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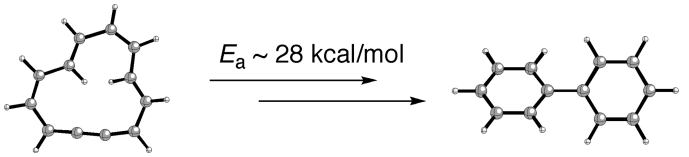
Dehydro[12]annulenes: Structures, Energetics, and Dynamic Processes

Lawrence A. Januar,[†] Vivian Huynh,[†] Taylor S. Wood,[†] Claire Castro,*[,†] and William L. Karney*[,†,‡]

[†]*Departments of Chemistry and* [‡]*Environmental Science, University of San Francisco, 2130 Fulton Street, San Francisco, California 94117, United States*

**castroc@usfca.edu; karney@usfca.edu*

Received September 7, 2010



Density functional and coupled cluster calculations on neutral monodehydro[12]annulenes ($C_{12}H_{10}$) reveal a global minimum that should be kinetically stable. At the CCSD(T)/cc-pVDZ//BHLYP/6-31G* level, the unsymmetrical CTCTC conformer **1a** lies at least 3 kcal/mol below all other isomers studied. The two isomers closest in energy to **1a** are Möbius structure **5a** (CCTCC) and all-cis **6a**. Isomer **1a** can undergo conformational automerization with E_a = 3.9 kcal/mol, implying that this process would be rapid on the NMR time scale, and computed ^{1}H NMR parameters (GIAO-B3LYP/6-311+G**//RHF/6-31G*) are presented. Cumulenic dehydro[12]annulene isomers, with 1,2,3-butatriene subunits, were found to be reactive intermediates in the interconversion of different configurations of the alkyne forms. Pathways for configuration change of **1a**, and for subsequent rearrangement to biphenyl, were investigated. The 28 kcal/mol overall barrier for the lowest energy pathway connecting **1a** to biphenyl suggests that **1a** is kinetically stable with respect to valence isomerization.

Introduction

Cousins to the annulenes, 1,2-dehydroannulenes[1−3] such as benzyne and higher analogues have inspired numerous theoretical and experimental studies as a result of their usefulness as aromaticity probes,[4] as manifolds for generating novel topologies,[5] as potential intermediates in the mechanism of action of enediyne antitumor agents,[6] and as building blocks for extended carbon frameworks.[7] Extensive synthetic work on unsubstituted, parent dehydroannulenes was carried out by Sondheimer and others decades ago.[1,8−13] From that era, the best characterized medium-sized dehydroannulenes are those with two or more acetylenic units. Of the monodehydro series, only dehydro[14]annulene was synthesized and characterized by NMR.[9,13]

Beginning in 2005 a series of papers by Stevenson et al. presented evidence for the syntheses of dehydro[12]annulenes **1**−**4** (both alkyne and cumulene forms).[14−16] However, Christl and Hopf recently showed that the NMR spectra assigned to configurations **1**, **2**, and **3** were in reality due to mixtures of *cis*- and *trans*-1,3-hexadien-5-yne, which formed when the starting material, 1,5-hexadiyne, reacted with

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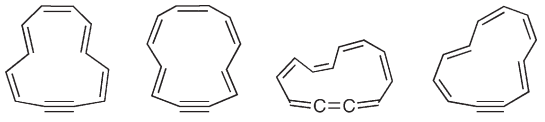
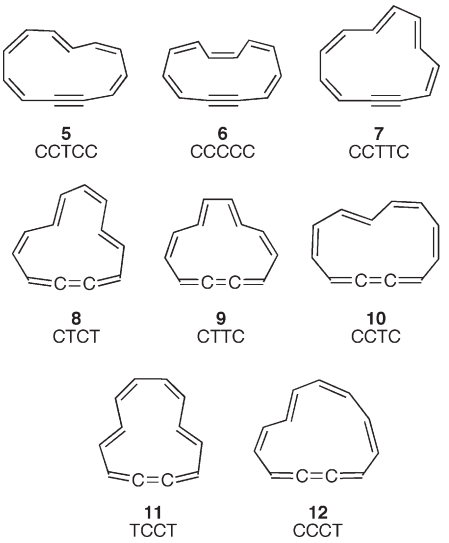
DOI: 10.1021/jo1017537 Published on Web 12/30/2010

base,[17] a reaction reported much earlier by Sondheimer.[18] Base-promoted rearrangement of numerous C_6H_6 isomers was thoroughly studied by Hopf,[19] and the proton NMR chemical shifts for 1,3-hexadien-5-ynes were published in 1997.[20] The preparation of isomer **4** was unique and did not draw on base condensation of 1,5-hexadiyne; rather its synthesis began with hexabromocyclododecane.[14] While no direct NMR was presented for neutral **4**, the ESR spectrum was reported for its radical anion.[14]



1 CTCTC **2** TCCCT **3** CCCC **4** CTCCT

The difficulty in preparing and characterizing neutral dehydro[12]annulenes motivated us to explore the $C_{12}H_{10}$ hypersurface to locate the most stable isomer and find any likely conformational processes and escape routes. In addition to previously reported structures for dehydro[12]-annulenes **1**−**4**, other alkyne (**5**−**7**) and cumulene isomers (**8**−**12**) seemed worthy of consideration. Finally, if the global minimum were predicted to be kinetically stable, we hoped to simulate its proton NMR spectrum to aid experimentalists in its future identification.

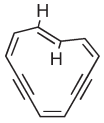


5 CCTCC **6** CCCCC **7** CCTTC
8 CTCT **9** CTTC **10** CCTC
11 TCCT **12** CCCT

Computational Methods

Geometries were optimized at the BHLYP/6-31G* and RHF/6-31G* levels. The B3LYP method is known to overestimate delocalization,[21] and the BHLYP (BHandHLYP) method is known to give more reliable geometries for annulenes, for purposes of correctly identifying stationary points and determining magnetic properties.[21,22] Vibrational analyses were performed at the same level as geometry optimizations to verify whether stationary points were minima or transition states, and to obtain zero point energies (ZPEs). Single point energies were obtained at the CCSD(T)/cc-pVDZ level by using the BHLYP/6-31G* geometries, and are corrected for differences in ZPE. Relaxed potential surface scans employed the BHLYP/6-31G* method.

Magnetic shieldings and coupling constants were computed by using the GIAO-B3LYP/6-311+G** method. ^{1}H NMR chemical shifts were then obtained by subtracting the shielding for a given proton from that for the protons in tetramethylsilane (TMS) obtained at the same level of theory.[23] Computed ^{1}H NMR chemical shifts for annulenes are extremely sensitive to the geometry that is used, especially for systems with inner hydrogens.[21] By comparison of computed chemical shifts with experimental ones for mono-*trans*-1,5-didehydro[12]annulene (**13**),[10,13] we found that chemical shifts computed with RHF/6-31G* geometries give best agreement with experiment (compared, for example, to those determined with BHLYP geometries). In general, BHLYP geometries yielded a chemical shift that was too high, whereas the RHF geometry gave one that was too low, for the inner hydrogen of **13**. However, the value obtained by using the RHF geometry was closer to the experimental one. (See the Supporting Information for details.) Finally, this method was applied to compute chemical shifts for the protons of *cis*/*trans*-1,3-hexadiene-5-yne and compared favorably with experimental values[17,20] (see the Supporting Information for details). Therefore, calculations of magnetic shieldings and chemical shifts employed the RHF/6-31G* geometries.



13

Nucleus-independent chemical shifts (NICS)[24] were computed at ring centers of selected species at the GIAO-B3LYP/6-311+G** level by using both RHF and BHLYP geometries. All calculations were performed with Gaussian 03.[25] NMR spectra were simulated with MacNUTS.[26]

Results and Discussion

Geometries of Minima. Figure 1 depicts the BHLYP/6-31G* optimized geometries of the most stable conformations of alkyne isomers **1**, **2**, and **4**−**7** and Figure 2 depicts those for the cumulene isomers **8**−**12**. No minimum was found for cumulene **3**; all attempts resulted in bond shifting to an alkyne. Four conformational minima were found for isomer **1** (**1a**−**d**). Two conformations each were located for configurations **2**, **5**, **6**, and **7**. (See the Supporting Information for the less stable conformations.) Only one minimum was found for the CTCCT configuration **4**.

For the alkyne isomers, CC triple-bond lengths ranged from 1.205 to 1.215 Å, and adjacent CC single bonds ranged from 1.415 to 1.424 Å. The slightly longer triple bond in

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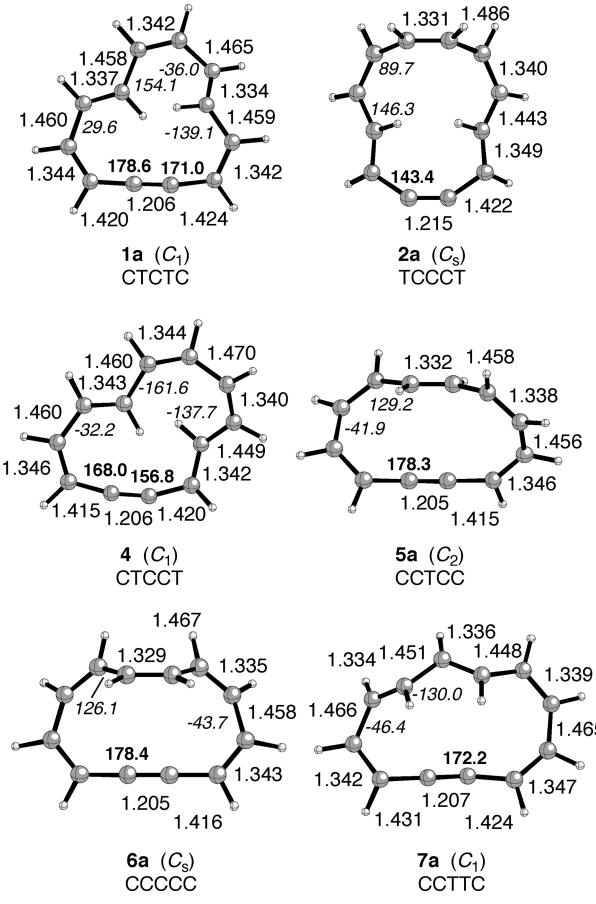


FIGURE 1. BHLYP/6-31G* geometries of most stable dehydro-[12]annulene minima for different alkyne configurations. Plain: C−C distances (Å); bold: alkyne CCC angles (deg); italics: CCCC dihedral angles (deg) centered on single bonds.

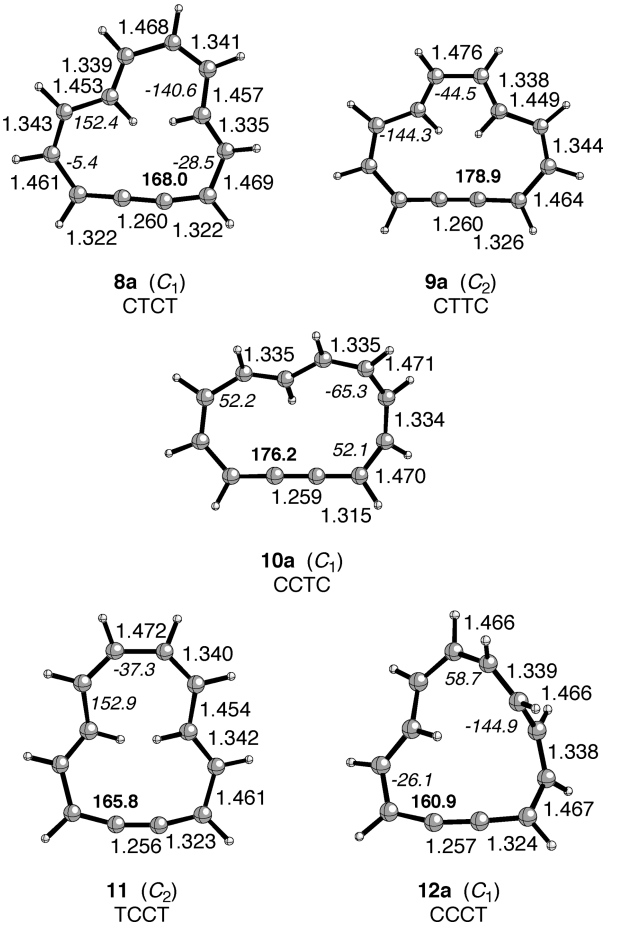


FIGURE 2. BHLYP/6-31G* geometries of most stable dehydro-[12]annulene minima for different cumulene configurations. Plain: C−C distances (Å); bold: CCC angles (deg); italics: CCCC dihedral angles (deg) centered on single bonds.

isomer **2a** (1.215 Å) arises from the highly bent acetylenic unit (CCC angles of 143.4°). The shortest adjacent CC bonds (to the alkyne unit) are 1.415 and 1.416 Å long in isomers **5a** and **6a**, respectively; these are the two isomers with the most linear acetylenic component. Interestingly, **5a** has Möbius topology (largest torsional angle of 50.8°), although evidence for its aromaticity is slim: bond alternation is strong ($\Delta r = 0.126$ Å) and the NICS(0) value of −6.7 ppm likely arises from the local effect of two π bonds pointing toward the ring center. For comparison, bond alternation for the Hückel isomers ranges from 0.128 (**1a**) to 0.138 Å (**6a**). NICS values were not computed for the Hückel isomers due to the close proximity of the internal hydrogens to the necessary ghost atom.

In contrast to the alkynes, the shortest bond in the cumulene isomers ranged from 1.256 to 1.260 Å with the adjacent π bonds being ca. 1.322 Å. All cumulene minima located had a cis geometry about the 1,2,3-butatriene subunit; attempts to locate isomers with a *trans*-butatriene moiety resulted in bond shifting to an alkyne. Other conformational minima were also located for the cumulene forms (see the Supporting Information).

Energetics. Table 1 gives relative energies for the lowest energy conformation of each dehydroannulene isomer and selected transition states.

Alkynes. As shown in Table 1, at the CCSD(T)/cc-pVDZ level the unsymmetrical CTCTC isomer **1a** is predicted to be the global minimum for dehydro[12]annulene. For the most part, the BHLYP method predicts the same energy ordering as does CCSD(T), though for most species the relative energy (compared to **1a**) decreases on going from BHLYP to CCSD(T). Möbius isomer **5a** and the all-cis **6a** are the two species that lie closest in energy to **1a** (< 4 kcal/mol). Neither of these two low-lying isomers has been proposed as possible structures in attempts to prepare dehydro[12]annulenes. The most unstable configuration is TCCCT isomer **2a** (computed to be ca. 36 kcal/mol above **1a**), which has two trans bonds flanking the triple bond. This, combined with the prediction that CTCCT isomer **4** (one trans double bond flanking the triple bond) is 10 kcal/mol above **1a**, indicates that trans C=C bonds adjacent to the triple bond cause substantial destabilization. In addition, the prediction that the CCTTC isomer **7a** is ca. 14 kcal/mol above **1a** suggests that sequential trans C=C bonds contribute considerable strain to the 12-membered ring.

Cumulenes. The most stable conformations of cumulene isomers are computed to be at least 10 kcal/mol higher in energy than the global minimum **1a** (range from ca. 11 to 21 kcal/mol). Interestingly, the lowest lying cumulene isomer **8a** is the structure that "mirrors" the global minimum **1a**, indicating that these are related by π-bond shifting. The relative high energy of the cumulenes makes them unlikely candidates for synthesis.

TABLE 1. Relative Energies (kcal/mol) for Dehydro[12]annulene Isomers, Transition States, and Valence Isomers[a]

species	sym	config	BHLYP rel E	NI	CCSD(T) rel E
			alkynes		
1a	C_1	CTCTC	0.0	0	0.0
2a	C_s	TCCCT	41.4	0	35.9
4	C_1	CTCCT	11.3	0	10.0
5a	C_2	CCTCC	3.4	0	3.3
6a	C_s	CCCCC	4.1	0	3.8
7a	C_1	CCTTC	16.2	0	14.4
			cumulenes		
8a	C_1	CTCT	11.4	0	11.3
9a	C_2	CTTC	17.3	0	16.7
10a	C_1	CCTC	14.0	0	15.0
11	C_2	TCCT	13.9	0	13.2
12a	C_1	CCCT	22.0	0	20.6
			transition states and valence isomers		
TS1	C_1	CTCTC	4.4	1	3.9
TS2	C_1		17.0[b]	0[b]	24.0[b]
TS3	C_1	CTCT	23.3	1	22.4
TS4	C_1		29.4	1	27.8
TS5	C_1		11.3	1	8.5
TS6	C_1		24.4	1	18.7
TS7	C_2		−19.0	1	−19.1
14	C_1		0.0	0	−3.1
15	C_2		−20.8	0	−21.2
16	D_2		−103.7	0	−95.5

[a]BHLYP = BHandHLYP/6-31G*. NI = number of imaginary frequencies. CCSD(T) = CCSD(T)/cc-pVDZ//BHLYP/6-31G*. Relative energies corrected for ZPE differences. [b]Computed for the triplet state. See ref 27 for details.

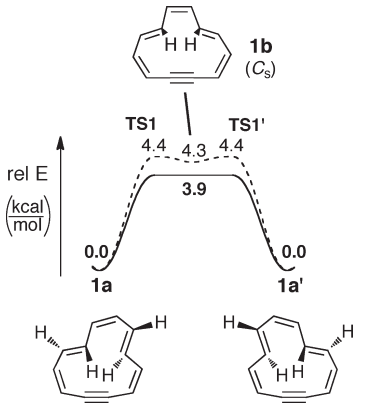
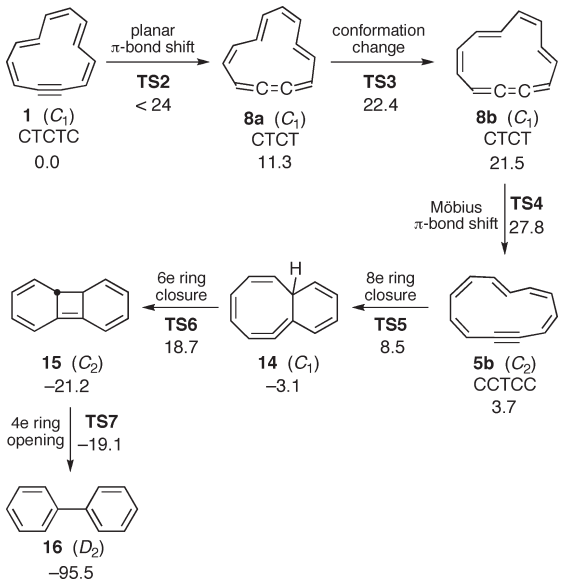


FIGURE 3. Potential energy curve for the lowest energy pathway for conformational automerization of CTCTC-dehydro[12]annulene **1a**. Relative energies in kcal/mol. Dashed lines: BHLYP/6-31G*. Solid lines: CCSD(T)/cc-pVDZ//BHLYP/6-31G*.

Automerization. Given that **1a** is the most stable isomer, the barrier for its conformational automerization is important, as it might influence the temperature dependence of the NMR spectrum. To locate possible automerization mechanisms, we probed the conformational space of isomer **1a** exhaustively as a function of two CCCC dihedral angles, chosen so as to flip both trans C=C bonds around. The detailed results of these relaxed potential surface scans are given in the Supporting Information (Figures S3 and S4). Of the numerous possible low-energy pathways, the one with the lowest barrier is depicted in Figure 3 and has a computed barrier of 3.9 kcal/mol at the CCSD(T) level. At the BHLYP/6-31G* level, the mechanism involves two steps, via **TS1** and

SCHEME 1. Pathway Connecting 1a to Biphenyl (16)[a]



[a]Relative energies in kcal/mol.

intermediate conformer **1b**. However, the shallow minimum **1b** and the transition state **TS1** become isoenergetic at the CCSD(T) level, resulting in a wide plateau-like transition region, with the C_s-symmetric structure **1b** at its center.

Valence Isomerization and "Escape" to Biphenyl. The feasibility of preparing and characterizing dehydro[12]annulene **1a** depends partly on its kinetic stability. Biphenyl is an extremely stable valence isomer of the dehydro[12]annulenes and is perhaps the most likely rearrangement product from these monocycles. A high barrier for isomerization to biphenyl would increase the likelihood of isolating a dehydro[12]-annulene. Working backward from biphenyl via thermally allowed electrocyclic reactions brings one to a bicyclic structure that could arise from electrocyclization of a dehydro[12]-annulene with short interannular distances and a favorable conformation. Isomers **5** and **10** represent the best candidates in this regard, so in part the problem reduces to finding a path from **1a** to one of these and subsequently to biphenyl.

Our results place the overall barrier for isomerization of **1a** to biphenyl (**16**) at ca. 28 kcal/mol (Scheme 1). The first part of this mechanism (**1a** → **5b**) highlights how different configurations of alkyne forms of dehydro[12]annulene can interconnect with each other and with cumulene isomers via π-bond shifting. The initial π-bond shift of **1a** provides **8a**, the most stable cumulene isomer, with a barrier less than 24 kcal/mol.[27] Subsequent Möbius π-bond shifting from a higher energy conformer of **8** (**8b**) forms **5b**. From **5b**, a series of electrocyclic reactions leads to biphenyl (**16**), with the final step being highly exothermic. Scheme 1 makes it clear that the cumulene isomers serve as reactive intermediates and would not be isolable. Further, the rate-determining step for

(27) This planar bond shifting step is expected to proceed via a singlet diradical transition state. Due to the difficulty of calculating the energy of such a species, the energy of the corresponding triplet was computed. The singlet and triplet states of **TS2** should be disjoint diradicals, which would give rise to the singlet state lying below the triplet.[28] Thus, the triplet energy of 24 kcal/mol, relative to **1a**, provides an upper bound to the true energy of the singlet diradical transition state. The CCSD(T) energy of triplet **TS2** was computed by using the RCCSD(T) method in Molpro.[29]

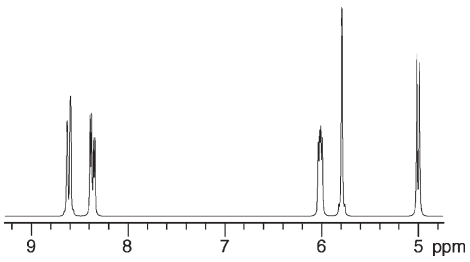


FIGURE 4. Simulated 400 MHz ^{1}H NMR spectrum of dehydro-[12]annulene **1a**, assuming rapid automerization and using GIAO-B3LYP/6-311+G**//RHF/6-31G* chemical shifts and coupling constants.

conversion of **1a** to biphenyl would be Möbius π-bond shifting.[30] Our results show that the different configurations can isomerize to the most stable dehydro[12]annulene (**1a**) and that this species is kinetically stable.

Compared to the mechanism in Scheme 1, the pathway to biphenyl that involves cumulene **10** has higher barriers for **1a** → **10** and for **10** → **16**, so it is not presented here. The mechanisms connecting **1a** to **10** and numerous other isomers are provided in the Supporting Information.

NMR Spectrum of 1a. Given that **1a** should be kinetically stable, computed NMR parameters for this species should aid its future characterization. Figure 4 shows the GIAO-B3LYP/6-311+G**//RHF/6-31G* predicted 400 MHz ^{1}H NMR spectrum for **1a** assuming fast automerization on the NMR time scale and a ten-spin system (AA′BB′CC′-DD′EE′).[31] The chemical shifts for the pairs of equivalent protons are well resolved. The four trans protons, which spend some of their time inside the ring, appear in the 8−9 ppm region while the external protons appear much further upfield (for computed coupling constants and shifts see the Supporting Information). Given the tendency of the RHF geometries to underestimate the chemical shifts of internal protons in a system such as this one, the actual shifts for the internal protons would be slightly higher, though still probably in the range 8−9 ppm.

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(30) The relationship between biphenyl and dehydro[12]annulene was previously explored by Stevenson et al.,[15] although the focus was on a pathway on the radical anion potential surface.

(31) Günther, H., *NMR Spectroscopy*, 2nd ed.; Wiley: New York, 1995; Chapter 5.

Conclusion

CCSD(T)/cc-pVDZ//BHLYP/6-31G* calculations on numerous configurations and conformations of dehydro-[12]annulene suggest that CTCTC isomer **1a** is the global minimum, lying > 3 kcal/mol below all other isomers. Möbius CCTCC isomer **5a** and all-cis **6a** were computed to be within 4 kcal/mol of **1a**. Cumulene forms were found to be higher in energy relative to their alkyne counterparts and can readily isomerize to the alkyne isomers via π-bond shifting. The isomerization of **1a** to biphenyl is a highly exothermic reaction, although the predicted overall barrier of 27.8 kcal/mol suggests that **1a** should be kinetically stable. Conformational automerization of **1a** was computed to occur with a 3.9 kcal/mol barrier. Thus, the automerization of **1a** would be rapid at ambient temperature. The GIAO-B3LYP/6-311+G**//RHF/6-31G* computed time-averaged ^{1}H NMR spectrum of **1a** exhibits two distinct signals for the two pairs of trans protons at δ 8.3−8.7 ppm, and separate peaks for the three pairs of cis protons at 5.0−6.0 ppm.

Acknowledgment. We thank the National Science Foundation (CHE-0910971) and the American Chemical Society Petroleum Research Fund for supporting this work.

Supporting Information Available: Absolute energies and Cartesian coordinates for all stationary points; structures of transition states, valence isomers, and additional conformers; details of other pathways for automerization of **1a**; mechanisms for configuration change among dehydro-[12]annulenes; and computed NMR data for **1a**. This material is available free of charge via the Internet at http://pubs.acs.org.