Pergamon

Tetrahedron Letters 39 (1998) 6795–6798

TETRAHEDRON
LETTERS

Synthesis of Expanded Planar Dehydrobenzoannulenes: Weakly Diatropic, Weakly Paratropic, or Atropic?

W. Brad Wan, David B. Kimball, and Michael M. Haley*

Department of Chemistry, University of Oregon, Eugene, Oregon 97403-1253

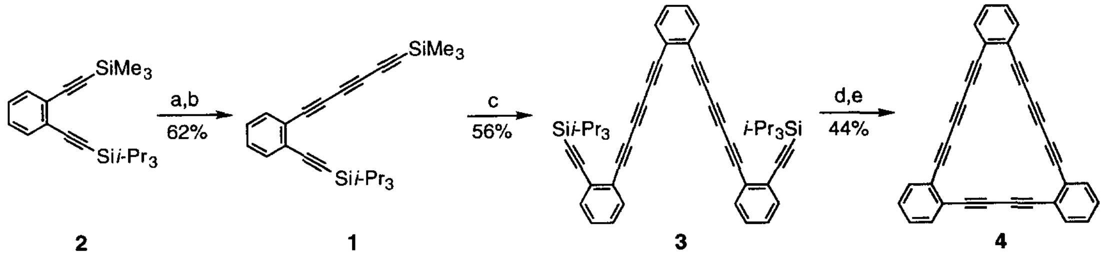
Received 16 June 1998; accepted 21 July 1998

Abstract: Use of a Cu/Pd cross-coupling strategy has led to the synthesis of the first dehydrobenzoannulenes containing triacetylenic linkages. NMR studies of these macrocycles and comparison with other known systems indicate that, in spite of their large size and extensive benzannelation, dehydrobenzoannulenes possess weak induced ring currents. © 1998 Elsevier Science Ltd. All rights reserved.

Keywords: Annulene; Aromaticity; Alkynes

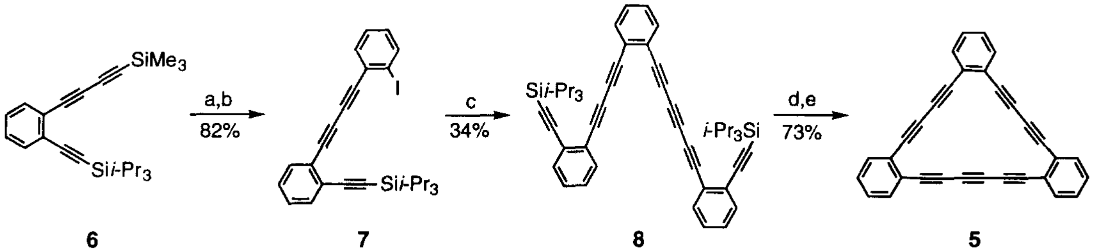
The recent revival of dehydrobenzoannulene (DBA) chemistry has led to the synthesis and study of a plethora of new macrocycles exhibiting fascinating physiochemical properties.[1] A vast majority of these examples have been either monoyne- and/or diyne-linked molecules.[2] Although the first tetrayne-connected DBAs were recently reported,[3] the non-planarity of the macrocycles precluded the possibility of ring currents in the annulenic core. The synthesis of planar triyne-connected (and larger) systems has been restricted due primarily to the method of annulene formation. Standard Cu-mediated dimerization/cyclooligomerization reactions of α,ω-diacetylenes typically produce complex mixtures of diyne-linked products that are difficult to separate[2c] and often provide low isolated yields of a desired macrocycle.[2b] Using Cu-coupling methods, systems with an odd number of acetylenes (three or greater) would require two different alkyne-containing partners, further complicating the product mixtures. Additionally, a vast majority of terminal diynes and triynes needed for higher DBA synthesis are sensitive molecules prone to rapid decomposition.[4] We recently reported a synthetic strategy that utilizes an intramolecular ring closure of α,ω-polyynes, giving rise to singular DBA products in relatively high overall yields.[5] The following report describes extension of this method to formation of the first triyne-linked dehydrobenzoannulenes, as well as preparation of related macrocycles containing a single alkene unit, and discussion of the induced ring currents in these systems.

The essential intermediate in the assembly of triyne-linked DBAs was phenylhexatriyne synthon **1** (Scheme 1). Protiodesilylation of **2**[5a] and subsequent exposure to modified Cadiot-Chodkiewicz conditions[6] using $Me_3Si–C{\equiv}CC{\equiv}C–Br$[7] gave **1** in 62% yield. Although the synthesis of 1-phenyl-1,3,5-hexatriyne has been



Scheme 1. a) K_2CO_3, MeOH, Et_2O; b) i] BuLi, THF, ii] CuBr, iii] $Me_3SiC{\equiv}CC{\equiv}CBr$, pyridine; c) *o*-diiodobenzene, $PdCl_2(PPh_3)_2$, $Pd(PPh_3)_4$, CuI, Et_3N, THF, KOH, H_2O; d) Bu_4NF, THF, EtOH; e) CuCl, $Cu(OAc)_2{\bullet}H_2O$, pyridine.

PII: S0040-4039(98)01583-4

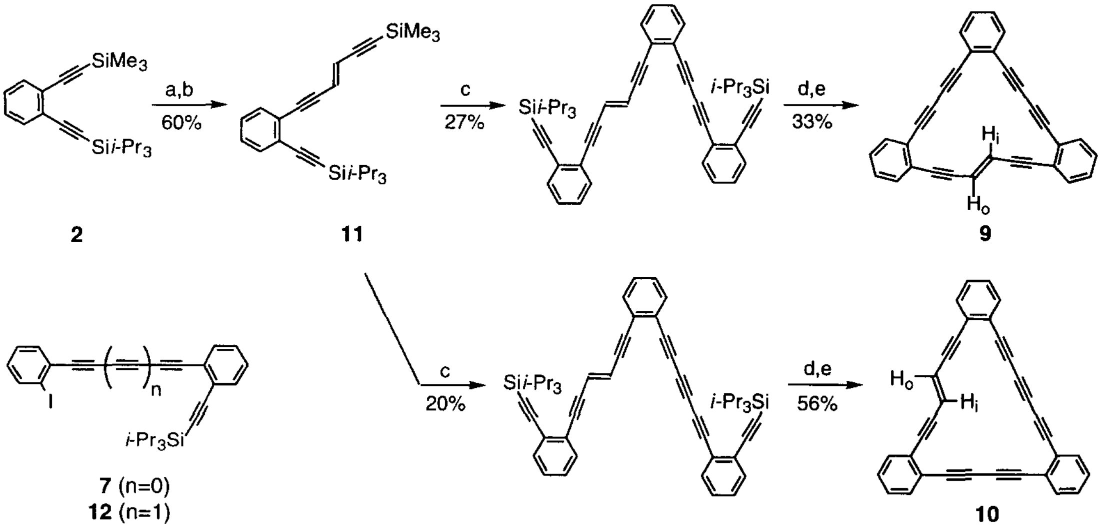


Scheme 2. a) *N*,*N*-tetramethylene-*o*-(iodophenyl)triazene, $PdCl_2(PPh_3)_2$, $Pd(PPh_3)_4$, CuI, Et_3N, THF, KOH, H_2O; b) MeI, 120 °C; c) **1**, $PdCl_2(PPh_3)_2$, $Pd(PPh_3)_4$, CuI, Et_3N, THF, KOH, H_2O; d) Bu_4NF, THF, EtOH; e) CuCl, $Cu(OAc)_2{\bullet}H_2O$, pyridine.

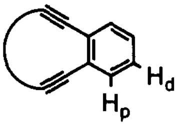
reported previously, identification of the extremely unstable parent molecule was limited to UV spectroscopy.[8] *In situ* generation of the reactive intermediate under Pd-coupling conditions,[5] however, gratifyingly afforded octayne **3** in 56% yield. Sequential desilylation and intramolecular oxidative dimerization furnished [22]annulene **4**.[9] Construction of the corresponding [20]annulene **5** was accomplished using the *in situ* deprotection/alkynylation reaction in two key steps (via **6** and **7**), as shown in Scheme 2. Cyclization of **8** using analogous chemistry gave **5** in good overall yield.

Replacement of one acetylene moiety with a *trans*-ethylene unit should provide DBAs **9** and **10** with protons directly attached to the macrocycles in question, and thus are superior probes for ring currents. The requisite enediyne **11** was cross-coupled with either iodide **7** or **12**[10] using the *in situ* deprotection/alkynylation protocol (Scheme 3). Subsequent desilylation and oxidative dimerization afforded monoene-DBAs **9** and **10**. In all cases the macrocycles were isolated as tan solids that exhibited modest solubility in common solvents.

Considerable debate in the literature over the last thirty years has focused on whether dehydrobenzoannulenes are able to sustain induced ring currents.[11] Although fusion of arenes to the annulenic core provides rigidity and stability, this also weakens the diatropicity/paratropicity of the macrocycle significantly. Until quite recently, the number of planar systems available for study was limited; however, with

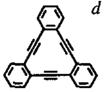
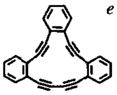
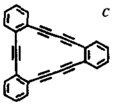
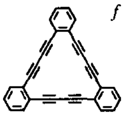


Scheme 3. a) K_2CO_3, MeOH, Et_2O; b) *E*-(4-chloro-3-buten-1-ynyl)trimethylsilane, $Pd(PPh_3)_4$, CuI, Et_3N, THF; c) **7** or **12**, $PdCl_2(PPh_3)_2$, $Pd(PPh_3)_4$, CuI, Et_3N, THF, KOH, H_2O; d) Bu_4NF, THF, EtOH; e) CuCl, $Cu(OAc)_2{\bullet}H_2O$, pyridine.



the addition of **4** and **5**,[12] the series of alkyne-linked, tribenzo-annelated DBAs is complete from [12]- to [22]annulene.[2a,5] A qualitative determination of the nature of the ring current can be made by comparing the chemical shift range of the proximal and distal protons (H_p and H_d, respectively) in the benzene rings of each DBA.[13] The arene proton environments in *o*-diethynylbenzene (ODEB) and **6**[5a] are used as suitable reference standards[14] due to their structural similarity, yet these simple DBA subunits lack the effects of macrocyclic delocalization as well as lack the anisotropic effects of dangling alkynes.[15]

Table 1. Chemical shift range for the two different arene proton environments in tribenzo-annelated DBAs and related reference molecules; mean values in parentheses.

cmpd	$H_p{}^a$	$H_d{}^a$
ODEB^b	7.49-7.51 (7.50)	7.28-7.30 (7.29)
6^c	7.44-7.49 (7.47)	7.22-7.32 (7.27)
 ^{d}	7.32-7.36 (7.34)	7.16-7.20 (7.18)
 ^{e}	7.58-7.88 (7.73)	7.38-7.46 (7.42)
 ^{c}	7.32-7.48 (7.40)	7.19-7.30 (7.25)
 ^{f}	7.66-7.70 (7.68)	7.40-7.44 (7.42)
5^g	7.44-7.53 (7.49)	7.23-7.38 (7.31)
9^g	7.36-7.54 (7.45)	7.24-7.36 (7.30)
4^g	7.56-7.71 (7.64)	7.35-7.43 (7.39)
10^g	7.50-7.68 (7.59)	7.29-7.45 (7.37)

^{a} As assigned above. ^{b} Reference 13. ^{c} Reference 5a. ^{d} Reference 11d. ^{e} Reference 2a. ^{f} Reference 5b. ^{g} This work.

As can be seen in Table 1, the DBAs display alternation between diatropic and paratropic character. All four of the $4n+2$ Hückel-type systems show distinct downfield shifts of their arene protons, while only two of the $4n$ systems ([12] and [16]) show opposite behavior. The mean chemical shifts for the [20]annulenes, on the other hand, are essentially the same as ODEB and **6**, and are virtually unchanged compared to the acyclic precursors. These data suggest that **5** and **9** are atropic. Although it is well known that ring currents lessen with increasing macrocycle size and that paratropicity diminishes faster than diatropicity,[11] we were surprised that, based on the arene protons, the 20-membered macrocycles seemed to lack a ring current.

The alkene protons of **9**, however, told a somewhat different story.[16] Whereas exchange of the in and out protons (H_i and H_o, respectively) of **9** gives the identical molecule, the same operation in **10** would result in an energetically less stable conformation. NMR experiments up to 100 °C showed that **10** adopted a static structure, which was most likely the same conformer that was found in the X-ray crystal structure (correctly depicted in Scheme 3).[12] The alkene protons resonated at 6.28 and 6.42 ppm (d, J=16.1 Hz) and are attributed to H_i and H_o, respectively.[11b] In contrast, the alkene protons of **9** were exchanging rapidly at room temperature and thus appeared as a singlet at 6.62 ppm. The signal remained unchanged upon cooling to –90 °C. Utilizing the alkene resonance in ***trans***-1,6-diphenyl-3-hexen-1,5-diyne as reference (δ=6.33),[17] the 0.29 ppm downfield shift roughly translates to $H_i \approx 6.9$ ppm for **9**. Taken together with previous monoene examples that exchange rapidly in solution,[11b,d] we therefore conclude that **9** (and thus likely **5**) is marginally paratropic.

The above results strongly suggest that expanded planar, highly alkynylated dehydrobenzoannulenes like **4**-**5** and **9**-**10** do indeed possess induced ring currents, albeit weakly so. While convincing, this work indicates further study is warranted in order to provide compelling evidence. Efforts to quantitate the ring current in DBAs are currently under way.

Acknowledgment. We gratefully acknowledge the National Science Foundation (CHE-9704171), the donors of The Petroleum Research Fund, administered by the ACS, and The Camille and Henry Dreyfus Foundation (Teacher-Scholar Award to MMH) for support of this research.

References and Notes

1. Haley, M.M. *Synlett* **1998**, 557, and references therein.
2. *Inter alia*: (a) Baldwin, K.P.; Matzger, A.J.; Scheiman, D.A.; Tessier, C.A.; Vollhardt, K.P.C.; Youngs, W.J. *Synlett* **1995**, 1215. (b) Boese, R.; Matzger, A.J.; Vollhardt, K.P.C. *J. Am. Chem. Soc.* **1997**, *112*, 2052. (c) Tovar, J.D.; Jux, N.; Jarrosson, T.; Khan, S.I.; Rubin, Y. *J. Org. Chem.* **1997**, *62*, 3432.
3. Haley, M.M.; Bell, M.; Brand, S.C.; Kimball, D.B.; Pak, J.J.; Wan, W.B. *Tetrahedron Lett.* **1997**, *38*, 7483.
4. Brandsma, L. *Preparative Acetylenic Chemistry*, Elsevier: Amsterdam, **1988**.
5. (a) Haley, M.M.; Bell, M.L.; English, J.J.; Johnson, C.A.; Weakley, T.J.R. *J. Am. Chem. Soc.* **1997**, *119*, 2956. (b) Haley, M.M.; Brand, S.C.; Pak, J.J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 836.
6. Rubin, Y.; Parker, T.C.; Khan, S.I.; Holliman, C.L.; McElvany, S.W. *J. Am. Chem. Soc.* **1996**, *118*, 5308.
7. de Graaf, W.; Smits, A.; Boersma, J.; van Koten, G.; Hoekstra, W.P.M. *Tetrahedron* **1988**, *44*, 6699.
8. Eastmond, R.; Walton, D.M.R. *Tetrahedron* **1972**, *28*, 4591.
9. Selected spectral data (^{1}H NMR: 300 MHz, ^{13}C NMR: 75.5 MHz, $CDCl_3$): **1**: ^{1}H NMR 7.43-7.52 (m, 2H), 7.20-7.38 (m, 2H), 1.18 (s, 21H), 0.25 (s, 9H); ^{13}C NMR 133.27, 132.40, 129.14, 127.96, 127.86, 123.83, 104.27, 96.51, 89.18, 88.11, 77.91, 75.54, 67.77, 61.68, 18.64, 11.31, –0.52. **4**: ^{13}C NMR 133.87, 133.33, 131.48, 129.15, 129.09, 128.78, 125.77, 124.98, 122.75, 80.70, 78.55, 77.49, 77.40, 76.61, 76.53, 67.42, 66.94. **5**: ^{13}C NMR 135.06, 133.18, 131.40, 129.44, 129.07, 129.01, 128.02, 124.75, 124.33, 81.55, 81.07, 79.26, 78.74, 78.56, 78.32, 68.85. **9**: ^{13}C NMR 134.75, 132.79, 130.68, 129.08, 128.96, 128.44, 126.68, 125.65, 124.39, 121.44, 94.17, 93.91, 81.71, 81.18, 78.20. **10**: ^{13}C NMR 133.55, 133.47, 133.50, 132.40, 132.19, 130.95, 129.23, 128.95, 128.80, 128.33, 128.26, 127.88, 125.89, 125.77, 124.15, 123.99, 123.92, 12242, 120.84, 94.12, 93.80, 93.41, 92.86, 81.51, 80.46, 78.78, 78.31, 77.68, 76.70, 67.56, 67.49. **11**: ^{1}H NMR 7.42-7.52 (m, 2H), 7.21-7.28 (m, 2H), 6.22 (d, J=16.1 Hz, 1H), 6.06 (d, J=16.1 Hz, 1H), 1.15 (s, 21H), 0.22 (s, 9H); ^{13}C NMR 132.66, 132.12, 128.18, 127.96, 125.82, 125.46, 121.93, 120.77, 105.02, 103.25, 100.69, 95.40, 93.85, 91.37, 18.68, 11.30, –0.20.
10. Prepared from **1** (41% yield) in a manner analogous to **7** (Scheme 2).
11. (a) Garratt, P.J. *Aromaticity*, Wiley: New York, **1986**. (b) Balaban, A.T.; Banciu, M.; Ciorba, V. *Annulenes, Benzo-, Hetero-, Homo- Derivatives and their Valence Isomers, Vol. 1-3*, CRC Press: Boca Raton, **1987**. (c) Minkin, V.I.; Glukhovtsev, M.N.; Simkin, B.Ya. *Aromaticity and Antiaromaticity*, Wiley: New York, **1994**. (d) Staab, H.A.; Günther, P. *Chem. Ber.* **1977**, *110*, 619, and references therein.
12. The planarity of **4**, **5**, and **9** is assumed due to the fact that X-ray crystal structures of [12]- to [18]-annulene and derivatives show that the macrocyclic ring in every tribenzo- case is essentially flat. Additionally, we recently obtained a crystal structure of **10** which confirmed its planarity. This cannot be discussed here due to space limitations: Wan, W.B., Weakley, T.J.R., Haley, M.M., unpublished results.
13. Matzger, A.J., Vollhardt, K.P.C., *Tetrahedron Lett.* **1998**, *39*, 6791. This group has assigned H_p and H_d in [12]- to [16]annulene using 2D–NMR techniques. The corresponding protons in [18]- to [22]annulene were assigned by analogy. We thank Professor Vollhardt for sharing this information prior to publication.
14. A quick survey of *ca.* 12 simple *o*-bisalkynylated benzenes in the literature gave an average value of H_p and H_d of 7.50 and 7.30 ppm, respectively. ODEB and **6** were chosen as representative examples.
15. Although the acyclic precursors to the DBAs might be, in theory, better models for comparative purposes, in practice this does not work due to their comformational flexibility and thus the influence on the NMR chemical shifts by magnetic anisotropy of dangling alkyne units.
16. We feel the monoene comparison is valid since the overall change in the expanded structures is minimal; however, since the effects we are attemptimg to qualify are small, this comparison might not hold true. We put forth these results in order to stimulate further discussion. See also references 11b, 11d, and 13.
17. Vollhardt, K.P.C.; Winn, L.S. *Tetrahedron Lett.* **1985**, *26*, 709.