DOI: 10.1002/ejoc.200900297

Dihydroazulene Photoswitches: The First Synthetic Protocol for Functionalizing the Seven-Membered Ring

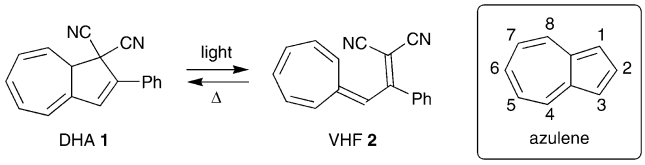
Michael Åxman Petersen,[a] Søren Lindbæk Broman,[a] Anders Kadziola,[a] Kristine Kilså,[a] and Mogens Brøndsted Nielsen*[a]

Keywords: Alkynes / Cross-coupling / Dihydroazulene / Photoswitches / Vinylheptafulvene / Photochemistry

The first synthetic protocol for functionalizing the dihydroazulene (DHA) photoswitch in its seven-membered ring has been developed. This protocol is based on regioselective bromination, followed by regioselective elimination of HBr, and finally a palladium-catalyzed cross-coupling reaction with a terminal alkyne. The position of functionalization (C-7) was confirmed by X-ray crystal structure analysis. Light-induced ring opening of this compound to its vinylheptafulvene (VHF) isomer followed by thermal ring closure provides a mixture of two DHA regioisomers in a ratio that depends on the wavelength of irradiation and solvent polarity.

Introduction

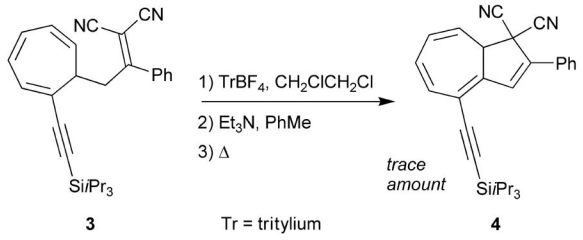
Molecular switches are systems that possess at least two reversibly interconvertible molecular states and are in particular important within the field of molecular electronics.[1] The dihydroazulene/vinylheptafulvene (DHA/VHF) system represents one such switch: DHA undergoes a photochemically induced ring-opening reaction to VHF that in turn undergoes a thermally assisted ring closure back to DHA.[2,3] The pioneering work by Daub and co-workers[2] has allowed ready functionalization of the five-membered ring of DHA by an aryl group and the DHA/VHF system **1/2** (Scheme 1) has been investigated in detail. However, functionalization of the seven-membered ring has not yet been accomplished. For exploitation of the DHA/VHF system as a light-controlled wire for molecular electronics, it is highly desirable to attach two handles to the system, one in each ring, in order to allow it to span two electrodes.



Scheme 1.

Results and Discussion

In an initial approach, we synthesized the DHA precursor **3** (Scheme 2) starting from an alkyne-functionalized tropylium, but otherwise in accordance to the originally developed strategy, involving, however, tedious separation of **3** from other formed regioisomers. Unfortunately, the elimination reaction as presented in Scheme 2 only furnished the DHA **4** in trace amounts, as judged from TLC and mass spectrometric analyses.



Scheme 2.

Instead of forming the DHA in the final step, we turned to a strategy involving conversion of already formed DHA. We have recently reported that bromination of **1** occurs selectively at the 7,8-positions in quantitative yield to provide the dibromide **5** (confirmed by X-ray crystal structure analysis, Figure 1) as a pair of enantiomers.[4] In fact, treatment with two molar equivalents of bromine selectively furnished the tetrabromide **6**, while treatment with three (or more) equivalents furnished the hexabromide **7** as confirmed by X-ray crystal structure analysis (Figure 1). Treating dibromide **5** with ca. 3 molar equivalents of lithium acetylide generated from trimethylsilylacetylene and butyllithium produced the 7-bromo DHA **8**. Highest yields (50–60%) were obtained by adding the base in three subsequent steps. Yields were judged from ^{1}H NMR spectroscopic analysis of the crude reaction mixtures. Isolation of **8** is possible by column chromatography, but is unfortunately

[a] Department of Chemistry, University of Copenhagen, Universitetsparken 5, 2100 Copenhagen Ø, Denmark
E-mail: mbn@kiku.dk

Supporting information for this article is available on the WWW under http://www.eurjoc.org or from the author.

accompanied by substantial decomposition. Both **1** as well as 2-phenylazulene-1-carbonitrile were formed as by-products. Using 1 molar equivalent of the acetylide only provided the product **8** in a yield of ca. 20%. Employing instead 1 molar equivalent of $LiN(SiMe_3)_2$ gave, however, **8** in a yield of >90%. Bases such as pyridine, DBU, Et_3N or Hünig's base were all unable to generate the desired product, while 2.5 molar equivalents of KO*t*Bu (freshly sublimed) furnished **8** in a yield of 40–50%. Using a larger excess of KO*t*Bu (3.6 molar equiv.) generated a mixture of azulenes from which the 7-bromoazulene **9** was isolated pure (9%) (Scheme 3). The X-ray crystal structure of **9** is shown in Figure 1 together with the related 1,3-dicyano-2-phenylazulene, a decomposition product formed from solid **5** upon standing.

Next, we subjected crude DHA **8** to a Sonogashira cross-coupling reaction[5] with triisopropylsilylacetylene. First, **5** was treated with $LiN(SiMe_3)_2$ in THF at room temp. for 2 h to produce **8** (ca. 90%), and a subsequent cross-coupling reaction provided the acetylenic DHA **10**. The overall yield of the conversion of **5** to **10** was 45% after column chromatographic work-up. Single crystals of **10** were grown from pentane and subjected to X-ray crystal structure analysis (Figure 1), confirming the proposed substitution pattern. The structure reveals that the seven-membered ring adopts a boat conformation, in agreement with previously reported structures.[3a] The alkyne unit is in the same plane as C6–C7–C8–C8a, which is twisted by 56.1° relative to the plane defined by C2–C3–C3a–C4–C5. In consequence, the alkyne unit is not in conjugation with the major part of the DHA

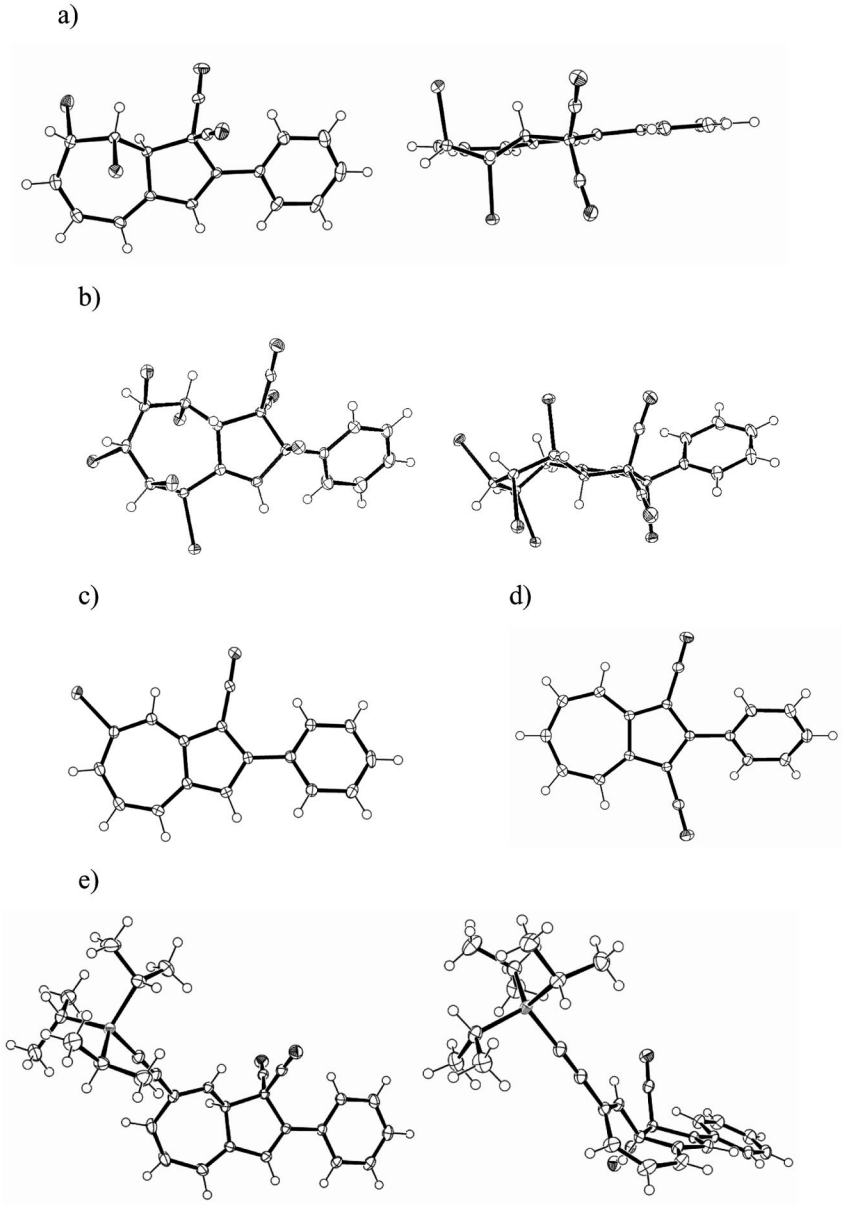
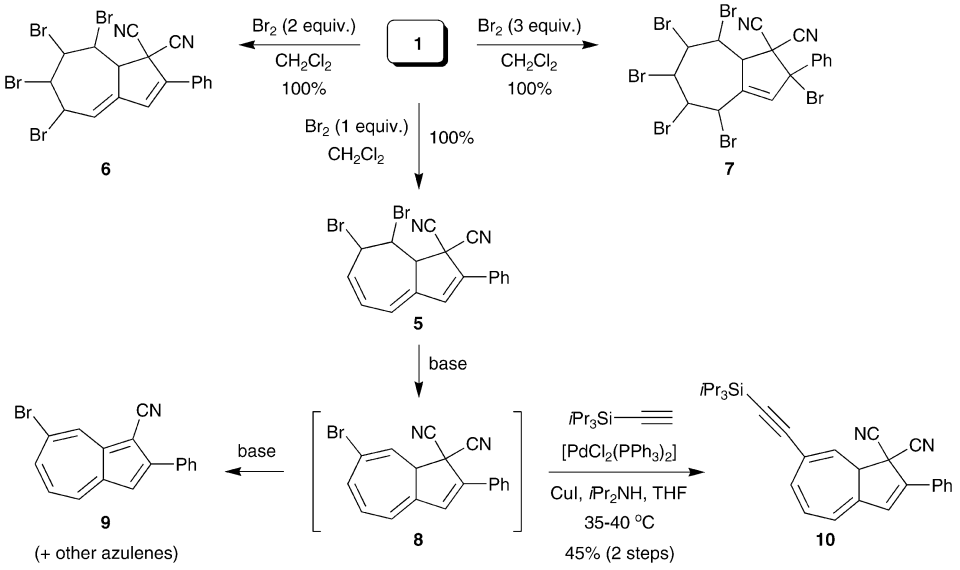


Figure 1. X-ray crystal structures of compounds **5** (a), **7** (b), **9** (c), 2-phenylazulene-1,3-dicarbonitrile (d), and **10** (e).



Scheme 3.

unit, which is nicely reflected in the fact that **10** exhibits a longest-wavelength absorption maximum of 355 nm, which is similar to that of DHA **1**.

The new DHA derivative **10** was subjected to photoswitching studies. Irradiating a sample in MeCN with light of 355 nm resulted in conversion of the DHA unit to a VHF unit exhibiting a characteristic absorption at 477 nm (Figure 2). The conversion was complete within the same time needed to convert DHA **1** into VHF **2** (90 s under the current conditions), which indicates that the quantum yield for converting **10** is similar to that of **1** ($\phi_{DHA-VHF} \approx 0.55$[6]). Thermal VHF–DHA conversion proceeded smoothly, but interestingly, the resulting DHA absorption is red-shifted to 376 nm. An Arrhenius plot provides an activation energy for the thermal back reaction of $E_a = 93.8$ kJ mol^{-1} and an preexponential factor of $A = 4.66 \times 10^{11}$ s^{-1}, while those of **2** were previously reported to $E_a = 84.9$ kJ mol^{-1} and $A = 3.0 \times 10^{10}$ s^{-1}.[6] By extrapolation, the rate constant and half-life at 25 °C are found to $k = 1.7 \times 10^{-5}$ s^{-1} and $t_{1/2} = 670$ min, while the values for **2** are $k = 7.0 \times 10^{-5}$ s^{-1} and $t_{1/2} = 165$ min.[6] Thus, the presence of the ethynyl group slows down the back reaction relative to that of **2**. The red-shifted DHA absorption indicates that a new DHA is formed. We therefore performed the photolysis and thermal reactions in CD_3CN and analyzed the products by ^{1}H NMR spectroscopy. It transpires that the two regioisomeric VHFs **11** and **12** (Scheme 4) are formed during photolysis of **10** as judged by two sets of *i*Pr$_3$ resonances and overlapping resonances in the aromatic region. These two VHFs are thermally converted into DHAs **10** and **13** in a ratio of 1:2. The two DHAs are readily distuingished by ^{1}H NMR spectroscopy, and a COSY spectrum confirmed substitution at the C-6 position of **13**. Repeated ring-opening/closure cycles do not change the ratio between the regioisomers. The absorption maximum of **13** is estimated to ca. 381 nm by subtracting the absorption spectrum of **10** from that of the mixture of **10** and **13**. This red-shifted absorption is readily explained by the fact that moving the alkyne unit to the 6-position renders it part of the larger conjugated system of the boat-shaped DHA. The different absorption characteristics open up for control of the ratio of the regioisomers simply by changing the wavelength of irradiation. Thus, by irradiation with 430-nm light, it is possible to change the ratio of regioisomers (**10**/**13**) to ca. 5.5:4.5 (after three cycles). In principle, repeated cycles should ultimately change the ratio completely in favor of **10**. The isomerization reaction is strongly solvent dependent. Thus, subjecting **10** to irradiation/heat cycles in cyclohexane does not result in formation of **13** but regeneration of **10** itself.

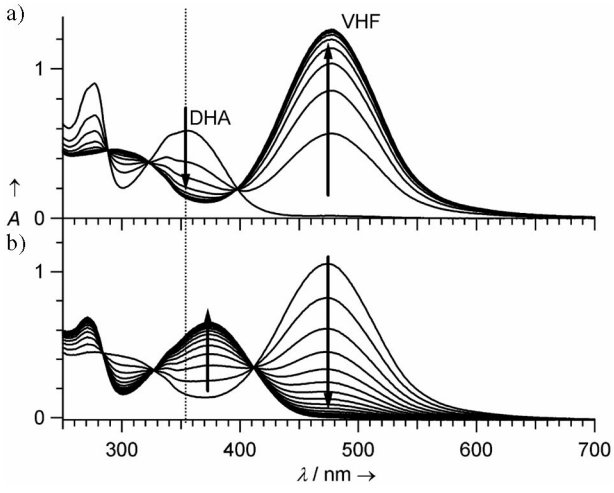
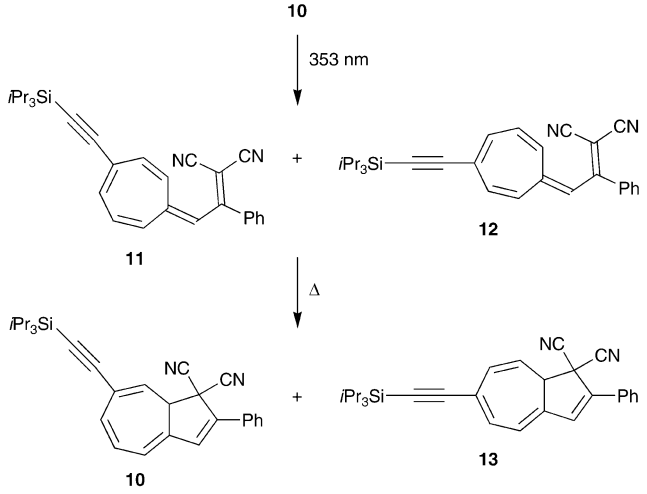


Figure 2. a) Irradiation of compound **10** in MeCN (3.0 mL, 3.6×10^{-5} M) with light (353 nm) 0–90 s, 10-s steps. b) Thermal back-reaction monitored at 70 °C, 2-min steps. The DHA absorption red-shifts after one cycle.

In conclusion, we have developed the first procedure for functionalizing dihydroazulenes in the seven-membered ring. The reaction proceeds regioselectively to provide the 7-substituted DHA, but this compound can be converted



Scheme 4.

partly to the 6-substituted isomer by irradiation followed by thermal ring closure in the polar solvent acetonitrile. As the two regioisomers exhibit different absorption maxima, their ratio can be controlled by the wavelength of irradiation. Isomerization can, however, be completely avoided by using a nonpolar solvent. Access to DHA derivatives functionalized in both the five- and seven-membered rings is important for the future exploitation of the DHA/VHF switch in for example molecular electronics devices.

Experimental Section

2-Phenyl-7-[(triisopropylsilyl)ethynyl]-1,8a-dihydroazulene-1,1-dicarbonitrile (10): Dibromide **5** (416 mg, 1.00 mmol) was dissolved in dry THF (20 mL) at 0 °C. Lithium bis(trimethylsilyl)amide (1.00 mL, 1.00 mmol, 1 M in toluene) was added dropwise, and the solution was stirred for 2 h, while the temperature was slowly raised to room temperature. The reaction mixture was diluted with Et_2O (100 mL) and then washed with saturated aqueous NH_4Cl (2×100 mL). The organic phase was dried with $MgSO_4$, filtered, and the solvents evaporated in vacuo yielding a black solid containing the bromide **8** plus minor by-products (according to NMR analysis). [**8**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.74 (m, 2 H), 7.48 (m, 3 H), 6.89 (s, 1 H), 6.52 (m, 2 H), 6.30 (m, 1 H), 6.13 (dd, J = 4.4, 0.9 Hz, 1 H), 3.80 (dd, J = 4.4, 1.8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.6, 141.1, 132.9, 132.3, 131.8, 130.7, 131.1, 129.5, 126.6, 120.3, 120.2, 120.0, 114.8, 112.6, 51.2, 44.8 ppm.] The crude batch of **8** was redissolved in dry, argon-degassed THF (10 mL). Then $[PdCl_2(PPh_3)_2]$ (70.19 mg, 0.10 mmol) and CuI (3.81 mg, 0.02 mmol) were added under argon, followed by iPr$_2$NH (0.3 mL) and (triisopropylsilyl)acetylene (0.5 mL, 2.2 mmol). The reaction mixture was stirred at 35–40 °C for 5 h, whereupon it was diluted with Et_2O (100 mL) and washed with saturated aqueous NH_4Cl (2×100 mL). The organic phase was dried with $MgSO_4$, filtered, and the solvents evaporated in vacuo. Purification by column chromatography (SiO_2, 40% CH_2Cl_2/heptane) yielded **10** (196 mg, 45%) as a yellow to green solid. Crystals were grown from pentane. M.p. 126–127 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.72–7.76 (m, 2 H), 7.44–7.51 (m, 3 H), 6.88 (s, 1 H), 6.51–6.63 (m, 2 H), 6.31 (d, J = 5.9 Hz, 1 H), 6.16 (d, J = 4.6 Hz, 1 H), 3.80 (dd, J = 4.6, 1.5 Hz, 1 H), 1.09 (s, 21 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.3, 140.3, 132.7, 131.5, 130.5, 129.5, 126.6, 124.9, 123.3, 120.7, 115.1, 112.7, 105.3, 91.5, 51.0, 45.0, 18.9, 11.5 ppm; two overlapping signals. $C_{29}H_{32}N_2Si$ (436.67): calcd. C 79.77, H 7.39, N 6.42; found C 79.66, H 7.49, N 6.33. HR-MS (ES): m/z = 437.2385 [MH$^+$]. $C_{29}H_{33}N_2Si$: m/z = 437.2413.

CCDC-718205 (for **7**), 718204 (for 2-phenylazulene-1,3-dicarbonitrile), 718206 (for **9**), 718207 (for **10**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see also the footnote on the first page of this article): NMR spectra of **3**, **10**, and **13**; spectral evolution upon irradiation of **10** in comparison to **1**; detailed photolysis experiments on **10**; frontier orbitals of **10**–**13** devoid of silyl substituents.

Acknowledgments

The Danish Research Agency is gratefully acknowledged for supporting this work (272-08-0540).

[1] a) V. Balzani, M. Gómez-López, J. F. Stoddart, *Acc. Chem. Res.* **1998**, *31*, 405–414; b) *Molecular Switches* (Ed.: B. L. Feringa), Wiley-VCH, Weinheim, Germany, **2001**; c) H. Tian, S. J. Yang, *Chem. Soc. Rev.* **2004**, *33*, 85–97.

[2] a) J. Daub, T. Knöchel, A. Mannschreck, *Angew. Chem.* **1984**, *96*, 980–981; *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 960–961; b) J. Daub, S. Gierisch, U. Klement, T. Knöchel, G. Maas, U. Seitz, *Chem. Ber.* **1986**, *119*, 2631–2646; c) S. Gierisch, J. Daub, *Chem. Ber.* **1989**, *122*, 69–75; d) S. Gierisch, W. Bauer, T. Burgemeister, J. Daub, *Chem. Ber.* **1989**, *122*, 2341–2349; e) J. Daub, S. Gierisch, J. Salbeck, *Tetrahedron Lett.* **1990**, *31*, 3113–3116; f) J. Achatz, C. Fischer, J. Salbeck, J. Daub, *J. Chem. Soc., Chem. Commun.* **1991**, 504–507; g) H. Spreitzer, J. Daub, *Chem. Eur. J.* **1996**, *2*, 1150–1158.

[3] a) M. Å. Petersen, L. Zhu, S. H. Jensen, A. S. Andersson, A. Kadziola, K. Kilså, M. B. Nielsen, *Adv. Funct. Mater.* **2007**, *17*, 797–804; b) M. Å. Petersen, A. S. Andersson, K. Kilså, M. B. Nielsen, *Eur. J. Org. Chem.* **2009**, 1855–1858.

[4] M. Å. Petersen, K. Kilså, A. Kadziola, M. B. Nielsen, *Eur. J. Org. Chem.* **2007**, 1415–1418.

[5] K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, *16*, 4467–4470.

[6] H. Görner, C. Fischer, S. Gierisch, J. Daub, *J. Phys. Chem.* **1993**, *97*, 4110–4117.

Received: March 19, 2009
Published Online: April 29, 2009

