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Synthesis and Properties of 9-Alkyl- and 9-Arylcyclopenta[*a*]phenalenes

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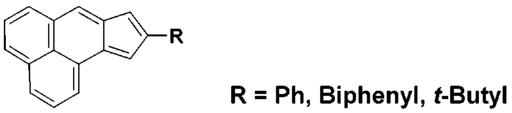
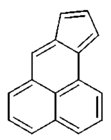
ABSTRACT



Two strategies for the synthesis of cyclopenta[*a*]phenalenes are described. NMR, X-ray diffraction, and cyclic voltammetry studies of simple alkyl- and aryl-substituted derivatives are reported for the first time.

Nearly 50 years ago, D. H. Reid proposed that cyclopenta[*a*]phenalene (**1**) should constitute the prototype for a new class of novel nonalternant polycyclic aromatic compounds.[1] Cognizant of the exceptional stability of phenalenyl cations, Reid further predicted that this system should exhibit significant ground-state dipolar character in analogy to the well-known polar aromatic hydrocarbon azulene. While a number of theoretical studies have since confirmed Reid's prediction that cyclopenta[*a*]phenalenes should exhibit "aromatic character",[2] the synthesis of **1** has yet to be achieved. Despite considerable effort, only a few penta- and hexacyclic benzo-fused[3] and heterosubstituted derivatives have been prepared to date. Most notably, Sugihara et al. achieved the synthesis of 7-methoxycyclopenta[*a*]phenalene in 1986[4] and reported data consistent with a dipolar ground state and the presence of a diamagnetic ring current in the molecule.



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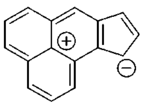
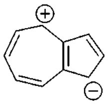
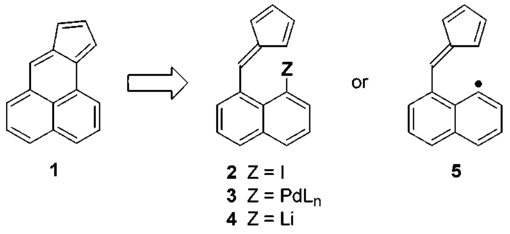




Our interest in cyclopenta[*a*]phenalene originated with the realization that silyl-substituted derivatives might be accessible in one step by the reaction of phenalenyl cations with allenylsilanes in a [3 + 2] annulation analogous to that previously employed in our laboratory for the synthesis of substituted azulenes.[5] When a review of the literature revealed that neither **1** nor any simple alkyl-substituted derivatives were known, we decided to undertake the synthesis and characterization of this elusive molecule. Herein we report two general strategies for the synthesis of substituted cyclopenta[*a*]phenalenes, as well as the first syntheses of simple alkyl- and aryl-substituted derivatives.

Operating on the assumption that cyclopenta[*a*]phenalene would be a relatively robust, azulene-like compound, we initially focused our attention on an expeditious strategy based on the cyclization of the versatile (iodonaphthyl)-fulvene intermediate **2** (Scheme 1). Particularly attractive to us was the prospect that we might achieve the desired key cyclization by way of any of several alternative tactics, including intramolecular Heck reaction, or via cyclization

Scheme 1



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[1] (a) Reid, D. H. *Angew. Chem.* **1955**, *67*, 761. (b) Reid, D. H. *Tetrahedron* **1958**, *3*, 339.

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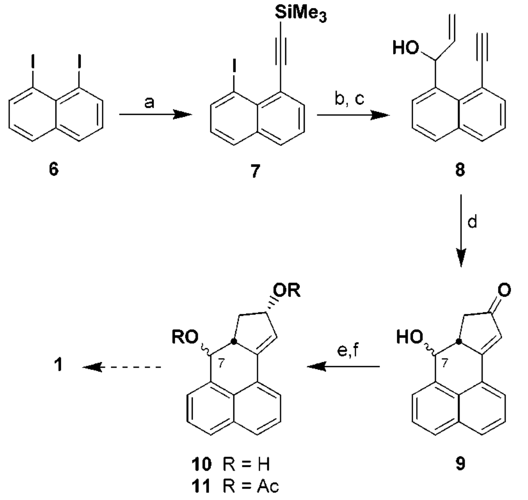
of an organolithium (**4**) or free radical (**5**) intermediate. While we recognized that steric and conformational considerations might work against the desired transformation, the ready availability of cyclization substrate **2** in one step from 8-iodo-1-naphthaldehyde[6] made this an appealing route for our initial studies. In the event, however, we were unable to effect the desired transformation under any of a variety of conditions, obtaining from each experiment either unreacted **2**, or a complex mixture of uncharacterizable products.

We next turned our attention to a less direct route to cyclopenta[*a*]phenalene in which a tetrahydro derivative would first be constructed and then the requisite additional unsaturation introduced in a stepwise fashion under carefully controlled conditions. In this approach an intramolecular Pauson−Khand reaction[7] serves as the key step for the assembly of the cyclopenta[*a*]phenalene carbon skeleton. Synthesis of the Pauson−Khand substrate **8** proceeded smoothly as outlined in Scheme 2. Thus, Sonogashira coupling[8] of trimethylsilylacetylene with 1,8-diiodonaphthalene[9] afforded the known naphthyl iodide **7**,[10] which was transformed to **8** by addition of the corresponding naphthyllithium species to acrolein followed by desilylation. The key intramolecular Pauson−Khand reaction[11] then proceeded in good yield to furnish the desired cyclopentenone **9** as an 87:13 mixture of isomers in which the C-7 hydroxyl is cis to the adjacent ring junction hydrogen in the major product. Reduction of **9** was accomplished smoothly and with high stereoselectivity using Li(s-Bu_3)BH to furnish diol **10** (87:13 ratio at C-7), which was also converted to the corresponding diacetate (**11**) using standard acetylation conditions.

Scheme 2

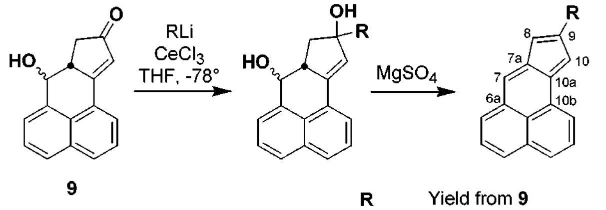


[a] Key: (a) 1.2 equiv of $Me_3SiC{\equiv}CH$, 0.04 equiv of $Pd(PPh_3)_2Cl_2$, 0.08 equiv of CuI, Et_3N, 16 h, 50−65%; (b) 1.1 equiv of *n*-BuLi, Et_2O, −30 °C, 15 min; then 2.0 equiv of acrolein, −78 °C, 1 h, 77−83%; (c) 0.1 equiv of K_2CO_3, MeOH, 2 h, 86−94%; (d) 1.1 equiv of $Co_2(CO)_8$, CH_2Cl_2; then 8.0 equiv of NMO, 4 h, 69−73%; (e) 1.1 equiv of Li(s-Bu_3)BH, THF, −78 °C, 15 min, 77−80%; (f) 20 equiv of Ac_2O, cat. DMAP, pyridine, 5 h, 76%.

Unfortunately, all attempts to achieve the transformation of these intermediates to cyclopenta[*a*]phenalene proved unsuccessful. No cyclopenta[*a*]phenalene could be detected among the products of either stepwise or "double elimination" reactions of diol **10** or its derivatives under a wide variety of conditions, and attempts to effect the desired elimination via flash vacuum pyrolysis of diacetate **11** (trapping of products at −198 °C) also proved fruitless. Surmising now that cyclopenta[*a*]phenalene might in fact be less stable than prior theoretical studies had suggested, we turned our attention to the application of cyclopentenone **9** in the synthesis of *substituted* cyclopenta[*a*]phenalenes that we anticipated might exhibit greater stability than the parent compound.

Scheme 3 outlines the results of this study, which eventuated in the first syntheses of simple alkyl- and aryl-substituted cyclopenta[*a*]phenalenes. The preparation of 9-phenylcyclopenta[*a*]phenalene was examined first. Addition of phenyllithium to cyclopentenone **9** proceeded poorly,

Scheme 3



R	Yield from **9**	
Phenyl	17-23%	**12**
Biphenyl	60%	**13**
t-Butyl	10-14%	**14**

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(2) (a) Zahradnik, R.; Michl, J.; Koutechy, J. *Collect. Czech. Chem. Commun.* **1964**, *29*, 1932. (b) Zahradnik, R.; Michl, J. *Collect. Czech. Chem. Commun.* **1965**, *30*, 520. (c) Andes Hess, B., Jr.; Schaad, L. J. *J. Org. Chem.* **1971**, *36*, 3418. (d) Aihara, J. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 2689. (e) Zhou, Z.; Parr, R. G. *J. Am. Chem. Soc.* **1989**, *111*, 7371. (f) Ghosh, G.; Ghosh, D.; Das Gupta, N. K. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 3109.

(3) (a) Aitken, I. M.; Reid, D. H. *J. Chem. Soc.* **1956**, 3487. (b) Kemp, W.; Storie, I. T.; Tulloch, C. D. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2812. (c) Blum, J.; Baidosi, W.; Badrieh, Y.; Hoffman, R. E. *J. Org. Chem.* **1995**, *60*, 4738 and references therein.

(4) (a) Sugihara, Y.; Fujita, H.; Murata, I. *J. Chem. Soc., Chem. Commun.* **1986**, 1130. (b) Sugihara, Y.; Hashimoto, R.; Fujita, H.; Abe, N.; Yamamoto, H.; Sugimura, T.; Murata, I. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2813.

(5) Becker, D. A.; Danheiser, R. L. *J. Am. Chem. Soc.* **1989**, *111*, 389.

(6) Bailey, R. J.; Card, P. J.; Shechter, H. *J. Am. Chem. Soc.* **1983**, *105*, 6096.

(7) Schore, N. E. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Kidlington, 1995; Vol. 12, pp 703−739.

(8) Sonogashira, K. In *Metal-catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998; pp 203−230.

(9) Diiodide **6** was prepared in one step from the corresponding commercially available diamine by the procedure of House et al.: House, H. O.; Koepsell, D. G.; Campbell, W. J. *J. Org. Chem.* **1972**, *37*, 1003.

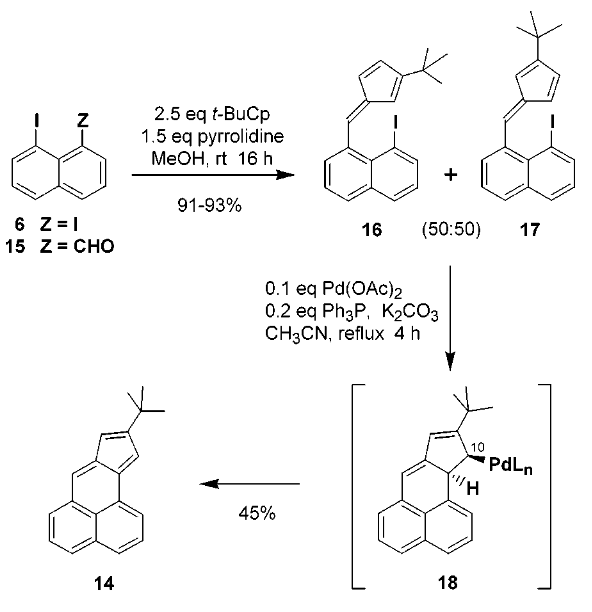
(10) For previous routes to this compound, see: (a) Feldman, K. S.; Ruckle, R. E., Jr.; Ensel, S. M.; Weinreb, P. H. *Tetrahedron Lett.* **1992**, *33*, 7101. (b) Cobas, A.; Guitián, E.; Castedo, L. *J. Org. Chem.* **1997**, *62*, 4896.

(11) Best results were obtained using the general procedure of Shambayati et al.: Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *Tetrahedron Lett.* **1990**, *31*, 5289.

but the corresponding organocerium reagent[12] reacted cleanly to furnish the desired 1,2-adduct in good yield. Following workup, a solution of the crude addition product in Et_2O−THF was simply stirred over anhydrous magnesium sulfate for 20 min at room temperature to effect the desired double dehydration. Column chromatography on alumina furnished phenylcyclopenta[*a*]phenalene (**12**) in 17−23% overall yield as a brown solid, mp 118−123 °C. By using a similar protocol, enone **9** was transformed to the biphenyl-substituted cyclopenta[*a*]phenalene **13** in 60% overall yield; the structure of this green crystalline solid was established by X-ray diffraction analysis (vide infra). Finally, the *tert*-butyl-substituted cyclopenta[*a*]phenalene **14** was prepared in an analogous fashion, although in this case the overall yield was limited by the poor efficiency of the organocerium addition step.

An investigation of the properties of the *tert*-butyl derivative **14** revealed that this substituted cyclopenta[*a*]phenalene is quite stable at room temperature and is even recovered unchanged after heating overnight in refluxing benzene. These observations encouraged us to revisit our original intramolecular Heck strategy to determine whether that very direct route might prove more successful when applied to the generation of stable cyclopenta[*a*]phenalene derivatives. As outlined in Scheme 4, we have found that this approach indeed provides efficient access to 9-*tert*-butylcyclopenta[*a*]phenalene in only three steps beginning with diodide **6**. Thus, addition of the monolithium derivative of **6**[13] to DMF provided the known aldehyde **15**,[6] which was transformed to a 1:1 mixture of fulvenes **16** and **17** by reaction with *tert*-butylcyclopentadiene according to the general protocol of Stone and Little.[14] Exposure of this mixture to the action of catalytic palladium acetate under standard Heck reaction conditions[15] then led to the formation of 9-*tert*-butylcyclopenta[*a*]phenalene (**14**) in 45% yield[16] after purification by silica gel chromatography.

Scheme 4



Several features of this key intramolecular Heck reaction deserve comment. First, inspection of molecular models reveals that the transition state for the alkene insertion step must involve a "twisted" orientation of the reacting carbon−palladium σ bond and alkene π bond rather than the "eclipsed" alignment that has been suggested to be favored in these reactions.[17] Also noteworthy is the apparent "anti" β-hydride elimination required for the conversion of intermediate **18** to 9-*tert*-butylcyclopenta[*a*]phenalene.[18] Although several mechanisms can be envisioned to account for this process, we suggest that the formation of **14** proceeds via initial epimerization of **18** at C-10 via a (π-allyl)palladium intermediate[19] followed by normal syn-β-hydride elimination.[20]

The structures of cyclopenta[*a*]phenalenes **12**−**14** were established through extensive 2D NMR analysis (TOCSY, HMQC, and HMBC) and in the case of **13**, X-ray crystallography. Figure 1 presents ORTEP plots for the planar biphenyl-substituted cyclopenta[*a*]phenalene **13**. Bond distances for this molecule and several pertinent reference compounds[21] are shown in Figure 2. Comparison of structural data for these compounds reveals that bond lengths in the cyclopenta[*a*]phenalene core of **13** do not deviate significantly from the corresponding bond lengths in naphthalene

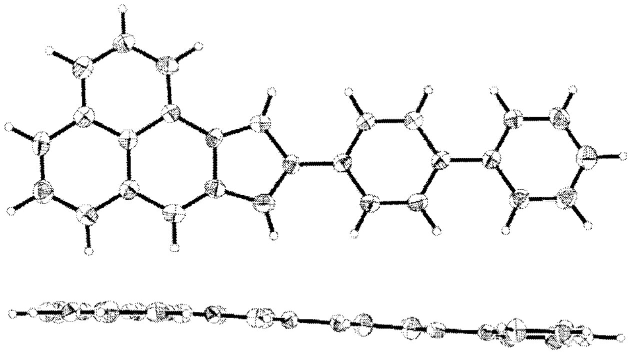


Figure 1. ORTEP views of **13**.

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[12] Imamoto, T. *Lanthanides in Organic Synthesis*; Academic Press: New York, 1994; pp 80−91.

[13] Monolithiation of diiodide **6** was carried out using a modification of the procedure of Katz: Katz, H. E. *Organometallics* **1986**, *5*, 2308.

[14] Stone, K. J.; Little, R. D. *J. Org. Chem.* **1987**, *49*, 1849.

[15] For reviews, see: (a) Bräse, S.; de Meijere, A. In *Metal-catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998; pp 99−166. (b) Link, J. T.; Overman, L. E. In *Metal-catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998; pp 231−270.

[16] In this reaction we believe that only fulvene isomer **17** undergoes cyclization.

[17] (a) Overman, L. E.; Abelman, M. M.; Kucera, D. J.; Tran, V. D.; Ricca, D. J. *Pure Appl. Chem.* **1992**, *64*, 1813. (b) Abelman, M. M.; Overman, L. E.; Tran, V. D. *J. Am. Chem. Soc.* **1990**, *112*, 6959.

[18] For a review of intramolecular Heck reactions involving formal "*anti*-eliminations," see: Ikeda, M.; El Bialy, S. A. A.; Yakura, T. *Heterocycles* **1999**, *51*, 1957.

[19] Granberg, K. L.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **1992**, *114*, 6858.

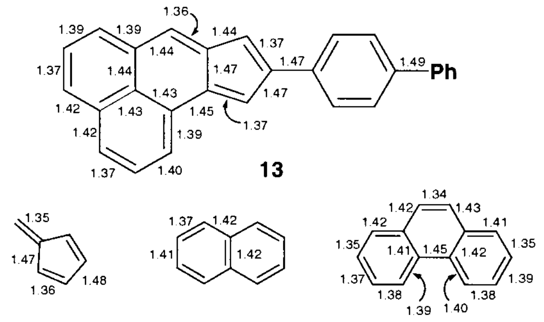

Figure 2. Bond distances (Å) for **13**, fulvene, naphthalene, and phenanthrene.

and fulvene; however, the $C_{6a}-C_7$ and $C_{10a}-C_{10b}$ single bonds in **13** are shorter than is typically observed (1.47 Å)[22] for $C_{sp2}-C_{sp2}$ single bonds. It should be noted that although the X-ray structure of this cyclopenta[*a*]phenalene reveals significant bond alternation, the variation in bond lengths is no larger than is observed in a number of well-known polycyclic aromatic hydrocarbons such as phenanthrene.

Figure 3 presents ^{1}H NMR chemical shift data for cyclopenta[*a*]phenalenes **12** and **14**. Also shown here is data for naphthylfulvenes **19** and **20**, which were prepared as reference compounds via the reaction of 1-naphthaldehyde with *tert*-butylcyclopentadiene. Historically, abnormal chemical shifts (relative to appropriate reference compounds) have been cited as evidence for the presence of diamagnetic ring currents and aromatic character in cyclic conjugated molecules.[23] Of particular relevance to this discussion, Sugihara et al. have reported that the chemical shifts of the five-membered ring protons in 7-methoxycyclopenta[*a*]phenalene appear 0.5−1.0 ppm downfield relative to the corresponding resonances in fulvene reference compounds.[4] In the case of the simple alkyl- and aryl-substituted cyclopenta[*a*]phenalenes **12** and **14**, however, we observe no dramatic deviation in chemical shift values. It should be noted, though, that this analysis is complicated by the fact that a number of factors contribute to determining the chemical shift of protons in these molecules, and the utility of **19**−**21** as reference compounds is compromised by the fact that these fulvenes are expected to prefer a nonplanar geometry[24,25] in contrast to cyclopenta[*a*]phenalene **14**.

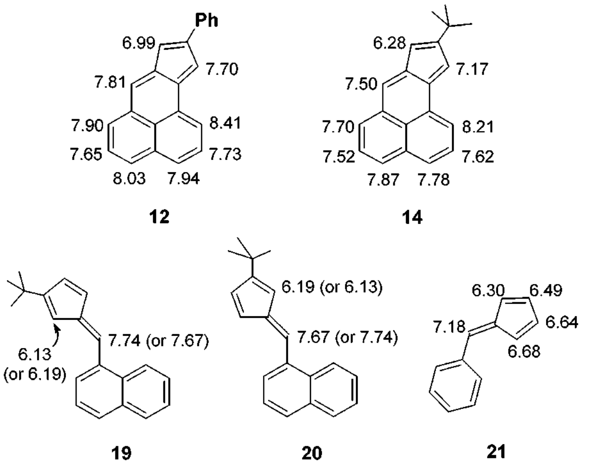

Figure 3. ^{1}H NMR (500 MHz) chemical shifts (ppm) for selected protons in **12** (acetone-d_6), **14** ($CDCl_3$), and **19**−**21** ($CDCl_3$).

The development of two efficient strategies for the preparation of cyclopenta[*a*]phenalenes has enabled us to begin the systematic investigation of the chemistry and physical properties of this novel class of nonalternant hydrocarbons. For example, we have carried out cyclic voltammetry studies to compare the redox behavior of cyclopenta[*a*]phenalene **14** and azulene.[26] Interestingly, both compounds are oxidized irreversibly at similar peak potentials ($E^{ox} = 0.65$ V for azulene and 0.69 V for **14**), while the cyclopenta[*a*]phenalene is reduced reversibly and considerably more easily ($E^{1/2} = -1.65$ V) than azulene ($E^{red} = -2.01$ V, irreversible).

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Supporting Information Available: Experimental procedures for the preparation of **12**, **13**, and **14**, characterization data for **8**, **9**, **12**−**14**, **16**, and **17**, and crystallographic data for **13**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(20) For other examples of Heck reactions that require formal anti β-hydride eliminations that may proceed via (π-allyl)palladium-mediated isomerization pathways, see: (a) Grigg, R.; Sridharan, V.; Stevenson, P.; Sukirthalingam, S.; Workun, T. *Tetrahedron* **1990**, *46*, 4003. (b) Grigg, R.; Fretwell, P.; Meerholtz, C.; Sridharan, V. *Tetrahedron* **1994**, *50*, 359. (c) Sperandio, D.; Hansen, H.-J. *Helv. Chim. Acta* **1995**, *78*, 765. (d) Wang, L.; Shevlin, P. B. *Tetrahedron Lett.* **2000**, *41*, 285.

(21) (a) Fulvene: Baron, P. A.; Brown, R. D.; Burden, F. R.; Domaille, P. J.; Kent, J. E. *J. Mol. Struct.* **1972**, *43*, 401. (b) Naphthalene: Cruickshank, D. W. J. *Tetrahedron* **1962**, *17*, 155. (c) Phenanthrene: Petricek, I.; Cisarova, I.; Hummel, L.; Kroupa, J.; Brezina, B. *Acta Crystallogr., Sect. B* **1990**, *46*, 830.

(22) Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2* **1987**, S1.

(23) For recent discussions of the definition of "aromaticity", see: (a) Minkin, V. I.; Glukhovtsev, M. N.; Simkin, B. Y. *Aromaticity and Antiaromaticity: Electronic and Structural Aspects*; John Wiley & Sons: New York, 1994. (b) Schleyer, P. v. R.; Jiao, H. *Pure Appl. Chem.* **1996**, *68*, 209. (c) Krygowski, T. M.; Cyrañski, M. K.; Czarnocki, Z.; Häfelinger, G.; Katrizky, A. R. *Tetrahedron* **2000**, *56*, 1783.

(24) For computational studies on the structure of 6-arylfulvenes, see: Sardella, D. J.; Keane, C. M.; Lemonias, P. *J. Am. Chem. Soc.* **1984**, *106*, 4962.

(25) For NMR studies of 6-phenylfulvene, see: Bönzli, P.; Otter, A.; Neuenschwander, M.; Huber, H.; Kellerhals, H. P. *Helv. Chim. Acta* **1986**, *69*, 1052.

(26) Cyclic voltammetry studies on **14** and azulene were performed under identical conditions (see Supporting Information).