M. *Chem. Rev.* **2006**, *106*, 5344.

(2) (a) Castro, C.; Karney, W. L.; Vu, C. M. H.; Burkhardt, S. E.; Valencia, M. A. *J. Org. Chem.* **2005**, *70*, 3602. (b) Castro, C.; Karney, W. L.; Valencia, M. A.; Vu, C. M. H.; Pemberton, R. P. *J. Am. Chem. Soc.* **2005**, *127*, 9704. (c) Castro, C.; Isborn, C. M.; Karney, W. L.; Mauksch, M.; Schleyer, P. v. R. *Org. Lett.* **2002**, *4*, 3431−3434. (d) Eichberg, M. J.; Houk, K. N.; Lehmann, J.; Leonard, P. W.; Märker, A.; Norton, J. E.; Sawicka, D.; Vollhardt, K. P. C.; Whitener, G. D.; Wolff, S. *Angew. Chem., Int. Ed.* **2007**, *46*, 6894.

(3) (a) Gard, M. N.; Reiter, R. C.; Stevenson, C. D. *Org. Lett.* **2004**, *6*, 393. (b) Kiesewetter, M. K.; Gard, M. N.; Reiter, R. C.; Stevenson, C. D. *J. Am. Chem. Soc.* **2006**, *128*, 15618.

(4) For a review of [4*n*]annulenes, see: Wiberg, K. B. *Chem. Rev.* **2001**, *101*, 1317.

10.1021/jo702412d CCC: $40.75

Recent computational investigations support the early assignment of the NMR spectrum to the tri-*trans*-[12]annulene **1**,[5] despite the prediction that the all-*cis* isomer **2** is isoenergetic with **1**.[2a] Further, **1** was computationally determined to undergo facile thermal isomerization to the intermediate di-*trans* isomer **3**.[2b]

Experimental investigations by Stevenson and co-workers suggested that di-*trans* isomers **3** and **4** were synthesized based on EPR analysis of the trapped radical anions; however, no NMR data for the neutral systems were provided.[3]

In the course of our investigation on configuration change in [12]annulene, we located a new mono-*trans* minimum **5** (CCCCCT, Figure 1) that was computed to be 1.5 kcal/mol more stable (CCSD(T)/cc-pVDZ//BHHLYP/6-311+G**) than that of the tri-*trans* **1** (CTCTCT) or all-*cis* isomer **2** (CCCCCC).[6] This result raises several questions: (1) Is **5** the global minimum for [12]annulene? (2) If so, has the mono-*trans* isomer unknowingly been synthesized? (3) If it has not been synthesized, what is the kinetic stability of **5**, that is, what dynamic processes (e.g., conformational, configurational, and electrocyclization) does **5** undergo? If these barriers are high, they might allow for a thorough spectroscopic study of the molecule.

Results and Discussion

In addition to locating **5** via intrinsic reaction coordinate calculations starting from a Möbius bond-shifting transition state,[2b] we also performed an exhaustive Monte Carlo search of conformational and configurational space for [12]annulene as an independent route to finding the global minimum. Local minima found with this method were reoptimized with the PM3 method and the B3LYP/6-31G* method. After eliminating duplicate species, 22 unique structures were identified within 20 kcal mol^{-1} of the global minimum. These structures were reoptimized at the BHHLYP/6-311+G** level, followed by single-point energy calculations using CCSD(T)/cc-pVDZ.[7] Five of these structures converged to transition states with very small (23−110 cm^{-1}) imaginary frequencies, leaving 17 structures remaining as minima. Of these, mono-*trans* isomer **5** is the lowest in energy (see Supporting Information for details). Unless otherwise stated, all discussion of relative energies refers to results at the CCSD(T)/cc-pVDZ//BHHLYP/6-311+G** + ZPE level. Proton chemical shifts were calculated at the GIAO-B3LYP/6-311+G** level on the BHHLYP geometries and referenced to TMS.[7,8]

The optimized geometry of **5** is shown in Figure 2. That **5** is 1.5 kcal/mol more stable than tri-*trans* isomer **1** is likely due to the lack of any steric interactions among internal hydrogens. Bond angle strain does not appear to play a significant role; both suffer from approximately the same number of large CCC angles (e.g., 127−132°).

Whereas neutral [12]annulene is elusive and difficult to characterize directly, [12]annulene dianions are more stable and thus provide a better opportunity for comparison of computed and experimental spectra. The computed proton NMR chemical shifts of both **5** and its corresponding dianion **5**$^{2-}$ are shown in Figure 3. For comparison, computed values for the tri-*trans* isomer **1**, its dianion **1**$^{2-}$, di-*trans* isomer **4**, and its dianion **4**$^{2-}$ are also presented. The results for mono-*trans*-**5** and -**5**$^{2-}$ are clearly not in agreement with the experimental values for [12]-

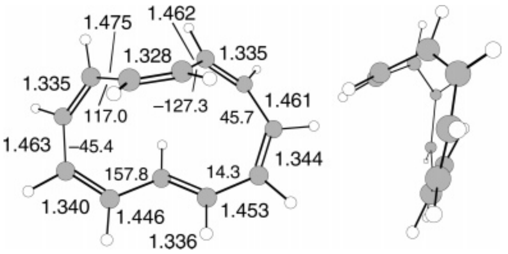


FIGURE 2. BHHLYP/6-311+G** geometry of mono-*trans*-[12]annulene **5**, showing C−C distances (Å) and CCCC dihedral angles (°) centered on single bonds.

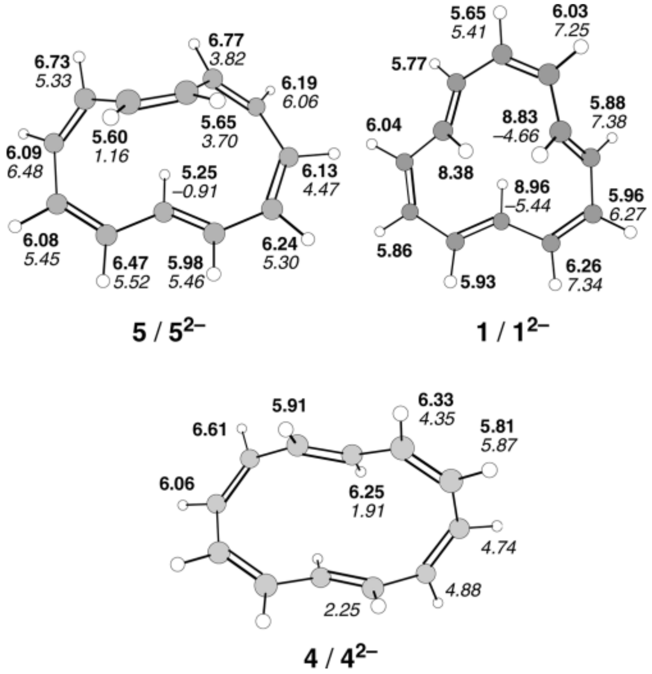


FIGURE 3. GIAO-B3LYP/6-311+G**//BHHLYP/6-311+G** proton chemical shifts (ppm, referenced to TMS) for **5**/**5**$^{2-}$, **1**/**1**$^{2-}$, and **4**/**4**$^{2-}$. Bold: neutral; italics: dianion. See Supporting Information for dianion structures. Data for neutral **1** and **4** taken from ref 2a.

---

[5] (a) Oth, J. F. M.; Röttele, H.; Schröder, G. *Tetrahedron Lett.* **1970**, 61. (b) Oth, J. F. M.; Gilles, J.-M.; Schröder, G. *Tetrahedron Lett.* **1970**, 67.

[6] See footnote 29 of ref 2b. The relative energy of **5** was incorrectly reported in that paper as being −2.6 kcal/mol.

[7] (a) For the use of BHHLYP geometries when computing magnetic criteria for annulenes, and for obtaining correct relative ordering, see ref 2a and: Wannere, C. S.; Sattelmeyer, K. W.; Schaefer, H. F., III; Schleyer, P. v. R. *Angew. Chem., Int. Ed.* **2004**, *43*, 4200. (b) For the use of CCSD(T)/cc-pVDZ energies on DFT geometries of [12]annulenes, see ref 2a and references therein.

[8] All calculations were performed using Gaussian 03: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision D.01; Gaussian, Inc.: Wallingford, CT, 2004.

TABLE 1. Experimental ^{1}H NMR Results for [12]Annulene and [12]Annulene Dianions

species	temperature	δ (ppm)	integral
[12]annulene, **1**[a]	−170 °C	7.8	3H
		5.9	9H
[12]annulene dianion, $\mathbf{1}^{2-}$ [b]	−90 to 30 °C	−4.6	3H
		6.2−7.0	9H
[12]annulene dianion, $\mathbf{4}^{2-}$ [c]	−100 °C	4.5−4.7	10H
		−0.2	2H

[a] Data from ref 5b. [b] Data taken from ref 9. Although the chemical shifts as originally reported were referenced to benzene, here we report them relative to tetramethylsilane (TMS). [c] Data taken from ref 3b.

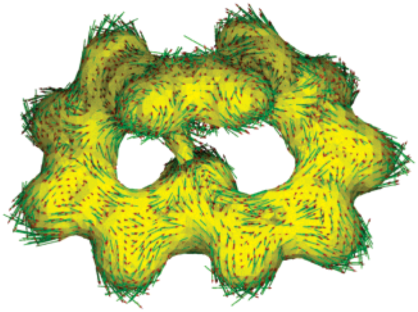


FIGURE 4. Ring currents and transannular interaction in **5**. The current density vectors (green arrows) are drawn onto the ACID isosurface (yellow, isosurface value 0.05).

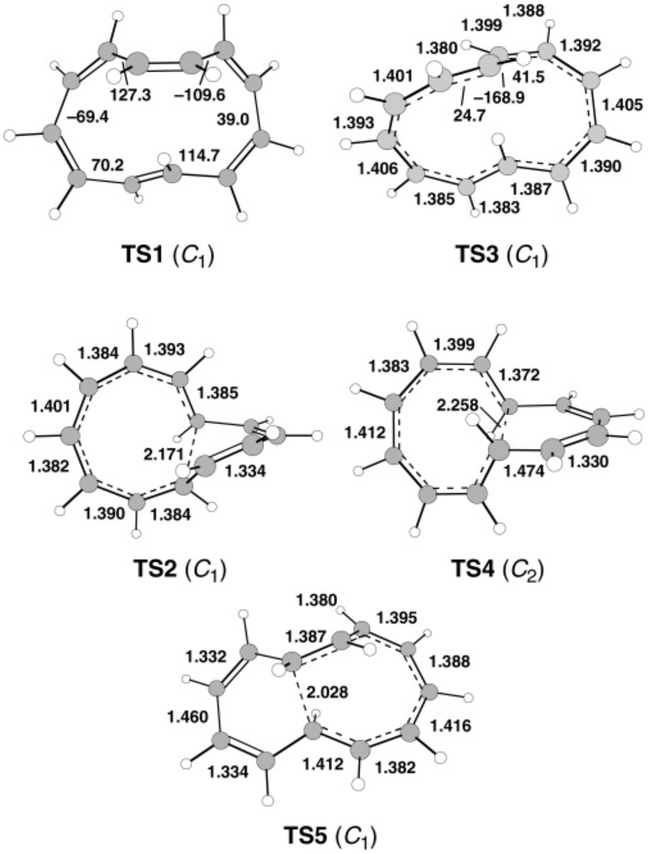


FIGURE 5. BHHLYP/6-311+G** geometries of transition states for dynamic processes of [12]annulene isomer **5**. Selected C−C distances (Å) and CCCC dihedral angles (°) are shown.

annulene[5b] and its dianion[9] as prepared by Oth (Table 1), while the values computed for $\mathbf{1}/\mathbf{1}^{2-}$ agree well. Unlike **1**, there is no evidence for paratropicity in **5**. While both **1** and **5** have two large torsional angles (66.2, 51.3° and 63.0, 52.7°, respectively), **5** suffers from the presence of two additional torsional angles greater than 40° (45.7 and 45.4°), which hinder a ring current.

Further evidence for the lack of paratropicity in **5** is the very small value for its computed magnetic susceptibility exaltation (MSE), +3.8 cgs·ppm.[10] In addition, the anisotropy of the induced current density (ACID)[11] plot (Figure 4) shows no clear overall direction for the ring currents, characteristic of a nonaromatic species. Thus, **5** belongs to the group of annulenes for which the most stable isomers are neither aromatic nor antiaromatic (e.g., COT, [10]annulene), but rather are cyclic polyenes, without strong cyclic π-delocalization. Even more striking is the lack of diatropicity in $\mathbf{5}^{2-}$. The computed proton shift values of $\mathbf{5}^{2-}$ range from −0.91 to 6.48 ppm, suggestive of local effects due to excess electron density, rather than full delocalization. This is a case of a parent [4*n*]annulene that resists delocalizing (and becoming aromatic) with the addition of two electrons.[12]

On the basis of the NMR evidence, **5** is not the isomer that was characterized by Oth and Schröder. Because experimental NMR data for di-*trans* isomer **4** are lacking, it is not possible to compare our computed results with experimental values. However, the computed ^{1}H NMR shift values for an identified minimum of **4** have been previously computed (Figure 3).[2a] The range of these values (5.81 to 6.61 ppm) are not strikingly distinct from those for **5** (5.25 to 6.77 ppm). Reoptimizing **4** as its dianion and computing NMR shift values revealed that these do not agree well with the reported experimental values (Figure 3).[3] On the other hand, the computed NMR values for $\mathbf{5}^{2-}$ (Figure 3) seem more consistent with the observed data for $\mathbf{4}^{2-}$: namely, one region of shielding (−0.9 to1.2 ppm) and a region of alkenyl shifts (3.8 to 6.5 ppm).[13]

To evaluate the feasibility of detecting **5**, we investigated its kinetic stability. This involved studying conformation change, configuration change, and electrocyclic ring closure. The transition states for these mechanisms are shown in Figure 5.

Conformational mobility in medium-sized annulenes generally involves rotation of *trans* double bonds about the adjacent single bonds.[2a,12,14] Potential surface scans of **5** that explored different conformations revealed that **5** is the only conformational minimum for the CCCCCT configuration, and it can undergo conformational automerization via **TS1**, with E_a= 11.2 kcal/mol (Scheme 1). This process interchanges the two hydrogens on the *trans* C═C bond.

Thermal 8-electron electrocyclization directly from **5** can occur in three ways. Formation of *cis*-[6.4.0]dodecapentaene

---

[9] Oth, J. F. M.; Schröder, G. *J. Chem Soc. (B)* **1971**, 904.

[10] For comparison, the computed MSEs at the same level of theory (CSGT-B3LYP/6−311+G**//BHHLYP/6−311+G** for both tri-*trans*-[12]-annulene and known S_4 symmetric [16]annulene are +10.6 and +49.6 cgs·ppm, respectively. MSEs were computed as in ref 2b. For [16]annulene, see: Johnson, S. M.; Paul, I. C.; King, G. S. D. *J. Chem. Soc. (B)* **1970**, 643.

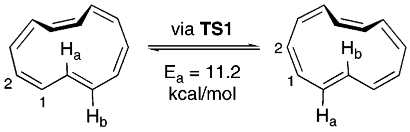
[11] Geuenich, D.; Hess, K.; Köhler, F.; Herges, R. *Chem. Rev.* **2005**, *105*, 3758.

[12] Oth, J. F. M. *Pure Appl. Chem.* **1971**, *25*, 573.

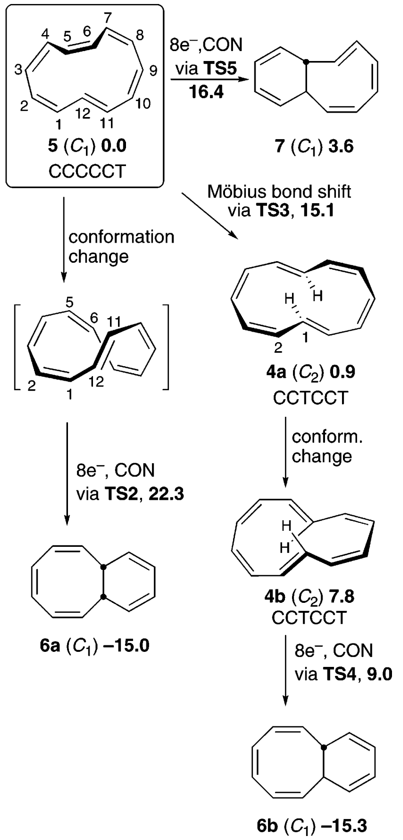
[13] In addition, the conformational mobility of both the dianions $\mathbf{4}^{2-}$ and $\mathbf{5}^{2-}$ would need to be clarified to understand peak averaging on the NMR time scale. This work is currently being investigated.

[14] Pemberton, R. P.; McShane, C. M.; Castro, C.; Karney, W. L. *J. Am. Chem. Soc.* **2006**, *128*, 16692.

SCHEME 1



SCHEME 2[a]



[a] Relative energies in kcal/mol.

(**6a**) occurs via **TS2** (Figure 5) with a prohibitive barrier, ca. 22 kcal/mol (Scheme 2).[15] A more accessible pathway for ring closure leads to *trans* bicyclic product **6b**. In this case, configuration change must first occur to form di-*trans* isomer **4a**. This proceeds via Möbius aromatic bond shifting transition state (**TS3**), with $E_a = 15.1$ kcal/mol, and is the rate-determining step. Conformation change from **4a** to **4b**, followed by 8-electron cyclization via **TS4** (1.2 kcal/mol barrier relative to **4b**), then provides **6b**. Finally, the ACID plot of **5** (Figure 3) reveals a significant transannular interaction, suggesting a possible electrocyclization route to form the relatively unstable bicyclic **7**, which has a *trans* double bond in the eight-membered ring. The barrier for this isomerization (16.4 kcal/mol) is also higher than that for Möbius π-bond shift/electrocyclization leading to **6b** and should not be a competitive process.

As mentioned earlier, our automated Monte Carlo search routine found 22 structures within 20 kcal/mol relative to the global minimum **5**. Five of these structures were found to have very small imaginary frequencies (23−110 cm^{-1}) and are transition states for conformation change of various isomers. Details for these additional species are provided in Supporting Information.

The dynamic processes outlined above indicate that **5** should be observable by NMR spectroscopy. Due to the lack of symmetry, the spectrum at very low temperature will be complicated. At higher temperatures, where the conformational automerization (E_a = 11.2 kcal/mol) is rapid, six pairs of magnetically equivalent protons result: 1/10, 2/9, 3/8, 4/7, 5/6, and 11/12 (see Scheme 2 for atom numbering). Using the chemical shifts in Figure 3, the simplified spectrum should consist of signals around 5.6 ppm (H5, H6, H11, H12), 6.2 ppm (H1, H2, H3, H8, H9, H10), and 6.75 ppm (H4, H7). At still higher temperatures, bicyclic product **6b** should be formed. Further, our results on the dianion of **5** open the possibility that the NMR spectrum[3b] attributed to 1,7-di-*trans*-[12]annulene dianion, $\mathbf{4}^{2-}$, might in fact be due to the presence of the mono-*trans* isomer $\mathbf{5}^{2-}$. If **5** were formed instead of **4** at −100 °C (the temperature at which [12]annulene was formed by exhaustive elimination of hexabromododecane[3]), it is unlikely that **5** would isomerize to **4**−the computed E_a is simply too high. However, the dynamic processes of the radical anion of **5** (as well as the radical anion of **4**) remain to be studied. Perhaps addition of an electron lowers the energy barrier to Möbius π-bond shift.

Conclusion

Using both density functional and coupled cluster methods, we have identified the mono-*trans* isomer **5** as the global minimum for [12]annulene. Unlike tri-*trans*-[12]annulene (**1**), this mono-*trans* isomer should be viewed as a cyclic polyene with no paratropic ring current. While it is computed to be 1.5 kcal/mol more stable than the tri-*trans* isomer synthesized by Oth and 2.4 kcal/mol more stable than the di-*trans* isomer **4** reported by Stevenson, it remains to be detected. Our computed escape routes reveal that it is conformationally rather inflexible, with the lowest energy pathway ($E_a \sim 11$ kcal/mol) being that of automerization. In addition, the lowest energy rearrangement for **5** involves configuration change via Möbius π-bond shifting ($E_a \sim 15$ kcal/mol), analogous to the cases of **1**[2b] and [16]annulene.[14] The bond shift product **4** should then cyclize to bicyclic species **6b**. The computed barrier heights suggest that it should be possible to characterize **5** by low-temperature NMR spectroscopy.

Acknowledgment. The authors gratefully acknowledge financial support from the Arthur Furst Scholarship Fund (M.N.B.), the National Science Foundation (CHE-0553402), and the American Chemical Society Petroleum Research Fund.

Supporting Information Available: Details of computational methods, absolute energies, and Cartesian coordinates for all stationary points. This material is available free of charge via the Internet at http://pubs.acs.org.

JO702412D

---

[15] Of the different electrocyclization pathways conceivable for **5**, those involving six electrons are not feasible, due to the difficulty of attaining the necessary conformation.