ORGANIC LETTERS

2004
Vol. 6, No. 13
2249−2252

Syntheses of Syn and Anti Doublebent [5]Phenylene†

Dennis T.-Y. Bong, Eugene W. L. Chan, Rainer Diercks, Peter I. Dosa, Michael M. Haley, Adam J. Matzger, Ognjen Š. Miljanić, and K. Peter C. Vollhardt*

Center for New Directions in Organic Synthesis, Department of Chemistry, University of California at Berkeley, and the Chemical Sciences Division, Lawrence Berkeley National Laboratory, Berkeley, California 94720-1460

Andrew D. Bond‡

University of Cambridge, Department of Chemistry, Lensfield Road, Cambridge, CB2 1EW, UK

Simon J. Teat

CCLRC Daresbury Laboratory, Warrington, Cheshire, WA4 4AD, UK

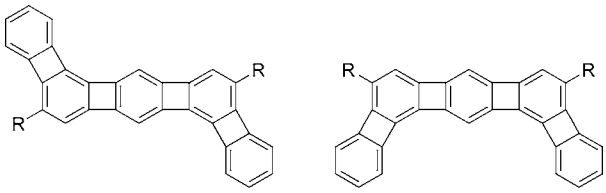
Amnon Stanger

Department of Chemistry, The Institute of Catalysis Science and Technology, and The Lise Meitner-Minerva Center for Computational Quantum Chemistry, Technion—Israel Institute of Technology, Haifa 32000, Israel

kpcv@berkeley.edu

Received April 27, 2004

ABSTRACT



1a: R = H
1b: R = Pr

2a: R = H
2b: R = Pr

The parent and dipropyl-substituted anti (1a,b) and syn doublebent (2a,b) [5]phenylenes have been assembled by CpCo-catalyzed double cyclization of regiospecifically constructed appropriate hexaynes. ^{1}H NMR, NICS, and an X-ray structural analysis of 1a reflect the aromatizing effect of double angular fusion on the central ring of the linear [3]phenylene substructure.

The various topological manifestations of the phenylenes are of fundamental synthetic[1] and theoretical interest.[2] In this context, hydrocarbons **1** and **2** are unusual in their mixed topology, composed of the respective linear and angular substructures **3**[3] and **4**[4] (Figure 1). The hitherto only example of this type is "bent" [4]phenylene **5**.[5] They also represent additional isolated[6] members of the family of 12 [5]-phenylenes[2d] and stand out in the series as the most stable unbranched isomers, despite the presence of linear substructures.[2d] To anticipate the properties of **1** and **2**, it is instructive to refer to those of their substructure **5**,[5] which

† CAS names: Benzo[1″,2″:3,4;5″,4″:3′,4′]dicyclobuta[1,2*a*:1′,2′*a*′]-bisbiphenylene (syn isomer) and benzo[1″,2″:3,4;4″,5″:3′,4′]dicyclobuta-[1,2-*a*:1′,2′-*a*′]bisbiphenylene (anti isomer).

‡ Present address: University of Southern Denmark, Department of Chemistry, Campusvej 55, 5230 Odense M, Denmark.

(1) For a review, see: (a) Vollhardt, K. P. C.; Mohler, D. L. In *Advances in Strain in Organic Chemistry*; Halton, B., Ed.; JAI: London, 1996; pp 121−160. For recent progress, see: (b) Han, S.; Bond, A. D.; Disch, R. L.; Holmes, D.; Schulman, J. M.; Teat, S. J.; Vollhardt, K. P. C.; Whitener, G. D. *Angew. Chem., Int. Ed.* **2002**, *41*, 3223. (c) Han, S.; Anderson, D. R.; Bond, A. D.; Chu, H. V.; Disch, R. L.; Holmes, D.; Schulman, J. M.; Teat, S. J.; Vollhardt, K. P. C.; Whitener, G. D. *Angew. Chem., Int. Ed.* **2002**, *41*, 3227. (d) Bruns, D.; Miura, H.; Vollhardt, K. P. C.; Stanger, A. *Org. Lett.* **2003**, *5*, 549.

10.1021/ol049225v CCC: $27.50
Published on Web 05/27/2004

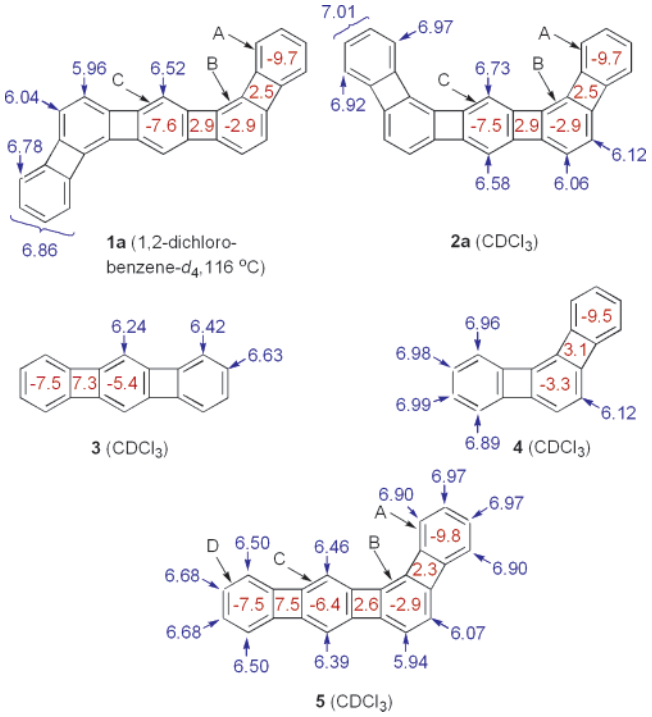
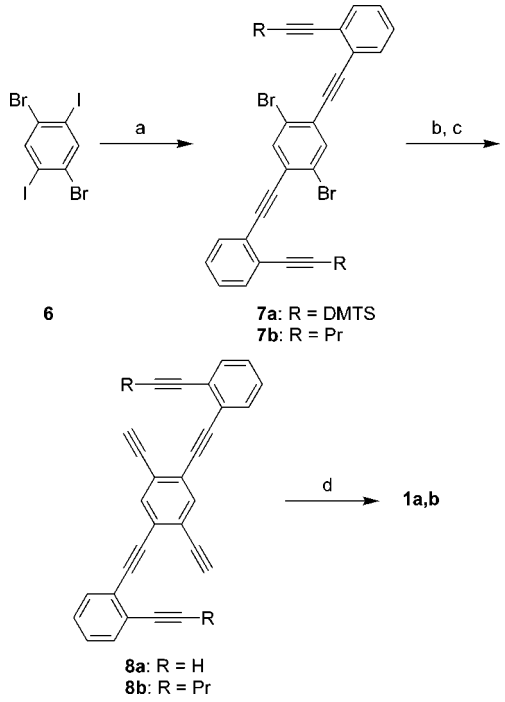


Figure 1. ^{1}H NMR chemical shifts (δ, ppm; blue) and NICS (1.0) values (red) for **1**−**5** (solvent).

reflects the effect of benzocyclobutadiene fusion to **3** and **4**, respectively. Thus, relative to the terminal ring in **3**, ring B exhibits increased bond alternation and lesser aromaticity (chemical shifts, NICS values; Figure 1). The result of this effect on B is decreased paratropism in the adjacent four-membered ring and slightly increased diatropism in ring C, causing the attached hydrogens to be relatively deshielded. Conversely, relative to the terminal ring in **4**, ring C undergoes distortion in the sense indicated in the structure depicted in Figure 1. The consequences of this distortion are subtly increased bond localization and hence decreased diatropism in B, relative to the central ring in **4**. In **1** and **2**, the seemingly fairly unperturbed "other side" of the linear substructure in **5** would be altered equally, and the determination of the consequences on C and of remote effects was deemed to be important.

Scheme 1[a]



[a] Reaction conditions: For **1a**: (a) 1-ethynyl-2-(dimethylthexylsilylethynyl)benzene, $PdCl_2(PPh_3)_2$, CuI, NEt_3, 72%. (b) TMSA, $PdCl_2(PPh_3)_2$, CuI, NEt_3, 120 °C, 70%. (c) $Bu_4N^+F^-$, THF, (95%). (d) (i) $CpCo(C_2H_4)_2$, THF, −25 °C; (ii) 1,3-cyclohexadiene, THF, 110 °C, 7% over two steps. For **1b**: (a) 1-ethynyl-2-(pent-1-ynyl)-benzene, $PdCl_2(PPh_3)_2$, CuI, NEt_3, 50 °C, 49%. (b) TMSA, $PdCl_2(PPh_3)_2$, CuI, NEt_3, 145 °C, 70%. (c) NaOH, THF, CH_3OH, 85%. (d) $CpCo(CO)_2$, *m*-xylene, *hν*, Δ, 2%.

The syntheses of **1a**,**b** (Scheme 1) started with tetrahalogenated benzene **6**[7] as a C_{2h} symmetric template. Elaboration by sequential Sonogashira couplings, first with the appropriate alkynyl(ethynyl)benzene and then with trimethylsilylacetylene (TMSA), followed by desilylation provided hexaynes **8a**,**b**, containing all the requisite carbon atoms. Cycloisomerization, while moderately successful toward **1b** when employing the standard protocol with $CpCo(CO)_2$,[1] failed for **1a** under these conditions, requiring a remarkably improved two-step protocol developed recently that utilizes $CpCo(C_2H_4)_2$.[8] The strategy en route to **2a**,**b** was identical, except that the starting haloarene was C_{2v}-symmetric **9** (Scheme 2).[9] A higher yielding alternative toward **2a** is depicted in Scheme 3 and proceeds through tetrabromoarene **12**, which could be subjected to 4-fold Sonogashira coupling to give **13** and then eventually the target.

(2) For an exposé of the significance of this class of molecules in graph theoretical treatments of aromaticity, see: (a) Randić, M. *Chem. Rev.* **2003**, *103*, 3449. For selected other studies, see: (b) Schulman, J. M.; Disch, R. L. *J. Phys. Chem. A.* **2003**, *107*, 5223. (c) Schulman, J. M.; Disch, R. L.; Jiao, H.; Schleyer, P. v. R. *J. Phys. Chem. A* **1998**, *102*, 8051. (d) Schulman, J. M.; Disch, R. L. *J. Phys. Chem. A* **1997**, *101*, 5596. The calculations reported in this paper were repeated at the B3LYP/6-31G* level of DFT theory in the present work; NICS (1.0) at GIAO/3-21G. See Supporting Information.

(3) (a) Schleifenbaum, A.; Feeder, N.; Vollhardt, K. P. C. *Tetrahedron Lett.* **2001**, *42*, 7329. (b) Berris, B. C.; Hovakeemian, G. H.; Lai, Y.-H.; Mestdagh, H.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1985**, *107*, 5670.

(4) Diercks, R.; Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 266.

(5) Bong, D. T.-Y.; Gentric, L.; Holmes, D.; Matzger, A. J.; Scherhag, F.; Vollhardt, K. P. C. *Chem. Commun.* **2002**, 278.

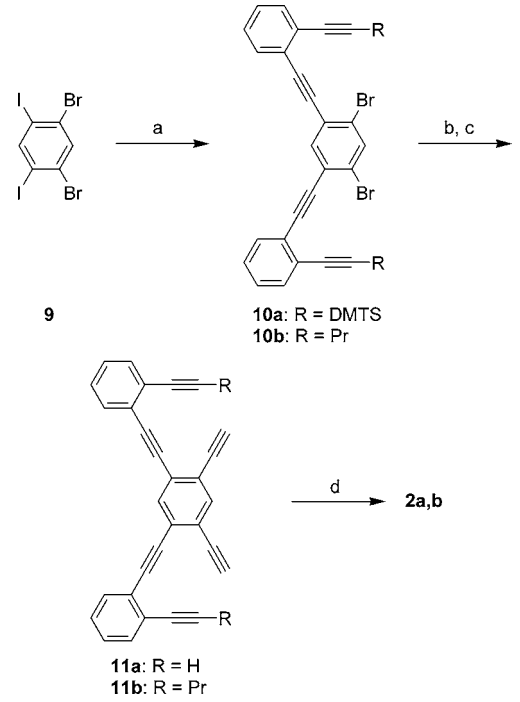
(6) Known topologies are linear: (a) Blanco, L.; Helson, H. E.; Hirthammer, M.; Mestdagh, H.; Spyroudis, S.; Vollhardt K. P. C. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1246. Angular: (b) Schmidt-Radde, R. H.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1992**, *114*, 9713. Zigzag: (c) Eickmeier, C.; Holmes, D.; Junga, H.; Matzger, A. J.; Scherhag, F.; Shim, M.; Vollhardt, K. P. C. *Angew. Chem., Int. Ed.* **1999**, *38*, 800. Y-shaped (C_{2v}) branched: (d) Boese, R.; Matzger, A. J.; Mohler, D. L.; Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1478.

(7) Hart, H.; Katsumasa, K.; Du, C.-J. F. *J. Org. Chem.* **1985**, *50*, 3104.

(8) Dosa, P. I.; Whitener, G. D.; Vollhardt, K. P. C.; Bond, A. D.; Teat, S. J. *Org. Lett.* **2002**, *4*, 2075.

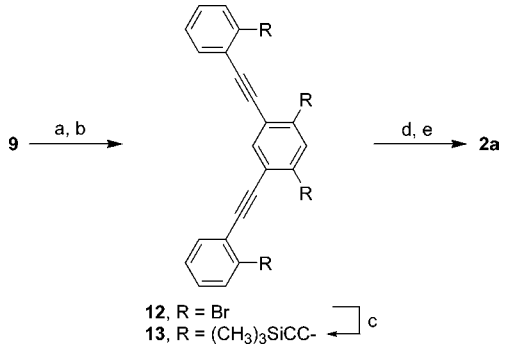
(9) Goldfinger, M. B.; Crawford, K. B.; Swager, T. M. *J. Am. Chem. Soc.* **1997**, *119*, 4578.

Scheme 2[a]



[a] Reaction conditions: For **2a**: (a) 1-ethynyl-2-(dimethylthexylsilylethynyl)benzene, $PdCl_2(PPh_3)_2$, CuI, NEt_3, 65%. (b) TMSA, $PdCl_2(PPh_3)_2$, CuI, NEt_3, 120 °C, 70%. (c) $Bu_4N^+F^-$, THF, 95%. (d) (i) $CpCo(C_2H_4)_2$, THF, −25 °C; (ii) 1,3-cyclohexadiene, THF, 110 °C, 14% over two steps. For **2b**: (a) 1-ethynyl-2-(pent-1-ynyl)benzene, $PdCl_2(PPh_3)_2$, CuI, NEt_3, 50 °C, 83%. (b) TMSA, $PdCl_2(PPh_3)_2$, CuI, NEt_3, 135 °C, 86%. (c) NaOH, THF, CH_3OH, 85%. (d) $CpCo(CO)_2$, *m*-xylene, *hν*, Δ, 1%.

Scheme 3[a]



[a] Reaction conditions: (a) TMSA, $PdCl_2(PPh_3)_2$, CuI, NEt_3, 96%. (b) (i) KOH, Et_2O/EtOH; (ii) 1-bromo-2-iodobenzene, $PdCl_2(PPh_3)_2$, CuI, NEt_3, 120 °C, 45% over two steps. (c) TMSA, $PdCl_2(PPh_3)_2$, CuI, NEt_3, 120 °C, 47%. (d) $Bu_4N^+F^-$, THF, (95%). (e) (i) $CpCo(C_2H_4)_2$, THF, −25 °C; (ii) 1,3-cyclohexadiene, THF, 110 °C, 14% over two steps.

The phenylenes **1** and **2** are orange-red solids that decompose in air, especially in solution. The parent systems are relatively insoluble (precluding ^{13}C NMR measurements), especially **1a**, the ^1H NMR spectrum of which necessitated the use of hot 1,2-dichlorobenzene. The electronic spectra exhibit the typical two sets of absorptions at higher ($\lambda_{max} \approx$ 350−390 nm) and lower energy (highest wavelength λ_{max} = 505 nm for **1a**, 507 nm for **1b**), devoid of any significant indication of the topological differences between the two isomers, unlike that observed for the series of angular vs zigzag phenylenes.[6b] In tune with a trend emerging in the electronic spectra of the lower phenylenes, i.e., λ_{max} (branched/angular) < λ_{max} (linear), [1a] these bands are at higher energy than that for the linear [5]phenylene frame (530 nm) but bathochromically shifted from those in the zigzag- (484 nm), Y-shaped (C_{2v}) branched (486 nm), and angular isomers (470 nm).[6] Most revealing are the comparative ^1H NMR spectra (Figure 1).[10] Focusing on **2a**, for which data could be obtained in $CDCl_3$, the effect of additional annelation is noticeably larger δ values for the hydrogens attached to ring C, in accord with the changes in NICS values. Thus, the central protons in the linear fragment experience increasing deshielding along the series **3** (δ = 6.24 ppm, NICS = −5.4) to **5** (δ = 6.46, 6.39 ppm, NICS = −6.4) to **2a** (δ = 6.73, 6.58 ppm, NICS = −7.5), the result of consecutive bond fixation in the terminal rings, in turn subtly increasing aromaticity in C and attenuating paratropism of cyclobutadienoid nuclei. In contrast, the central protons of the angular fragment, which are slightly shielded in **5** (δ = 5.94 and 6.07 ppm, NICS = −2.9) relative to **4** (δ = 6.12 ppm, NICS = −3.3, also vide supra), seem to be unchanged in **2a** (δ = 6.06 and 6.12 ppm, NICS = −2.9). The deshielding effect of the evolving "bay region" manifests itself in the increased $\Delta\delta$ of two protons on the C ring: 0.07 ppm in **5**, 0.15 ppm in **2a**. Finally, a long-range effect of symmetrization in going from **5** to **2a** seems to be absent, as indicated by the essentially identical NMR and NICS data for rings A and B.

While it was impossible to obtain solids suitable for conventional X-ray analysis of all the new [5]phenylenes reported, **1a** eventually yielded single crystals (by slow

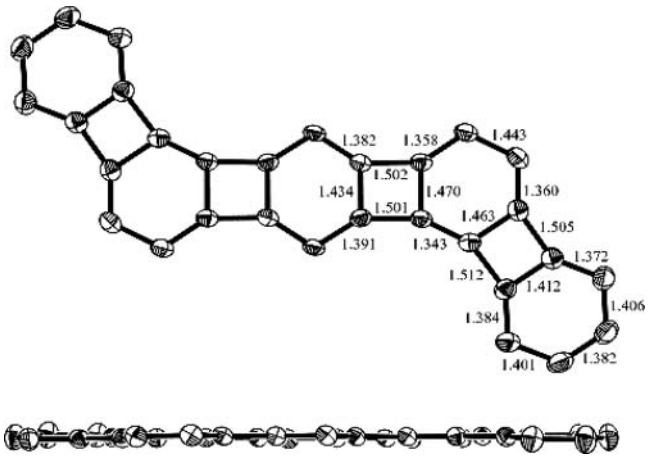


Figure 2. Synchrotron radiation crystal structure of **1a**: views from above (top) and the side (bottom). Bond lengths (Å; standard uncertainties = 0.003). Thermal ellipsoids are shown at 50% probability.

cooling of a sealed solution of dibutyl ether from 190 °C to room temperature) that were amenable to synchrotron diffraction (Figure 2). The crystallographically centrosymmetric molecule exhibits γ-packing[11] and is essentially planar, the dihedral angles between sets of consecutive four carbons along the periphery ranging from 0.2 to 3.5°. Ring C adopts the characteristic bisallylic pattern (average allyl bond length 1.387 Å) present also in **3** (1.392 Å)[3a] and (a silyl derivative of) 9,10-$(SiMe_3)_2$-**5** (1.389 Å).[5] Conversely, ring B exhibits even more bond fixation (66%) than the center of **4** (62%)[12] but the same as in B of silylated **5** (67%). The terminal rings in all systems are almost identically minimally distorted (vide supra). The calculated structure of **1a** (B3LYP/6-31G*) faithfully reproduces the experimentally determined data, with deviations $\Delta_{avg} = 0.008$ Å and $\Delta_{max} = 0.016$ Å. Computed **2a** is essentially identical, suggesting that the details in Figure 2 also apply to this isomer.

Finally, heats of formation calculations of the entire family of [5]phenylenes (see Supporting Information) reveal that **1a** and **2a**, despite the presence of the linear substructure, are not destabilized relative to their all-angular isomers **14**−**16** (Figure 3). We had traced this phenomenon to the opposing effects of the σ- (relatively stabilizing) and π-frames (relatively destabilizing) on the energetics of linear versus angular fusion.[1d] Since NICS (1.0) values are reflective primarily of the properties of the π-system, total NICS (i.e., the sum of all NICS values)[13] should rectify the relative ordering of these isomers. Indeed (Figure 3), such an effect is found, the entire series exhibiting a fairly good linear correlation between ΔH_f and total NICS ($R^2 = 0.9816$).

In summary, the synthesis of the title hydrocarbons constitutes a significant step in the understanding of the influence of topology on the properties of the phenylenes. Efforts continue to make the entire family of [5]phenylenes available for scrutiny in this respect.

(10) Assignments were made on the basis of signal multiplicity, including the simplification of the spectra in **1b** and **2b**, comparison to the NMR spectra of **3**−**5**, and calculated chemical shifts (see Supporting Information).

(11) Desiraju, G. R. *Chem. Commun.* **1997**, 1475.

(12) As defined in: Beckhaus, H.-D.; Faust, R.; Matzger, A. J.; Mohler, D. L.; Rogers, D. W.; Rüchardt, C.; Sawhney, A. K.; Verevkin, S. P.; Vollhardt, K. P. C.; Wolff, S. *J. Am. Chem. Soc.* **2000**, *122*, 7819.

(13) Moran, D.; Stahl, F.; Bettinger, H. F.; Schaefer, H. F., III; Schleyer, P. v. R. *J. Am. Chem. Soc.* **2003**, *125*, 6746.

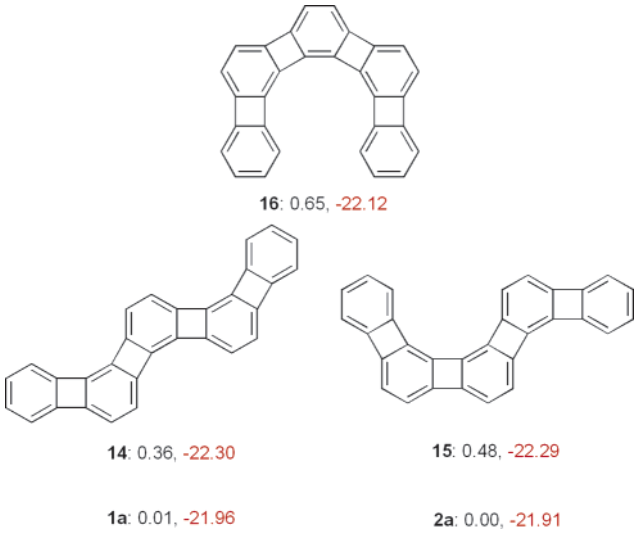


Figure 3. Relative heats of formation (kcal mol^{-1}) and total NICS (red) of **1a**, **2a**, and the all-angular [5]phenylenes **14**−**16**.

Acknowledgment. The NSF (CHE-0071887) funded this work. The Center for New Directions in Organic Synthesis is supported by Bristol-Myers Squibb as a Sponsoring Member and Novartis as a Supporting Member. We are grateful for postdoctoral fellowships to R.D. (NATO) and M.M.H. (NSF), graduate fellowship to A.J.M. (Syntex; ACS Division of Organic Chemistry, sponsored by Rohm and Haas Co.), and a US−Israel BSF grant (No. 2000136). A.S. thanks the VPR fund and the fund for promotion of research at the Technion for financial support.

Supporting Information Available: Computational and experimental procedures, characterization of all new compounds, CIF for **1a**, and XYZ files of calculated phenylenes. This material is available free of charge via the Internet at http://pubs.acs.org.

OL049225V