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A Bis(heptafulvenyl)-dicyanoethylene Thermoswitch with Two Sites for Ring Closure

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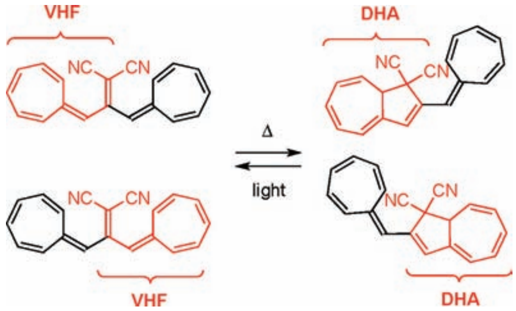
ABSTRACT



Suitably functionalized vinylheptafulvenes (VHFs) act as thermoswitches undergoing ring closure to the corresponding dihydroazulenes (DHAs). Here we present the synthesis of a new such thermoswitch incorporating two heptafulvene rings on a dicyanoethylene unit. The synthetic protocol explores both the tropylium species as an electrophile and as a leaving group in the generation of the heptafulvene units. The thermally induced ring closure was enhanced as a result of two accessible sites for the reaction to occur.

Molecular switches have attracted considerable interest in recent years as entities for molecular electronics, supramolecular chemistry, and biotechnology.[1] 1,8*a*-Dihydroazulene-1,1-dicarbonitrile (DHA) is a photochromic compound that undergoes a light-induced ring-opening reaction to form a vinylheptafulvene (VHF), which in turn undergoes a thermally induced conversion to DHA (Scheme 1).[2] We have recently observed that this event is accompanied by conductance switching in a single-molecule junction, which points toward further exploration of the system in molecular electronics.[3] In solution, the switching is accompanied by a color change from yellow (DHA) to red (VHF). The VHF is formed as an s-*cis* conformer that is in equilibrium with an s-*trans* conformer. The thermal conversion of the s-*cis* VHF conformer to DHA is finely tuned by substituent groups at the system; for example it is promoted by an electron-donating group at one end of the molecule and an electron-withdrawing group at the other.[4] Another way of

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[1] (a) Balzani, V.; Gómez-López, M.; Stoddart, J. F. *Acc. Chem. Res.* **1998**, *31*, 405. (b) *Chem. Rev.* **2000**, *100* (issue 5). (c) *Molecular Switches*; Feringa, B. L., Ed.; Wiley-VCH: Weinheim, Germany, 2001. (d) Areephog, J.; Browne, W. R.; Katsonis, N.; Feringa, B. L. *Chem. Commun.* **2006**, 3920. (e) Weibel, N.; Grunder, S.; Mayor, M. *Org. Biomol. Chem.* **2007**, *5*, 2343. (f) Matsuda, K.; Yamaguchi, H.; Sakano, T.; Ikeda, M.; Tanifuji, N.; Irie, M. *J. Phys. Chem. C* **2008**, *112*, 17005. (g) Banghart, M. R.; Mourot, A.; Fortin, D. L.; Yao, J. Z.; Kramer, R. H.; Trauner, D. *Angew. Chem., Int. Ed.* **2009**, *48*, 9097. (h) Berg, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 3218.

[2] (a) Daub, J.; Knöchel, T.; Mannschreck, A. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 960. (b) Nielsen, M. B.; Broman, S. L.; Petersen, M. Å.; Andersson, A. S.; Jensen, T. S.; Kilså, K.; Kadziola, A. *Pure Appl. Chem.* **2010**, *82*, 843 and references cited therein.

[3] Lara-Avila, S.; Danilov, A. V.; Kubatkin, S. E.; Broman, S. L.; Parker, C. R.; Nielsen, M. B. *J. Phys. Chem. C* **2011**, *115*, 18372.

[4] (a) Görner, H.; Fischer, C.; Gierisch, S.; Daub, J. *J. Phys. Chem.* **1993**, *97*, 4110. (b) Broman, S. L.; Petersen, M. Å.; Tortzen, C. G.; Kadziola, A.; Kilså, K.; Nielsen, M. B. *J. Am. Chem. Soc.* **2010**, *132*, 9165.

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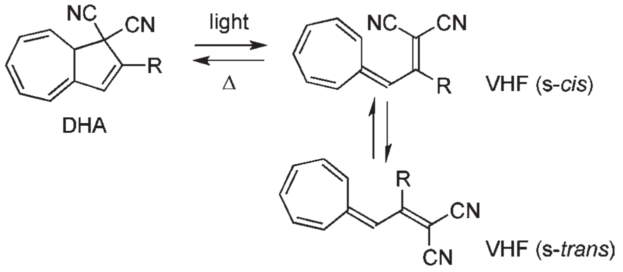
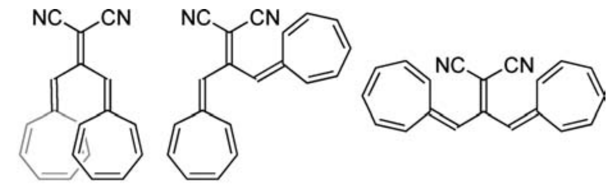
promoting the ring closure has been to lock the VHF in its reactive s-*cis* conformation by fusing the five-membered ring to another ring.[5]

Scheme 1. Dihydroazulene (DHA)/Vinylheptafulvene (VHF) Photo-/Thermoswitch



In the quest for thermoswitches that can respond quickly to a temperature variation by a color change, we became interested in enhancing the thermally induced conversion of VHF to DHA in another manner. We reasoned that if the dicyanoethylene unit is functionalized by two heptafulvenyl groups as in compound **1** (Figure 1), then two of the three possible conformations would be reactive for the ring-closure reaction (s-*cis*/s-*cis* and s-*trans*/s-*cis*).



1 (s-*trans*/s-*trans*) **1** (s-*trans*/s-*cis*) **1** (s-*cis*/s-*cis*)

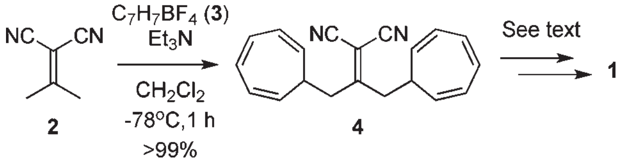
Figure 1. Structures of possible VHF conformations.

DFT calculations (B3LYP/6-311++G(2d,p)//B3LYP/6-31+G(d)) using the Gaussian03 program package[6] reveal that the s-*trans*/s-*trans* and s-*cis*/s-*trans* conformations of **1** are of equal energy (corrected for zero-point energy), while the s-*cis*/s-*cis* conformation is slightly more energetic (+4.3 kcal mol^{-1}). The fulvene rings are rotated relative to the ethylene unit by 34.5° in s-*trans*/s-*trans*-**1**, by 17.5° and 41.1° in s-*trans*/s-*cis*-**1**, and by 44.1° in s-*cis*/s-*cis*-**1** (Figure 2). Here we present the synthesis of this system and the kinetics for its thermal ring-closure reaction.

Our first synthetic approach starts from the known malononitrile derivative **2**[7] (Scheme 2), which is readily prepared by a Knoevenagel condensation between malononitrile and acetone in the presence of basic alumina (see Supporting Information). This compound **2** was treated with 2 mol equiv of tropylium tetrafluoroborate **3** in the presence of triethylamine to furnish the product **4**.[8] This product can be purified by either dry column vacuum chromatography or crystallization from CH_2Cl_2/heptanes, but the latter protocol provided a more stable compound for storage.[9] The structure of **4** was confirmed by X-ray crystallography (Figure 3).

Figure 2. Geometry-optimized structures (B3LYP/6-31+G(d)) of s-*trans*/s-*trans*-**1** (left), s-*trans*/s-*cis*-**1** (middle), and s-*cis*/s-*cis*-**1** (right) of relative energies 0, 0, and 4.3 kcal mol^{-1} (B3LYP/6-311++G(2d,p)).

Scheme 2. Synthesis of **4**



The subsequent oxidation step to provide the VHF **1** proved more difficult (Scheme 2). Hydride abstraction by tritylium tetrafluoroborate (Ph_3CBF_4) followed by proton abstraction by Et_3N or pyridine gave a mixture of the desired product **1** together with the monooxidized compound (**5**, one heptafulvene unit) in poor yield (< 5% isolated along with starting material). Oxidation of **4** with DDQ in boiling toluene only gave **5** in low yield (< 5% isolated). Other oxidizing agents such as chloroanil and $NOBF_4$ were not rewarding either. It should be noted that any thermally induced conversion of the intermediate VHF **5** to its corresponding DHA in the presence of

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(5) Gierisch, S.; Daub, J. *Chem. Ber.* **1989**, *122*, 69.

(6) Frisch, M. J. et al. . *Gaussian 03*, revision B.03; Gaussian, Inc.: Wallingford, CT, 2004.

(7) Texier-Boullet, F.; Foucand, A. *Tetrahedron Lett.* **1982**, *23*, 4927.

(8) **2-[1,3-Di(cyclohepta-2,4,6-trienyl)propan-2-ylidene]malononitrile (4).** Compounds **2** (1.09 g, 10.3 mmol) and **3** (4.40 g, 24.7 mmol) were suspended in CH_2Cl_2 (100 mL) by sonication under an argon atmosphere. The mixture was cooled to −78 °C, whereupon Et_3N (3.5 mL, 25 mmol) was added dropwise via a canula and the mixture was stirred for 1 h. It was then diluted with Et_2O (100 mL), washed with brine (2 × 50 mL), dried with $MgSO_4$, filtered, and concentrated in vacuo, affording **4** (3.54 g, > 99%) as a brown oil. An analytically pure sample was obtained by recrystallization from CH_2Cl_2/heptanes as colorless needles. TLC ($CHCl_3$/heptanes 4:1): $R_f = 0.45$. Mp 74.5−75.0 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 6.67 (t, $J = 3.2$ Hz, 4H), 6.21 (dt, $J = 9.0, 3.2$ Hz, 4H), 5.15 (dd, $J = 9.0, 6.1$ Hz, 4H), 2.81 (d, $J = 8.0$ Hz, 4H), 2.14−2.02 (m, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 181.3, 131.4, 126.5, 122.9, 112.0, 88.8, 37.7, 37.1 ppm. HR-MS (ESP+): m/z 309.1359 [MNa^+], calcd for $C_{20}H_{18}N_2Na$: 309.1368. Calcd for $C_{20}H_{18}N_2$: C, 83.88; H, 6.34; N, 9.78. Found: C, 83.83; H, 6.32; N, 9.76%.

(9) The recrystallization was, however, not always easy to perform as the product tended to form an oil.

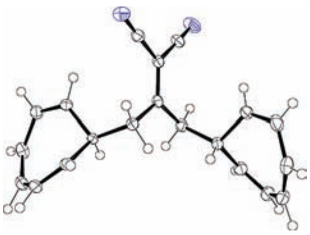
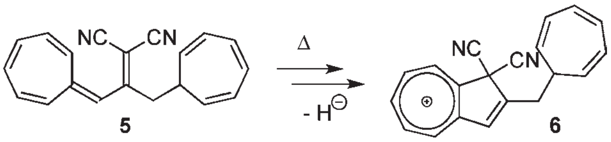


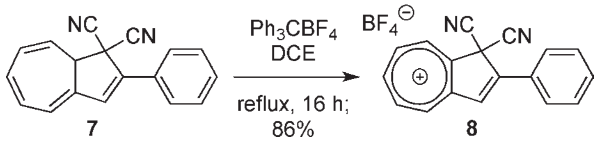
Figure 3. Molecular structure of **4** with displacement ellipsoids at 50% probability for non-H atoms (crystals grown from CH_2Cl_2/heptanes).

Ph_3CBF_4 poses a problem as the DHA unit would be prone to hydride abstraction, forming the tropylium species **6** (Scheme 3). Indeed, treating the known DHA **7**[4,5] with Ph_3CBF_4 in refluxing 1,2-dichloroethane (DCE) furnished the azulenium salt **8**[10] in good yield (Scheme 4).

Scheme 3. Possible Side Reaction



Scheme 4. Synthesis of an Azulenium Tetrafluoroborate by Hydride Abstraction from DHA



The structure of the salt **8** was confirmed by X-ray crystallography (Figure 4), revealing a completely planar fused ring system. We are currently exploring the reaction between this compound and different nucleophiles as it would offer a new convenient method for functionalizing the DHA system in the seven-membered ring.

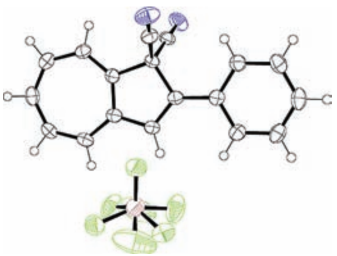
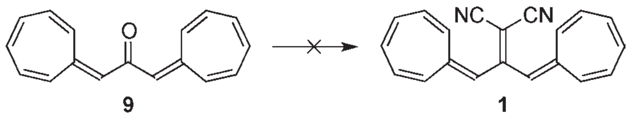


Figure 4. Molecular structure of **8** with displacement ellipsoids at 50% probability for non-H atoms (crystals grown from MeCN). The BF_4^- anion is modeled as disordered over two orientations.

Because of the unreliable oxidations of **4**, we decided to postpone the Knoevenagel condensation to the last step (Scheme 5). First, the 8,8′-diheptafulvenyl ketone **9** was prepared according to a previously reported route[11] from 1,3-bis(cycloheptatrienyl)acetone.[12] Unfortunately, however, a condensation with malononitrile did not provide the desired VHF **1**, but only decomposition.

Scheme 5. Another Attempt of Preparing Compound **1**



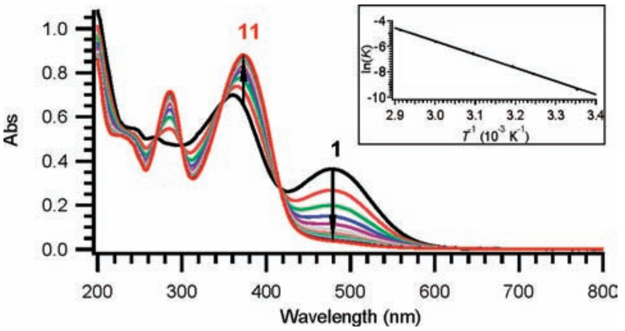


Figure 5. Thermal ring closure of **1** (black wave) to **11** (red wave) followed by UV–vis absorption spectroscopy at 25 °C in MeCN. Inset: Arrhenius plot for the ring closure; [*k*] = s^{-1}.

As it has been shown by Mrozek and Daub[13] that the tropylium cation can act as a leaving group, to generate

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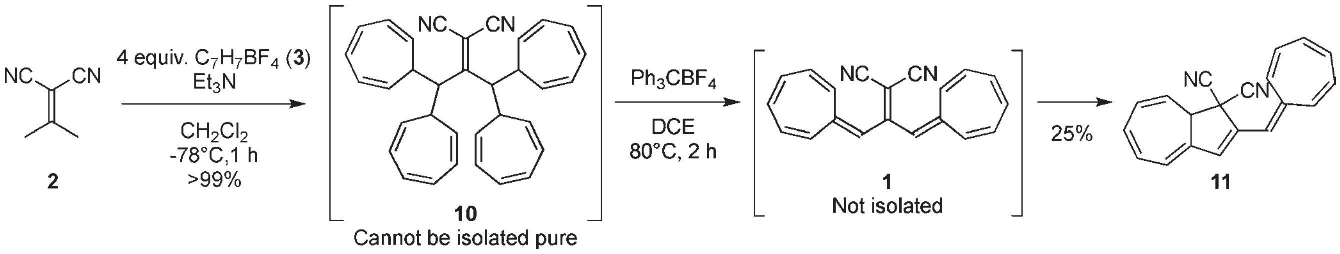
[10] **1,1-Dicyano-2-phenyl-1,8a-dihydroazulenium tetrafluoroborate (8).** A mixture of DHA **7** (3.68 g, 14.35 mmol) and Ph_3CBF_4 (5.07 g, 15.35 mmol) in DCE (100 mL) was refluxed overnight, while keeping the mixture shielded from light. The mixture was allowed to reach rt, and then dry Et_2O (150 mL) was added. The precipitate was filtered and washed with dry Et_2O, providing the product **8** as a light-brown powder (4.23 g, 86%). ^1H NMR (300 MHz, CD_3CN): δ 9.44 (dd, J = 8.9, 1.5 Hz, 1H), 9.18–9.09 (m, 2H), 9.08–8.97 (m, 2H), 8.29 (s, 1H), 8.23–8.16 (m, 2H), 7.86–7.73 (m, 3H) ppm. ^{13}C NMR (75 MHz, CD_3CN): δ 170.9, 157.6, 157.5, 155.5, 153.6, 153.1, 148.0, 147.7, 136.8, 135.7, 131.4, 129.8, 128.6, 110.4, 46.2 ppm. MS (FAB): m/z 255 $[M - BF_4]^+$. Calcd for $C_{18}H_{11}BF_4N_2$: C, 63.18; H, 3.24; N, 8.19. Found: C, 63.04; H, 3.00; N, 8.14%.

[11] Yagihara, M.; Kitahara, Y. *Chem. Lett.* **1972**, 653.

[12] Details are included in the Supporting Information.

[13] Mrozek, T. Ph.D. Thesis (Supervisor: Daub, J.), University of Regensburg, Germany, 2000.

Scheme 6. Successful Synthesis of **1**, Which after Thermal Ring Closure, Was Isolated as **11**



the VHF in a similar system, we decided to functionalize compound **2** with four cycloheptatrienyl units in order to explore this property in the final elimination steps (Scheme 6). Gratifyingly, a reaction between **2** and 4 molar equiv of tropylium tetrafluoroborate in the presence of Et_3N gave **10** in quantitative yield with no purification needed other than aqueous workup. This compound was then refluxed with 2 molar equiv of tritylium tetrafluoroborate in DCE, which ultimately generated DHA **11** via the VHF **1** as an intermediate. By a line of careful purifications by dry column vacuum chromatography, followed by a crystallization from heptanes, DHA **11**[14] was finally obtained in pure form. The rather low yield reflects the difficult purification.

DHA **11** exhibits an absorption maximum at 375 nm in MeCN (Figure 5), which is red-shifted by ca. 20 nm relative to that of DHA **7** owing to the extended conjugation in **11**. With this DHA in hand, we were able to study the thermoswitch properties of the corresponding VHF **1**. First, a sample of DHA **11** in MeCN was quantitatively ring-opened by light (375 nm) to provide **1** (Figure 5). This compound exhibits an absorption at λ_{max} 483 nm. The ring closure of **1** was then followed at 25 °C (Figure 5), and from the exponential decay (first-order kinetics) of the VHF absorption at λ_{max} 483 nm, the rate constant k for ring closure was found to be $9.64 \times 10^{-5}\ s^{-1}$ and the half-life $t_{1/2}$ to be 120 min. In line with the rationale behind the design, $t_{1/2}$ is reduced by almost a factor of 2 relative to that obtained previously at 25 °C for the VHF of DHA **7**.

An Arrhenius plot based on the rate constants obtained at six different temperatures is shown in Figure 5 (inset), from which we obtain an activation energy for the ring closure of **1** of 87.0 ± 0.7 kJ mol^{-1} and a preexponential factor of $1.71 \times 10^{11}\ s^{-1}$.

In summary, a new VHF thermoswitch **1** with two sites available for ring closure was prepared from a suitable precursor by subsequent hydride and tropylium removals, while procedures based on subsequent hydride and proton removals were unsuccessful. The two heptafulvene groups in the product result in an enhanced rate of thermal ring closure in comparison to a related VHF, due to the higher chance of accessing a reactive s-*cis* conformation for this thermoswitch. Future work will focus on enhancing the properties further by incorporating different functional groups in the two seven-membered rings. In addition, we have shown that the tropylium ring is readily obtained by hydride abstraction from DHA, furnishing a compound that may be used as an electrophilic species for further reactions.

Acknowledgment. Support from The Danish Council for Independent Research | Natural Sciences (#10-082088) is gratefully acknowledged.

Supporting Information Available. Experimental procedures, X-ray crystallographic data, and spectroscopic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) **2-(Cyclohepta-2,4,6-trienylidenemethyl)-1,8a-dihydroazulenedicarbonitrile (11)**. To a solution of **2** (0.57 g, 5.40 mmol) in CH_2Cl_2 (125 mL), compound **3** (4.61 g, 25.9 mmol) was added and the temperature was lowered to −78 °C. NEt_3 (3.5 mL, 25 mmol) was added dropwise over 1 h, and the mixture was stirred for 4 h while the temperature was allowed to slowly reach rt. The mixture was diluted with Et_2O (100 mL), then washed with brine (2 × 100 mL), dried with $MgSO_4$, filtered, and concentrated in vacuo. The resulting dark yellow oil (compound **10**) was redissolved in DCE (200 mL), and Ph_3CBF_4 (4.27 g, 13.0 mmol) was added. The mixture was stirred at 80 °C for 4 h, then washed with brine (2 × 100 mL), dried with $MgSO_4$, filtered, and concentrated in vacuo. Dry column vacuum chromatography (SiO_2, 12.6 cm^2, 0−100% toluene/heptanes, 10% steps, 40 mL fractions) followed by recrystallization from boiling heptanes gave **11** (381 mg, 25%) as a yellow solid. Mp 118.2−120.6 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, J = 7.5 Hz, 2H), 7.41−7.37 (m, 2H), 7.36−7.31 (m, 1H), 7.17 (d, J = 16.6 Hz, 1H), 6.94 (d, J = 16.6 Hz, 1H), 6.56 (dd, J = 11.2, 6.2 Hz, 1H), 6.52 (s, 1H), 6.46 (dd, J = 11.2, 6.2 Hz, 1H), 6.34−6.27 (m, 2H), 5.83 (dd, J = 10.1, 3.7 Hz, 1H), 3.73 (dt, J = 3.7, 1.9 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.4, 138.9, 135.8, 135.0, 134.6, 131.1, 131.1, 129.4, 129.0, 127.8, 127.3, 121.0, 119.4, 119.3, 115.0, 112.6, 50.9, 43.9 ppm (two signals missing due to overlap). Calcd for $C_{20}H_{14}N_2$: C, 85.08; H, 5.00; N, 9.92. Found: C, 84.90; H, 4.96; N, 9.87%.