ORGANIC LETTERS

2001
Vol. 3, No. 22
3599−3601

Diatropicity of Dehydrobenzo[14]annulenes: Comparative Analysis of the Bond-Fixing Ability of Benzene on the Parent 3,4,7,8,9,10,13,14-Octadehydro[14]annulene

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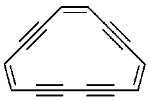
Received September 17, 2001

ABSTRACT



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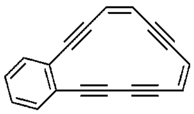

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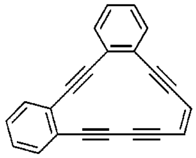

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We report the synthesis of 3,4,7,8,9,10,13,14-octadehydro[14]annulene (1) and detail a comparative aromaticity study with its benzannelated derivatives (e.g., 2 and 3).

An intensely debated area of dehydrobenzoannulene (DBA) chemistry is the extent of the delocalization in the macrocyclic ring.[1] While support of the diatropicity and paratropicity of DBAs has been presented,[2] skepticism still exists.[3] Our group has shown, qualitatively, that despite their large size and extensive benzannelation DBAs possess weak but discernible induced ring currents.[2a,c,d] While work has gone into utilizing molecular NMR probes to measure the aromaticity of DBAs[4] and other fused ring systems,[5] Bunz et al. recently turned the tables and used octadehydro[14]annulenes as a tool for making indirect, qualitative measurements of the aromaticity of ring systems fused to the [14]annulene skeleton.[6] Their arguments relied on the notion that macrocycle **1**, an unknown molecule, is an aromatic compound capable of ring current competition. Thus, the bond-fixing ability of the “study” ring systems could be determined qualitatively by the change in chemical shifts of the alkene protons going from the precyclized polyynes to cyclized annulenes. This raised the question of what are the observable effects of stepping down the aromaticity of the parent octadehydro[14]annulene via benzannelation? We expected to observe a distinguishable trend when additional ring systems were attached to **1**. In doing so, we hoped to find further support for the hypothesis that **1** and its DBA derivatives do in fact possess diatropic ring currents and to

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(2) (a) Kimball, D. B.; Wan, W. B.; Haley, M. M. *Tetrahedron Lett.* **1998**, *39*, 6795−6798. (b) Matzger, A. J.; Vollhardt, K. P. C. *Tetrahedron Lett.* **1998**, *39*, 6791−6794. (c) Bell, M. L.; Chiechi, R. C.; Johnson, C. A.; Kimball, D. B.; Matzger, A. J.; Wan, W. B.; Weakley, T. J. R.; Haley, M. M. *Tetrahedron* **2001**, *57*, 3507−3520. (d) Wan, W. B.; Chiechi, R. C.; Weakley, T. J. R.; Haley, M. M. *Eur. J. Org. Chem.* **2001**, 3485−3490.

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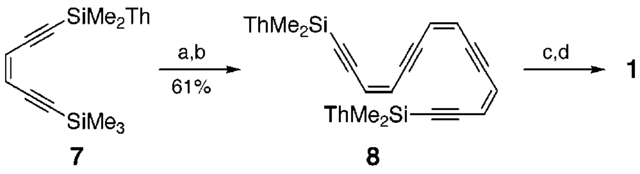
10.1021/ol016764g CCC: $20.00

show that **1** is sensitive enough to be used as a probe for aromaticity. To do this, we prepared **1** and compared its proton NMR data with those for a series of benzannelated derivatives, both new (**2**, **3**) as well as known (**4**,[7] **5**,[8] **6**[9]).

The straightforward synthetic route to the parent annulene **1** is shown in Scheme 1. Selective deprotection of enediyne **7**,[10] followed by Pd/Cu cross-coupling with (*Z*)-1,2-dichloroethene, gave α,*ω*-polyyne **8** in 61% yield. Stepwise deprotection and cyclization furnished 3,4,7,8,9,10,13,14-octadehydro[14]annulene (**1**), which proved to be stable only in dilute solutions.

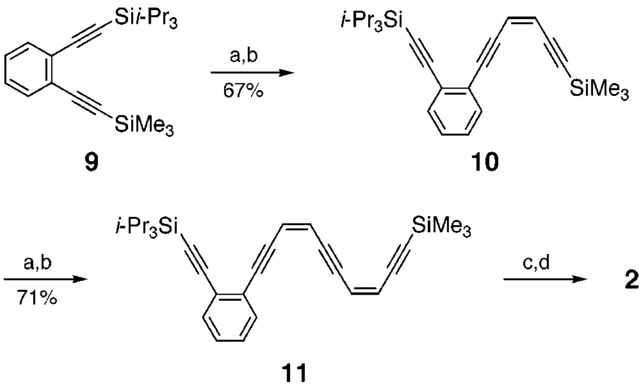
Scheme 1[a]



[a] Reagents: (a) K_2CO_3, MeOH, THF; (b) (*Z*)-1,2-dichloroethene, $Pd(PPh_3)_4$, CuI, $PrNH_2$, THF; (c) Bu_4NF, THF, MeOH; (d) $Cu(OAc)_2$, MeCN, reflux. (Th = 1,1,2-trimethylpropyl-).

As shown in Scheme 2, monobenzoannulene **2** was synthesized from known diethynylbenzene **9**[2c,11] via Pd/Cu cross-coupling with (*Z*)-(4-chloro-3-buten-1-ynyl)trimethylsilane[12] to furnish intermediate aryl enediyne **10**. Repeated deprotection and cross-coupling gave α,*ω*-polyyne **11** in 48% yield from **9**. Deprotection and cyclization resulted in formation of unstable benzocyclyne **2**.

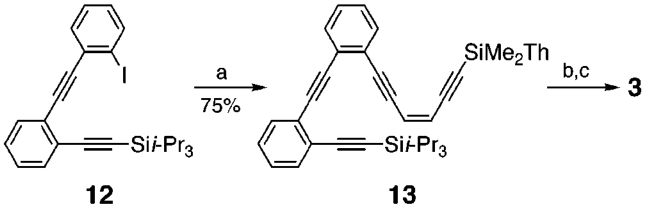
Scheme 2[a]



[a] Reagents: (a) K_2CO_3, MeOH, THF; (b) (*Z*)-(4-chloro-3-buten-1-ynyl)trimethylsilane, $Pd(PPh_3)_4$, CuI, $PrNH_2$, THF; (c) Bu_4NF, THF, MeOH; (d) $Cu(OAc)_2$, MeCN, reflux.

The synthesis of **3** (Scheme 3) required iodoarene **12**[2c,11] and enediyne **7**, which were subjected to an in situ deprotection/alkynylation procedure[2c,11] to yield polyyne **13**. Stepwise deprotection and cyclization gave unsymmetrical annulene **3**, which also could be handled only in dilute solutions. Concentrated solutions or solid samples of **1**−**3** rapidly polymerized to furnish dark, intractable materials. This instability precluded complete removal of the residual trialkylfluorosilane impurities.

Scheme 3[a]



[a] Reagents: (a) **7**, K_2CO_3, MeOH, $PdCl_2(PPh_3)_2$, CuI, Et_3N; (b) Bu_4NF, THF, MeOH; (c) $Cu(OAc)_2$, MeCN, reflux.

With solutions of **1**−**3** in hand, we examined the chemical shifts of the alkene and arene protons of all six octadehydro[14]annulenes (Figure 1). The average of the chemical shift

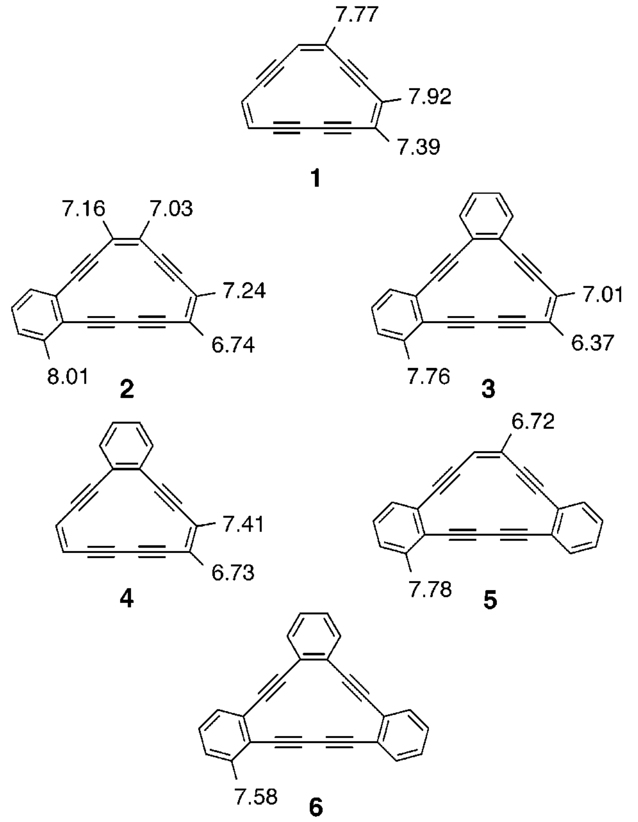


Figure 1. NMR chemical shifts of the alkene and selected arene protons for **1**−**6**.

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differences of the alkene protons show that in going from **1** to an annulene with one fused arene ring (**2**, **4**) results in an average upfield shift ($\Delta\delta$) of 0.67 ppm (Table 1). Attachment of a second benzene moiety gives a smaller upfield shift ($\Delta\delta$) of 0.38 ppm. One adjustment that is apparent from our data is a +0.15 ppm correction when the alkene proton is on a carbon γ to a benzene ring (e.g., H5 in going from **2** → **3**). It appears that this is the amount of change caused by steric deshielding of the nearby arene proton. It is interesting to note that the average change upon annelation of the second benzene ring is approximately half that of affixing the first. It is known that fusion of one benzene reduces the aromaticity of an annulene circuit by about one-half.[5,13] It follows that fusion of the second arene reduces the remaining ring current again by half. The mean $\Delta\delta$ values corroborate this notion.

Table 1. Chemical Shift Difference (ppm) of the Alkene Protons upon Successive Benzannelation

protons	**1** → **2**	**1** → **4**	**2** → **3**	**2** → **5**	**4** → **3**
H1	−0.61			−0.44	
H2	−0.74			−0.31	
H5	−0.68	−0.51	−0.23		−0.40
H6	−0.65	−0.66	−0.37		−0.36

A subtler trend can be extracted from examination of the arene protons. The sensitivity of these protons is much less than that shown for the alkene protons, as expected, but a consistent upfield shift is still observed for certain arene protons as the degree of benzannelation is increased. The protons *ortho* to the diacetylene bridge are compared, as these are the most consistent with regard to regiochemistry and do not experience steric deshielding effects. The $\Delta\delta$ values (with respect to monobenzo **2**) are 0.23 ppm for **5** and 0.25 ppm for **3**. When a third benzene ring is added (**6**), the $\Delta\delta$ value decreases to 0.19 ppm.

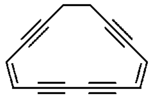
We considered the possibility of the $\Delta\delta$ trend to be simply a result of aryl substitution on the conjugated backbone. It was necessary, then, to compare the alkene chemical shifts of the precyclized polyynes (Table 2). If the results we observed in comparing the DBAs to the parent compound were an outcome of diatropicity in the annulene circuit, then the $\Delta\delta$ trend should be observable only in the aromatic (cyclized) target molecules, not in the nonaromatic polyynes. We were pleased to realize that the chemical shifts of each set of alkene protons in the polyynes were essentially the same, the range being only 0.04−0.12 ppm going from zero to two benzene rings.

Table 2. Chemical Shifts (ppm) of the Alkene Protons in Pre-Cyclized Compounds

protons	**8**	**11**	**13**	pre-**4**[a]	pre-**5**[b]
H1	6.07	6.11			6.11
H5	6.05	6.11	6.15	6.17	
H6	5.90	5.91	5.95	5.94	

[a] Reference 7. [b] Reference 8.

Another interesting comparison is that of annulene **1** with the 1,2-dihydro analogue **14** reported by Schreiber's group.[14] In the latter compound, the aromaticity is interrupted and the system is sufficiently "bond-fixed". If octadehydro[14]-annulene possesses a diatropic ring current, then this should manifest itself in a significant downfield shift of the 5,6-alkene protons relative to those of **14**. This is in fact what is observed. The alkene protons of **14** appear at 6.17 and 5.79 ppm and thus are close to the values of the *precyclized* compounds in Table 2, whereas in aromatic macrocycle **1** the analogous protons appear at 7.92 and 7.39 ppm. The large difference in chemical shifts cannot be ascribed to the anisotropy of the double bond; therefore, the difference must be a direct result of a diatropic ring current.



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These data, although qualitative, provide strong support for the aromaticity of **1** and thus uphold the idea of using dehydroannulenes as a means for evaluating the relative aromaticity of fused ring systems. The narrow ranges of the alkene chemical shift differences (typically 0.10−0.15 ppm), which are much less than the average $\Delta\delta$ values themselves, support the contention that the alkene protons of the parent macrocycle are sensitive enough to be used as a qualitative probe for relative aromaticity. Furthermore, the effects of the step-down in aromaticity by increasing benzannelation are clearly a result of competing ring currents in the annulenic systems. We are currently working toward further understanding the aromaticity of dehydro- and dehydrobenzoannulenes both theoretically and experimentally.

Acknowledgment. We thank the Petroleum Research Fund, administered by the American Chemical Society, and The Camille and Henry Dreyfus Foundation (Teacher−Scholar Award 1998−2003 to M.M.H.) for financial support.

Supporting Information Available: Selected spectroscopic data for compounds **1**−**3**, **8**, **10**, **11**, and **13**. This material is available free of charge via the Internet at http://pubs.acs.org.

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