

Synthesis and structure of polyunsaturated [10]paracyclophane annulated by two azulene rings

Shigeyasu Kuroda,^{a,*} Yuji Obata,^a Nguyen Chung Thanh,^a Ryuta Miyatake,^a Yoshikazu Horino^a and Mitsunori Oda^{b,*}

^aDepartment of Applied Chemistry, Graduate School of Science and Engineering, University of Toyama, Gofuku 3190, Toyama 930-8555, Japan

^bDepartment of Chemistry, Faculty of Science, Shinshu University, Asahi 3-1-1, Matsumoto, Nagano 390-8621, Japan

Received 11 September 2007; revised 10 November 2007; accepted 13 November 2007

Available online 17 November 2007

Abstract—The polyunsaturated [10]cyclophane **4** was synthesized from 1,4-diacetylbenzene by a four-step sequence involving the modified Yasunami azulene synthesis, introduction of two butenone units, and a subsequent McMurry coupling reaction. The crystal structures of **4** and the synthetic intermediate **8** was determined by X-ray crystallographic analysis and the results reveal that (1) the benzene ring of **4** is distorted as a boat form with relatively small bending angles and (2) the azulene rings of **8** show large out-of-plane deformation along the short azulene molecular axis.

© 2007 Elsevier Ltd. All rights reserved.

Unsaturation at the bridging part of cyclophane¹ is a challenging subject in cyclophane chemistry. Recent synthesis of highly unsaturated cyclophanes, such as cyclophynes,² toward carbon-rich aromatics has been extensively studied.³ The polyunsaturation of the bridging part of [10]paracyclophane (**1**), particularly those with a polyvinyl unit,⁴ in context of its molecular distortion, and CH– π and π – π interactions between the bridging part and benzene ring has interested us. DFT calculations⁵ for all-*cis*- and *cis,trans,cis,trans,cis*-pentane, **2** and **3**, predict the following: For **2**, all-*s-cis* structure has not been generated but the *s-cis-trans-trans-cis* structure was obtained. Both **2** and **3** possess a slightly bent benzene ring, and the latter has a slightly lower total energy than the former.⁶ A π – π interaction in **2** and CH– π interaction in **3** is possible; the minimum distance between a bridging carbon and the quaternary benzene carbon in **2** is 3.233 Å, and that between a bridging hydrogen and the quaternary benzene carbon in **3** is 2.478 Å. The C–H bond length (1.082 Å) of the vinyl group with the C–H interaction in **3** is slightly shorter than that of the benzene ring (1.086–1.088 Å)

and the other vinyl part (1.090–1.092 Å). Focusing on **2** or **3** as our ultimate goal to investigate the strain and interactions in detail, we initially studied the synthesis of diazuleno derivative **4** (Fig. 1). We describe the synthesis of polyunsaturated [10]cyclophane **4**, and provide X-ray crystallographic analysis of **4** and the synthetic intermediate **8**.

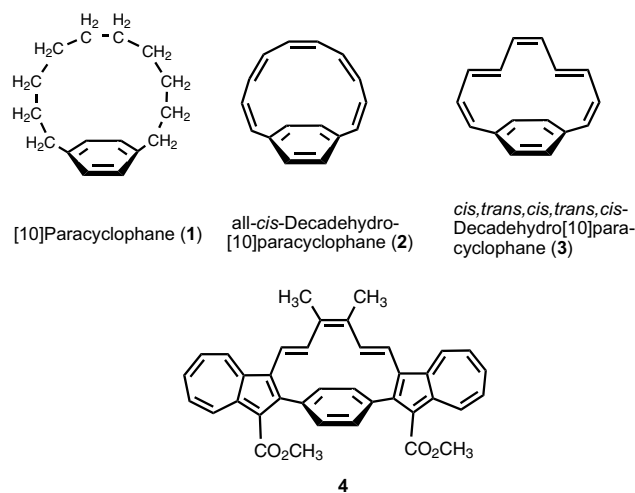
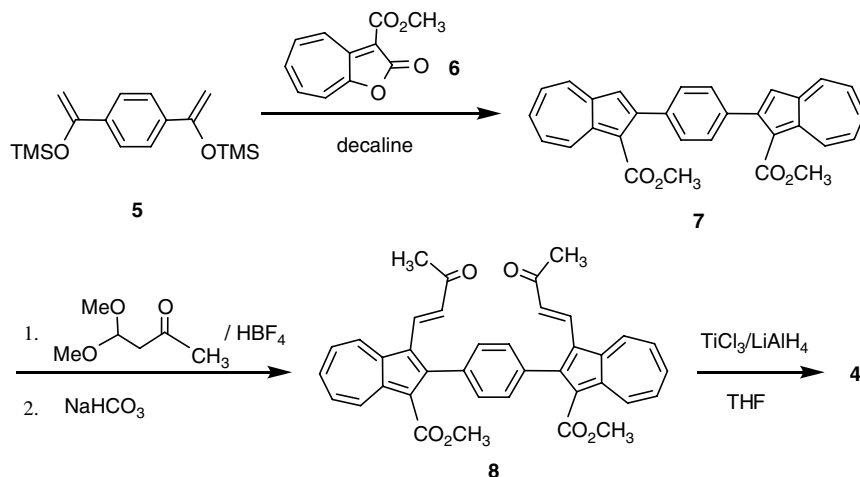


Figure 1. Various [10]paracyclophanes.

Keywords: Cyclophanes; X-ray crystallographic analysis; McMurry coupling; 2*H*-Cyclohepta[*b*]fura-2-one; Azulene.

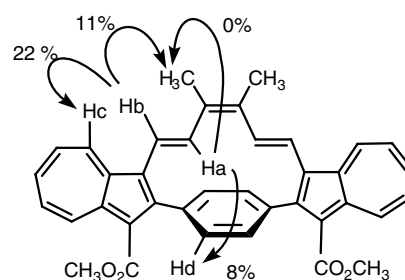
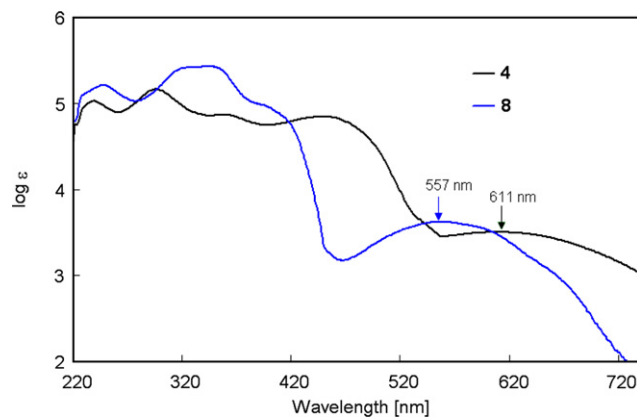
* Corresponding authors. Tel./fax: +81 76 445 6819 (S.K.); tel./fax: +81 263 37 3343 (M.O.); e-mail addresses: kuro@eng.u-toyama.ac.jp; mituoda@shinshu-u.ac.jp

Scheme 1. Synthesis of **4**.

The synthesis of **4** was accomplished as shown in Scheme 1. The azulene skeleton was constructed by the modified Yasunami–Takase azulene synthesis.⁷ Bistrimethylsilyl enol ether **5**⁸ of commercially available 1,4-diacetylbenzene reacts with 3-methoxycarbonyl-2*H*-cyclohepta[*b*]fura-2-one (**6**)⁹ in refluxing decaline for 4 hr to give 1,4-diazulenobenzene derivative **7** in 10% yield.¹⁰ Double elongation of a four-carbon unit in **7** was achieved by electrophilic substitution with 4,4-dimethoxybutan-2-one under acidic conditions and subsequent elimination of methanol under basic conditions,¹¹ to afford **8**, having all required carbons for **4**, in 28% yield. Stereochemistry of the formed C–C double bonds in **8** was confirmed as trans by the vicinal coupling constant in the NMR spectrum. Final intramolecular McMurry coupling¹² of **8** using titanium trichloride and lithium aluminum hydride in refluxing THF provided compound **4** in 20% yield.^{13,14}

Cyclophane **4** was obtained as stable dark green crystals with a relatively high melting point. In the ¹H NMR spectrum of **4** in CDCl₃, the ethenyl protons in the dimethylhexatrienyl bridge appear at 6.62 (H_a in Fig. 1) and 6.92 (H_b) ppm with a coupling constant of 16.0 Hz, which indicates that the stereochemistry around the C–C double bonds attached to the azulene ring remains as trans. Assignment of the ethenyl protons was confirmed by the results of the NOE experiments, as shown in Figure 2. Their chemical shifts were slightly deshielded compared with those of **8**. Since proton chemical shifts of azulene and benzene rings of **4**, **7**, and **8** are similar, they do not interact with each other in these compounds, thus, indicating an interplanar distortion between planes of these rings (vide infra). In the UV–visible spectrum of **4**, the long-wave absorption maximum, corresponding to π–π* excitation of the azulene part, exhibited a bathochromic shift compared with that of **8** because of the extended conjugation of two azulene parts through the hexatriene bridge (Fig. 3).

The crystal structures of **4** and **8** were determined by X-ray diffraction analysis and are shown in Figures 4 and 5. The interplanar angle between the benzene and

Figure 2. Results of NOE experiments of **4**.Figure 3. UV–vis spectra of **4** and **8**.

azulene rings in **4** is 70°. The benzene ring of **8** is nearly planar, while the benzene ring of **4** is non-planar, possessing a shallow boat form as expected. The bond angles of the benzene ring are approximately equal to that estimated for a regular hexagon, and the bond lengths are in the range 1.372–1.409 Å, exhibiting a difference between the right and the left parts (Fig. 6). The bending angles of **4** (Fig. 6) are smaller than those of tetrahydro[2.2]paracyclophane and are comparable to the values of the calculated structures of **2** and **3**.¹⁵ The bond angles and lengths of the azulene part are very

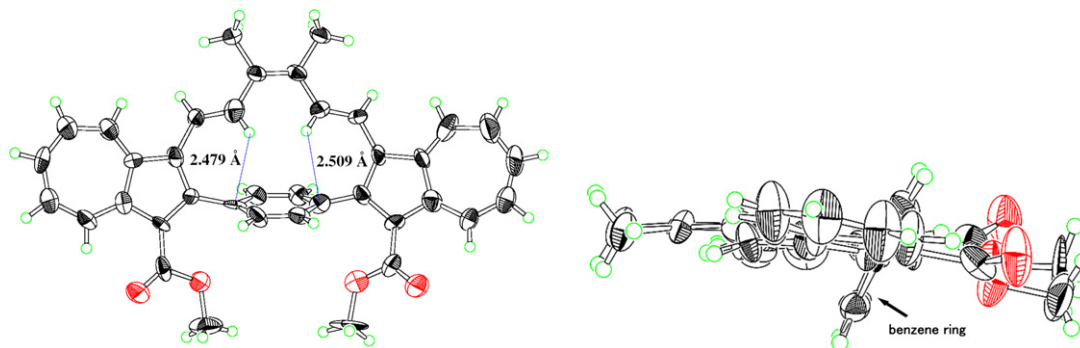


Figure 4. ORTEP drawings of **4**.

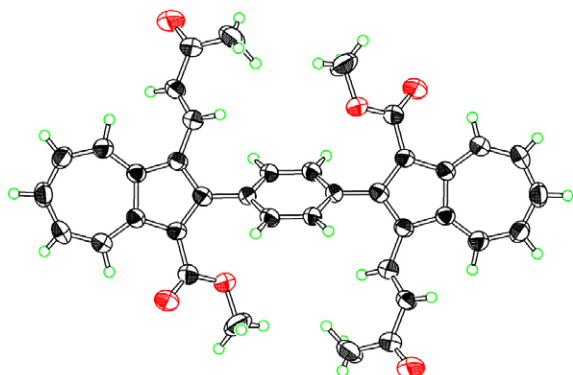


Figure 5. ORTEP drawing of **8**.

similar to those of **8**. The distances between the olefinic H_a protons and the nearest benzene carbon atoms are 2.509 and 2.479 Å, suggesting the possibility of CH– π interaction between them.¹⁶ Note that the latter distance is almost equal to the estimated value for **3** (vide ante).¹⁷ Also note that the azulene ring of **8** exhibits out-of-plane deformation along the short azulene molecular axis. We recently reported such a deformation in 1,3-diarylazulenes **10** and **11**.¹⁸ Twist angles¹⁹ for C1–C3 of **8** are greater than those of **10** and **11** (Table 1, Fig. 7), indicating that **8** has the greatest deformation.

In summary, we constructed the fully unsaturated [10]paracyclophane framework of **3** annulated by two azulene rings by four steps from the commercially available compound. The crystal structure of **4** indicates that the benzene ring has a shallow boat form and suggests the possibility of the CH– π interaction. In addition, it

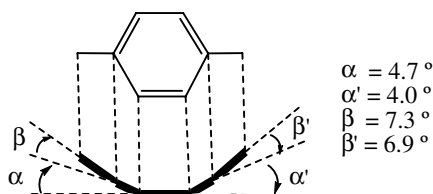
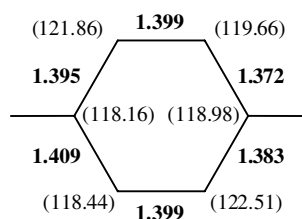


Figure 6. Bond lengths (Å, bold), bond angles (degree, in parentheses) and bending angles of the benzene ring in the crystal structure of **4**.

Table 1. Out-of-plane deformation of crystal structures of **8**, **10**, and **11**, as shown by twist angles

Compound	Twist angles (in degree) for C1–C3		
	C4–C10 ^a	C5–C9 ^a	C6–C8 ^a
8	2.25	9.02	13.30
10 ^b	1.39	4.80	6.56
11 ^b	3.16	7.27	9.69

^a Numbering is shown in Figures 6 and 7.

^b Taken from Ref. 18b.

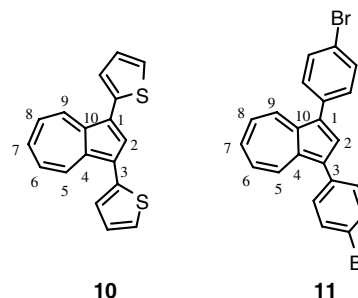


Figure 7. Structures of 1,3-diarylazulenes **10** and **11**.

was found that the crystal structure of the synthetic intermediate **8** showed another example of the azulene ring distortion along its short azulene molecular axis with large twist angles.

Acknowledgment

We thank an undergraduate student, Taihei Kano, at the University of Toyama for his technical assistance.

References and notes

- For books of cyclophanes, see: (a) Diederich, F. *Cyclophanes*; The Royal Society of Chemistry: Cambridge, UK, 1991; (b) Vögtle, F. *Cyclophane Chemistry*, Jones, P.R. (Trans.); John Wiley & Sons, New York, 1993; (c) *Cyclophane Chemistry for the 21st Century*; Takemura, H., Ed.; Research Signpost: Trivandrum, 2002; (d) *Modern Cyclophane Chemistry*; Gleiter, R., Hopf, H., Eds.; Wiley-VCH: Weinheim, 2004.
- Tobe, Y.; Sonoda, M. *Cyclophynes*; 2004, Chapter 1, pp 1–40, in Ref. 1d.
- Carbon-Rich Compounds*; Haley, M. M., Tykwinski, R. R., Eds.; Wiley-VCH: Weinheim, 2006.
- For an elegant generation of unsaturated [4]paracyclophanes, see: (a) Tsuji, T.; Nishida, S. *J. Am. Chem. Soc.* **1989**, *111*, 368–369; (b) Tsuji, T.; Okuyama, M.; Ohkita, M.; Kawai, H.; Suzuki, T. *J. Am. Chem. Soc.* **2003**, *125*, 951–961.
- DFT calculations were conducted at B3LYP/6-31G(d) level of theory by using the MULLIKEN (ver. 2.0.0, IBM Inc.) program.
- Bending angles in the calculated structures of **2** and **3** are as follows: 9.5° for α ($=\alpha'$) and 5.8° for β ($=\beta'$) in **2**, and 8.5° for α ($=\alpha'$) and 4.7° for β ($=\beta'$) in **3**. See Figure 4 for the angles, α and β . Total energies of **2** and **3** are -617.61943983 and -617.62960812 a.u., respectively.
- For the original azulene synthesis from enamines and 2*H*-cyclohepta[*b*]fura-2-ones by Yasunami and Takase, see: Yang, P.-W.; Yasunami, M.; Takase, K. *Tetrahedron Lett.* **1971**, 4275–4278. Yasunami et al. reported that azulenes can be synthesized from silylenol ethers with 2*H*-cyclohepta[*b*]fura-2-ones. The results were presented in the 84th Annual Meeting of Chemical Society; Yasunami, M.; Sato, T.; Watanabe, T. **2004**, p 1409 (3 PC-061).
- (a) Posner, G. H.; Ploypradith, P.; Parker, M. H.; O'Dowd, H.; Woo, S.-H.; Northrop, J.; Krasavin, M.; Dolan, P.; Kensler, T. W.; Xie, S.; Shapiro, T. A. *J. Med. Chem.* **1999**, *42*, 4275–4280; (b) Posner, G. H.; Northrop, J.; Paik, I.-H.; Borstnik, K.; Dolan, P.; Kensler, T. W.; Xie, S.; Shapiro, T. A. *Bioorg. Med. Chem.* **2002**, *10*, 227–232.
- Yang, P.-W.; Lin, L.-C. *Huaxue* **1973**, *1*, 1–6; Fujimori, K.; Fujita, T.; Yamane, K.; Yasunami, M.; Takase, K. *Chem. Lett.* **1983**, *11*, 1721–1724; Nozoe, T.; Wakabayashi, H.; Ishikawa, S.; Wu, C. P.; Yang, P. W. *Heterocycles* **1990**, *31*, 17–22.
- The monoazuleno product was obtained as the primary product in 30% yield. The best obtained yield of **4** is 10%, despite several efforts to improve it under various conditions.
- Hafner, K.; Pelster, H.; Schneider, J. *Liebigs Ann. Chem.* **1961**, *650*, 62–80.
- (a) McMurry, J. E. *Acc. Chem. Res.* **1983**, *16*, 405–411; (b) McMurry, J. E. *Chem. Rev.* **1989**, *89*, 1513–1524; (c) Lenoir, D. *Synthesis* **1989**, 883–897; (d) Furstner, A.; Bogdanovic, B. *Angew. Chem., Int. Ed.* **1996**, *35*, 2443–2469; (e) Furstner, A. *Pure Appl. Chem.* **1998**, *70*, 1071–1076; (f) Furstner, A. In *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 1, pp 449–468; (g) Ladipo, F. T. *Curr. Org. Chem.* **2006**, *10*, 965–980.
- All new compounds were characterized by spectral and combustion analyses. Selected data of new compounds are as follows: *Compound 4*: Dark green prisms, mp = 289–292 °C, $^1\text{H NMR}$ (CDCl_3) δ = 9.58 (d, J = 10.0 Hz, 2H), 8.84 (d, J = 10.0 Hz, 2H), 7.75 (t, J = 10.0 Hz, 2H), 7.50 (t, J = 10.0 Hz, 2H), 7.47 (s, 4H), 7.41 (t, J = 10.0 Hz, 2H), 6.92 (d, J = 16.0 Hz, 2H), 6.62 (d, J = 16.0 Hz, 2H), 3.78 (s, 6H), 2.00 (s, 6H) ppm; $^{13}\text{C NMR}$ (CDCl_3) δ = 166.3, 152.1, 141.7, 139.6, 139.3, 139.2, 137.7, 134.7, 132.4, 131.1, 128.4, 128.3, 126.6, 126.4, 116.5, 115.9, 50.8, 14.6 ppm; IR (KBr) ν_{max} = 1681s, 1390s, 1166s cm^{-1} ; UV (CH_2Cl_2) λ_{max} = 230sh (log ϵ = 4.46), 238 (4.52), 295 (4.66), 320sh (4.46), 357 (4.36), 450 (4.34), 611 (3.00) nm. *Compound 7*: Violet solids, mp = 260–265 °C, $^1\text{H NMR}$ (CDCl_3) δ = 9.42 (d, J = 10.0 Hz, 2H), 8.44 (d, J = 10.0 Hz, 2H), 7.77 (t, J = 10.0 Hz, 2H), 7.68 (s, 4H), 7.55 (t, J = 10.0 Hz, 2H), 7.45 (t, J = 10.0 Hz, 2H), 7.44 (s, 2H), 3.84 (s, 6H) ppm; $^{13}\text{C NMR}$ (CDCl_3) δ = 166.7, 153.1, 142.7, 142.1, 138.3, 137.5, 137.3, 137.2, 129.3, 127.8, 127.0, 119.5, 114.6, 51.0 ppm; IR (KBr) ν_{max} = 1690s, 1449s, 1410s, 1201s cm^{-1} ; UV (CH_2Cl_2) λ_{max} = 233 (log ϵ = 3.46), 238sh (3.44), 256sh (3.32), 280 (3.46), 330 (3.83), 366sh (3.36), 399 (3.36), 543 (3.07), 564sh (3.06), 617sh (2.72) nm. *Compound 8*: Blue solids, mp = 222–226 °C, $^1\text{H NMR}$ (CDCl_3) δ = 9.56 (d, J = 10.0 Hz, 2H), 8.87 (d, J = 10.0 Hz, 2H), 7.95 (d, J = 16.0 Hz, 2H), 7.91 (t, J = 10.0 Hz, 2H), 7.68 (t, J = 10 Hz, 2H), 7.64 (t, J = 10.0 Hz, 2H), 7.48 (s, 4H), 6.52 (d, J = 16 Hz, 2H), 3.79 (s, 6H), 2.32 (s, 6H) ppm; $^{13}\text{C NMR}$ (CDCl_3) δ = 198.3, 166.0, 154.0, 143.1, 141.0, 141.1, 138.4, 136.7, 136.3, 136.2, 129.9, 129.1, 128.9, 128.0, 122.4, 117.5, 51.2, 27.6 ppm; IR (KBr) ν_{max} = 1688s, 1650s, 1438s, 1219s cm^{-1} ; UV (CH_2Cl_2) λ_{max} = 229sh (log ϵ = 4.60), 249 (4.71), 324 (4.91), 344 (4.93), 395sh (4.48), 414sh (4.34), 557 (3.12), 594sh (3.05), 644sh (2.67) nm.
- The X-ray data for **4**: $\text{C}_{38}\text{H}_{30}\text{O}_4$, M_w = 550.65, $0.50 \times 0.30 \times 0.50 \text{ mm}^3$, monoclinic, space group $P2_1/n$ (#14), a = 21.222(2), b = 13.4566(9), c = 10.141(1) Å, β = 89.65(1)°, V = 2895.8(5) Å³, Z = 4, D_{calc} = 1.263 g cm^{-3} , $\mu(\text{Mo-K}\alpha)$ = 0.81 cm^{-1} , 2849 independent reflections, 388 parameters, R = 0.066, wR = 0.087, T = 298 K. Those for **8**: $\text{C}_{38}\text{H}_{30}\text{O}_6$, M_w = 528.65, $0.30 \times 0.30 \times 0.30 \text{ mm}^3$, triclinic, space group $P\bar{1}$ (#2), a = 8.679(1), b = 11.496(1), c = 7.835(1) Å, α = 95.28(1)°, β = 108.56(1)°, γ = 82.80(1)°, V = 734.0(2) Å³, Z = 1, D_{calc} = 1.318 g cm^{-3} , $\mu(\text{Mo-K}\alpha)$ = 0.88 cm^{-1} , 1523 independent reflections, 215 parameters, R = 0.052, wR = 0.066, T = 298 K. Estimated standard deviations for the bond lengths and angles are 0.004–0.007 (ang) and 0.2–0.4 (deg), respectively, for the non-hydrogen atoms. Crystallographic data excluding structures have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 658455 for **4** and CCDC 658456 for **8**, respectively. A copy of the data can be obtained free of charge from CCDC, 12 Union road, Cambridge CB2 1EZ, UK [DIRECT LINE: +44 1223 762910, Fax: +44 (0) 1223-336033 or e-mail: linstead@ccdc.cam.ac.uk; deposit@ccdc.cam.ac.uk].
- Tending angles of the benzene ring in X-ray structure of tetrahydro[2.2]paracyclophane at ambient temperature were 13.7° for α ($=\alpha'$) and 15.2° for β ($=\beta'$): de Meijere, A.; Kozhushkov, S. I.; Rauch, K.; Schill, H.; Verevkin, S. P.; Kümmerlin, M.; Beckhaus, H.-D.; Rüdhardt, C.; Yufit, D. S. *J. Am. Chem. Soc.* **2003**, *125*, 15110–15113. Bending angles in the calculated structures of **2** and **3** are as follows: 9.5° for α ($=\alpha'$) and 5.8° for β ($=\beta'$) in **2**, and 8.5° for α ($=\alpha'$) and 4.7° for β ($=\beta'$) in **3**.
- For non-bonded atomic contacts in cyclophanes, see review: Pascal, R. A., Jr. *Eur. J. Org. Chem.* **2004**, 3763–3771.
- The $^1\text{J}_{\text{C-H}}$ coupling constant of the vinyl C–H whose hydrogen is located inside the hexatriene bridge in **4** is 152.1 Hz, which is comparable to that (156 Hz) of an ethylene molecule. This result conflicts with the short CH– π distance determined from the X-ray structure of **4** and

the calculated short length of the vinyl C–H bond in **3**, indicating that the structure of **4** in the solution and that in the solid state may slightly differ.

18. For deformations of azulenes, see following recent papers and references in there: (a) Yamamura, K.; Kawabata, S.; Kimura, T.; Eda, K.; Hashimoto, M. *J. Org. Chem.* **2005**, *70*, 8902–8906; (b) Ohta, A.; Thanh, N. C.; Terasawa, K.; Fujimori, K.; Kuroda, S.; Oda, M. *Tetrahedron Lett.* **2006**, *47*, 2815–2819.
19. The twist angles were obtained by the way reported in the following reference: Symth, N.; Van Eugen, D.; Pascal, R. A., Jr. *J. Org. Chem.* **1990**, *55*, 1937–1940.