Optimized synthesis and detailed NMR spectroscopic characterization of the 1,8a-dihydroazulene-1,1-dicarbonitrile photoswitch

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Abstract

An economical and effective protocol for large scale synthesis of the 2-phenyl-1,8a-dihydroazulene-1,1-dicarbonitrile (DHA) photoswitch has been developed. This compound is ring-opened by light to a vinylheptafulvene (VHF), which is thermally closed back to DHA. This compound serves as an important starting material for dihydroazulene photoswitches incorporating a substituent in the seven-membered ring and as a reference compound for comparison of properties. A detailed NMR spectroscopic characterization has allowed the assignment of all proton and carbon signals. In addition, the compound was characterized by X-ray crystallography. A correlation between the rate constant for thermal ring-closure of VHF to DHA and empirical parameters of solvent polarity (E_T30) was established.

Keywords: Dihydroazulene, photoswitch, solvent polarity, thermoswitch, vinylheptafulvene

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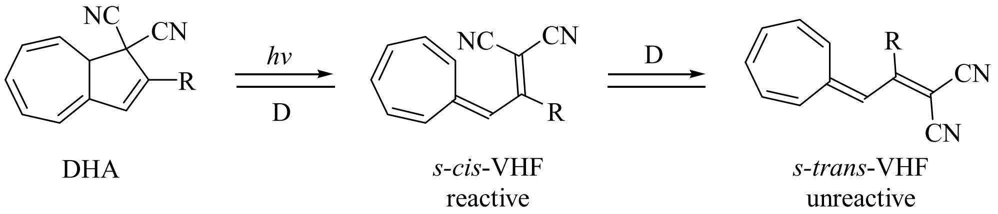
Introduction

Molecular switches possess at least two reversible interconvertible states.[1] A photochromic switch is a system where at least one of the conversions is light-induced.[2] These systems are particularly interesting within the fields of molecular electronics, materials science, supramolecular chemistry, and biotechnology.[3] Systems such as the azobenzene[4] and the dithienylethene[5] show great potential as future building blocks within molecular electronics. We have become interested in the dihydroazulene/vinylheptafulvene system (Scheme 1).[6] DHA undergoes a light-induced ring-opening reaction to VHF that in turn undergoes a thermal ring-closure back to DHA.



Scheme 1. Dihydroazulene / vinylheptafulvene photo/thermoswitch.

A wide variety of derivatives has been synthesized, incorporating both electron-withdrawing and –donating groups in the five-membered ring[7] and very recently also in the seven-membered ring.[8] To exploit the DHA/VHF system in molecular electronics a handle in both the seven-membered and the five-membered ring is needed. We reported in 2009 a procedure for incorporating a bromine atom selectively at C-7 (Figure 1) of the seven-membered ring of the DHA.[8a] This functionality was next employed for incorporation of an arylethynyl group at C-7 by a Sonogashira cross-coupling reaction.[8b] Studies on electron-donating and –withdrawing aryl substituents have shed light on the mechanism for the ring-closure reaction.[8b] Thus, the first step of ring-closure involves a change of conformation from an unreactive *s-trans* to a reactive *s-cis* conformation (Scheme 1) and the ring-closure goes through a zwitterionic transition state or intermediate.[8] The kinetics of the ring-closure was shown to follow a Hammett correlation when plotting ln(*k*) against σ_p^+ (Hammett constant including through-conjugation).[8b] The most advanced systems actually provide the possibility to control the switching abilities by the redox-state of the substituent,[9] or by the pH of the solution.[8b]

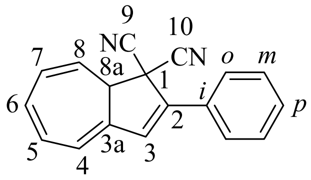
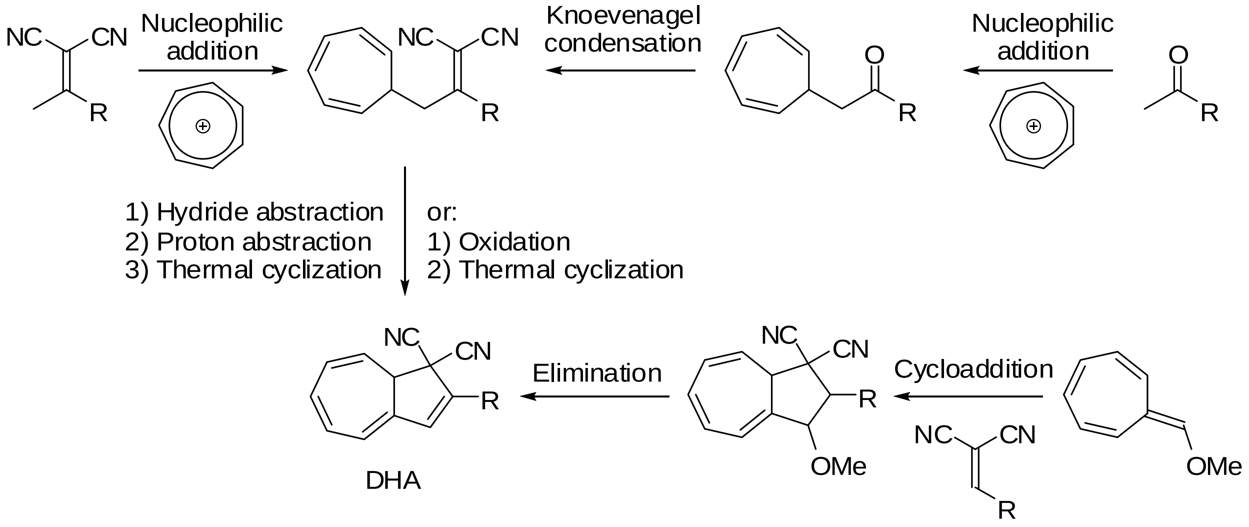


Figure 1. Numbering of the DHA.

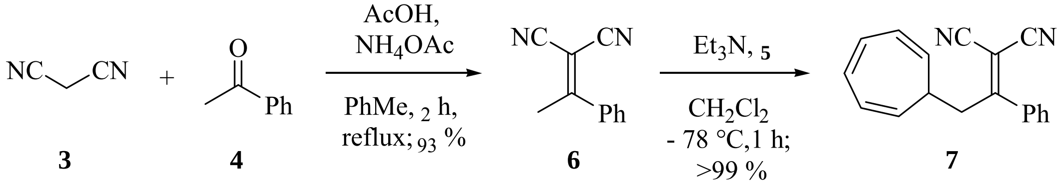
The DHA photoswitch has been much less studied than the two aforementioned systems. This is most likely due to the lack, until recently, of a protocol for functionalizing the system in both the five- and seven-membered rings. Moreover, access to DHA in large scale is a prerequisite for its wider applicability in advanced systems. 2-Phenyl-1,8a-dihydroazulene-1,1-dicarbonitrile **1** was one of the first photochromic DHAs to be reported by Daub and coworkers.[10] Different synthetic protocols for obtaining DHAs were developed. One protocol involves a [8+2] cycloaddition between 8-methoxyheptafulvene and a derivative of 1,1-dicyanoethylene, followed by elimination of methanol (Scheme 2).[10] In this route the DHA is formed directly in the final elimination step. In another route, the VHF precursor was first prepared.[11] The first step was here an acid-catalyzed nucleophilic addition of an acetophenone derivative to tropylium tetrafluoroborate. A Knoevenagel condensation with malononitrile, followed by hydride and proton abstractions, or by oxidation with DDQ or chloroanil,[11] provided the corresponding VHF that was then thermally converted to DHA. This protocol however had some limitations, for synthesis of multigram quantities.[12] A convenient modification was developed by Gobbi *et al.*[12] by performing the Knoevenagel condensation between the acetophenone derivative and malononitrile already in the first step. A subsequent nucleophilic addition under alkaline conditions to the tropylium ion followed by hydride and proton abstractions then generated the VHF, the immediate precursor for the DHA. This method was used to prepare 2-(4'-iodophenyl)-1,8a-dihydroazulene-1,1-dicarbonitrile **2** in a ca. 5-g scale (DHA with R = 4-iodophenyl in Scheme 2). We have optimized this procedure for large scale synthesis (ca. 15 g) of the simple 2-phenyl-1,8a-dihydroazulene-1,1-dicarbonitrile **1** (DHA with R = phenyl in Scheme 2), which is the starting material for our regioselective functionalization of DHA.[8] In addition, its detailed characterization by both 2D-NMR spectroscopy and X-ray crystallography will be presented. Moreover, we have looked in more detail on the thermal conversion of VHF and the possibility for establishing a correlation with empirical solvent polarity parameters.



Scheme 2. Existing routes to 2-substituted DHAs.

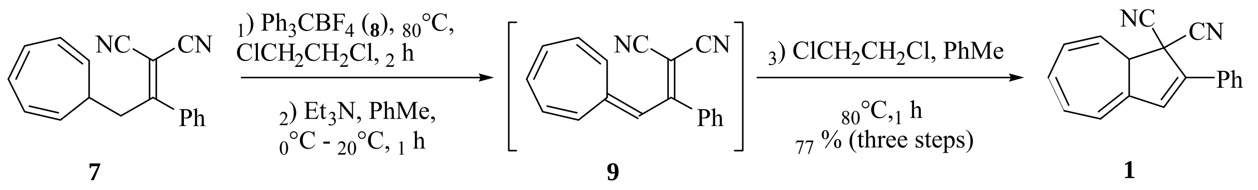
Results and Discussion

An optimization of the original cycloaddtion – elimination route was deliberately avoided. The first step of this procedure is an oxidation of cyclooctatetraene by either $Hg(OAc)_2$[13] or by electrolysis[14] (not shown in Scheme 2); one is toxic and the other inconvenient. Instead the first objective was to optimize the synthesis of the precursor for the VHF using the simple starting materials malononitrile **3**, acetophenone **4**, and tropylium tetrafluoroborate **5**. It was found that the order of Knoevenagel and nucleophilic addition reactions was important. Thus, it was advantageous to prepare the crotononitrile derivative **6** before **7** (Scheme 3) since the latter is not stable under the required reaction conditions of the Knoevenagel condensation. On the other hand a Knoevenagel condensation between **3** and **4** in the presence of AcOH and NH_4OAc gave **6** in high yield (Scheme 3). When following the analogous procedure of Gobbi *et al.*,[12] using three molar equivalents NH_4OAc in AcOH added in portions, the condensation can be accomplished in 3-4 days by reflux in toluene in a flask equipped with a Dean-Stark trap. We found that by adding the whole amount at once and heating the reaction mixture, the reaction time is reduced to only 2 hours and the yield is greatly improved, because of a much easier purification with almost no loss of material. A simple washing procedure gave the product in a yield of 98% on a 25-g scale. This product can be used directly in the next step, while recrystallization from heptanes gave a final yield of 93%. The resulting crotononitrile **6** was then treated with tropylium tetrafluoroborate **5** in the presence of a small excess of Et_3N in CH_2Cl_2 at –78 °C which gave the VHF precursor **7** in a quantitative yield. Higher temperature (–20 °C) resulted in unidentified by-products. The amount of solvent was reduced to only 1 L for 12.6 g (75 mmol) of the crotononitrile, but could not be further reduced as the tropylium tetrafluoroborate reactant is only poorly soluble in CH_2Cl_2. Tropylium tetrafluoroborate **5** was prepared by treating freshly distilled cycloheptatriene with tritylium tetrafluoroborate **8** using a slightly modified procedure of Dauben and coworkers.[15]



Scheme 3. Synthesis of crotononitrile derivative.

The final steps leading to DHA **1** are shown in Scheme 4. Compound **7** was oxidized in two steps. Thus, hydride abstraction with tritylium tetrafluoroborate followed by elimination with Et_3N gave the VHF **9**. Heating this compound in the dark for 1 hour at 80 ^{o}C promoted ring-closure to furnish the DHA **1** as a pair of enantiomers. The synthesis can be done in large scale (15 g) and does not require purification before the last step. While optimizing and scaling up the synthesis, the total amount of solvents used for the three steps was reduced from 2.2 L to only 750 mL, and by using this convenient protocol the product (ca. 15 g) can be purified using dry column chromatography.[16] This chromatographic work-up can be done with less than 2-L of technical solvents and a subsequent recrystallization from either heptanes or ethanol (96 %) makes it overall an economical and efficient purification.



Scheme 4. Optimized synthesis of DHA **1**.

The crystalline product is very stable and can be stored at ambient conditions for years with no need to exclude it from light. It can be kept in solution, in the dark, for months without decomposition. The compound can also be sublimed without decomposition.

The structure of crotononitrile derivative **7** was solved by 2D-NMR spectroscopy and X-ray crystallography (Figure 2).

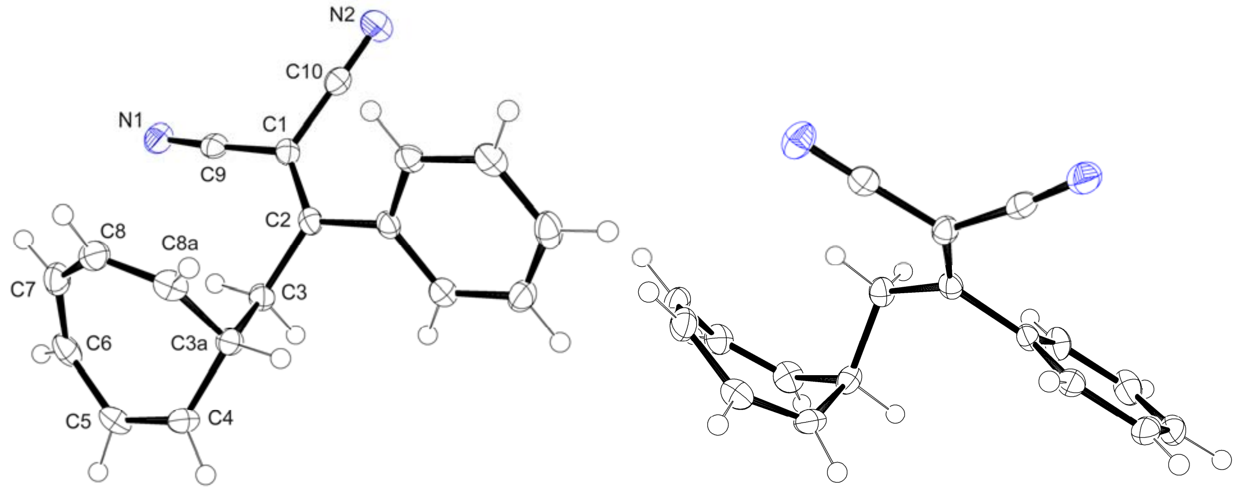


Figure 2. X-Ray crystal structure of **7** (crystals grown from heptanes). The atoms labeled C1-C8a correspond to the C1-C8a atoms in DHA (see Figure 1); for convenience this same numbering was chosen. CCDC 792112.

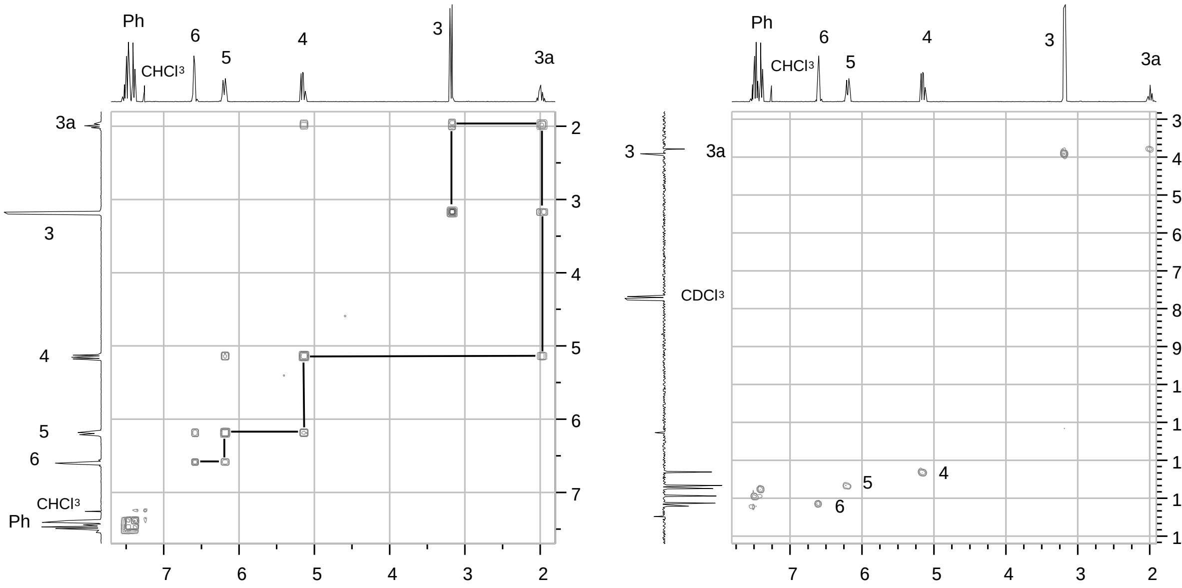


Figure 3. COSY- (left) and ^{1}H / ^{13}C HMQC-NMR (right) spectra of 2-(cyclohepta-2,4,6-trienyl-1-phenylethyliden)malononitrile **7** recorded in $CDCl_3$. Same numbering as used in crystal structure.

^{1}H-, ^{13}C-, COSY-, ^{1}H / ^{13}C HMQC- and ^{1}H / ^{13}C HMBC-NMR analyses were obtained for **7** at a 300-MHz instrument. Selected spectra are shown in Figure 3 (atom labeling of signals is that of the crystal structure, corresponding to that of DHA).

Acquiring a clean NMR-spectrum of the VHF in $CDCl_3$ is difficult, because of the relatively fast back-reaction in the polar solvent causing DHA reformation. Thus the NMR characterization of VHF **9** was performed in C_6D_6, in which the back-reaction is much slower. A relatively dilute sample of VHF was prepared by irradiating DHA in C_6D_6 at ambient temperature and ^{1}H, COSY, ^{13}C, ^{1}H / ^{13}C HSQC, NOESY1D, and TOCSY1D-NMR spectra were acquired. The HSQC-spectrum is shown in Figure 4.

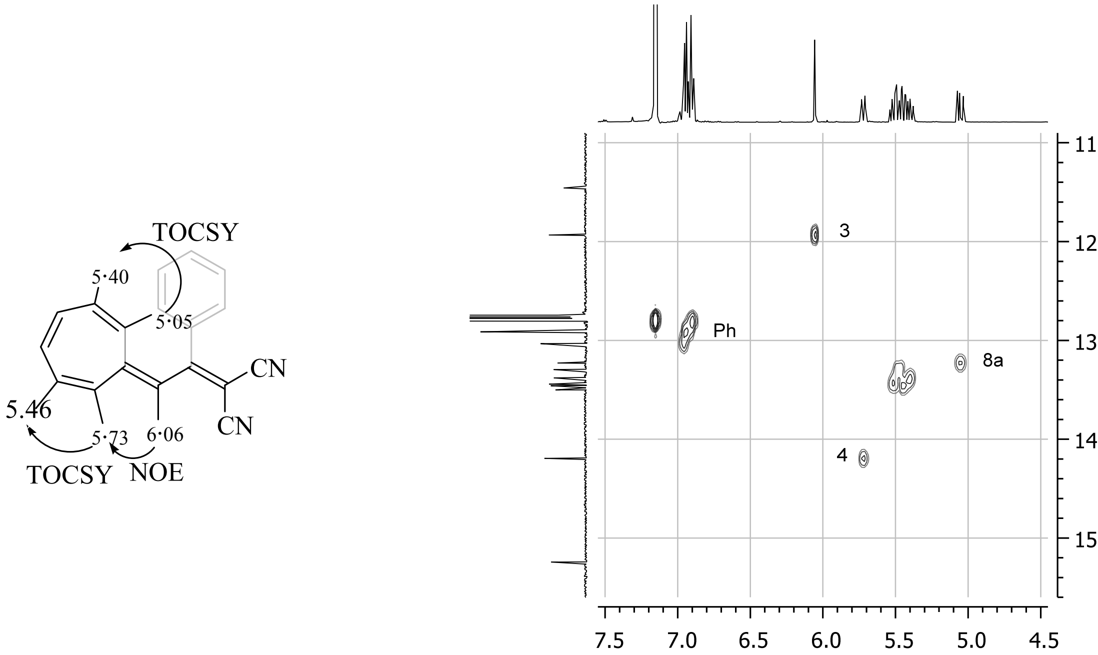


Figure 4. Coupling pattern and ^{1}H / ^{13}C HMQC-NMR spectrum of VHF **9** recorded in C_6D_6. Numbering according to DHA numbering. Assignment of signals can be found in the experimental section.

Because of overlapping signals, the proton signals could not be unambiguously assigned by COSY-NMR. But an NOE was seen between a singlet (assigned to H3) and a doublet (assigned to H4). By TOCSY1D H5, H8, and H8a were assigned as shown in Figure 4 (left).

The structure of the DHA **1** was solved by 2D-NMR spectroscopy and X-ray crystallography. The seven-membered ring adopts a boat form where the C7-C8 double bond is twisted out of the plane (Figure 5), which is characteristic for DHAs. This conformation explains the similar absorption spectra, previously observed, for DHAs incorporating a substituent at position C-7.[8]

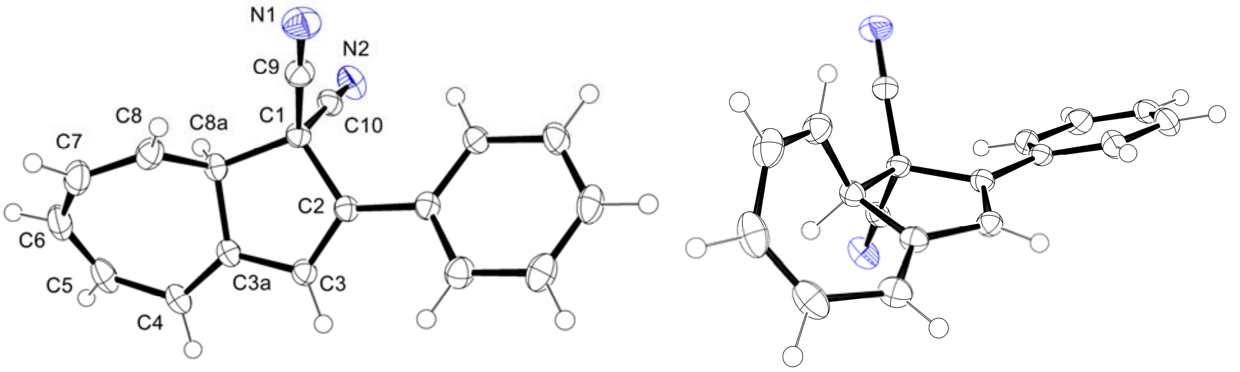


Figure 5. X-Ray crystal structure of 2-phenyl-1,8a-dihydroazulene-1,1-dicarbonitrile **1** (crystals grown from chloroform/ heptanes). CCDC 792113.

It remains a challenge when synthesizing new functionalized DHAs to unambiguously prove in which position a group is attached in the seven-membered ring. For this reason, we subjected DHA **1** to a detailed NMR analysis (^{1}H-, ^{13}C-, COSY-, ^{1}H / ^{13}C HMQC- and ^{1}H / ^{13}C HMBC-NMR, Figure 6) in order to assign all of the signals in the spectrum of this parent DHA as listed in Table 1.

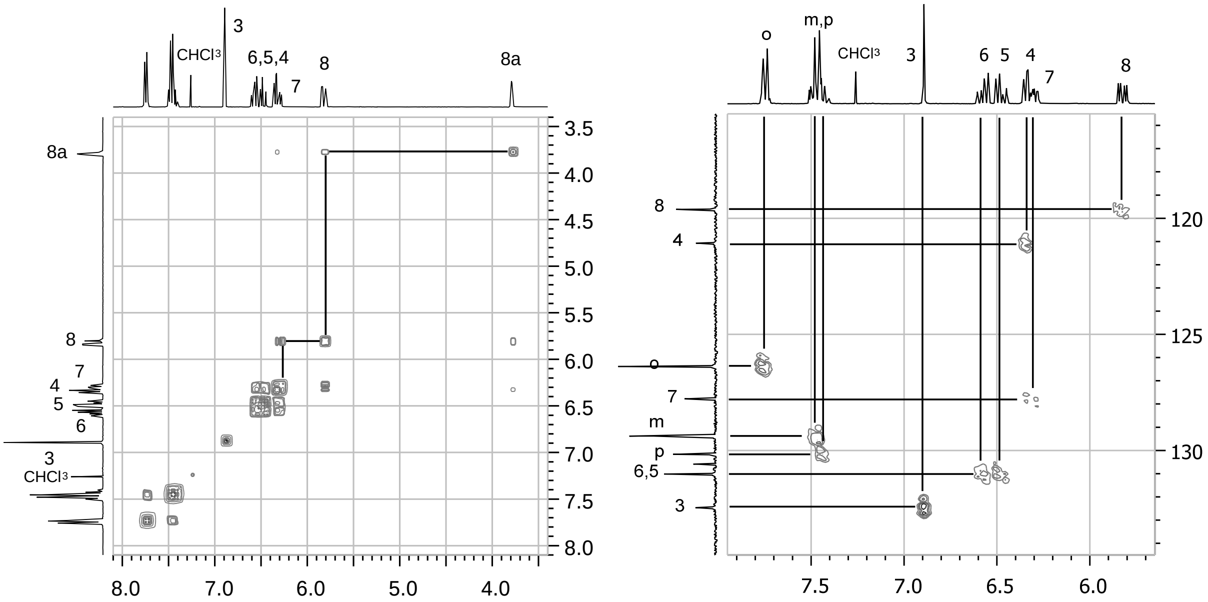


Figure 6. COSY- (left) and ^{1}H / ^{13}C HMQC-NMR (right) spectra of 2-phenyl-1,8a-dihydroazulene-1,1-dicarbonitrile **1** recorded in $CDCl_3$.

Table 1. Assigned signals (chemical shifts in ppm) in both ^{1}H- (300 MHz) and ^{13}C-NMR (75 MHz) in $CDCl_3$

	1	2	3	3a	4	5	6	7
δ_C	45.4	140.3[a]	132.5	130.6	121.1	131.0[b]	131.0[b]	127.8
δ_H	-	-	6.89	-	6.34	6.48	6.58	6.31
	8	8a	*I*	*o*	*m*	*P*	CN	CN
δ_C	119.6	51.3	138.8[a]	126.4	129.4	130.2	115.3	112.9
δ_H	5.82	3.79	-	7.7	7.5	7.4	-	-

[a]Assigned by ^{1}H / ^{13}C HMBC. [b]The signals for C5 and C6 are overlapping, but are clearly discernible in a 125-MHz spectrum.

The simple DHA **1** and its corresponding VHF are conveniently used as reference compounds when comparing the rate constant for the thermal back-reaction of newly synthesized DHA/VHFs. For this reason the back-reaction of the VHF of **1** was restudied in our lab to make sure that the already reported values[7] are compatible under our precise conditions. A solution of DHA **1** was irradiated at its absorption maximum and according to UV-Vis and NMR the compound was completely converted to VHF **9**. Heating the sample resulted in a clean conversion back to DHA and the thermal back-reaction was followed by UV-Vis and NMR using a kinetics program. The absorption spectra of DHA and VHF and the thermal back-reaction in acetonitrile are shown in Figure 7.

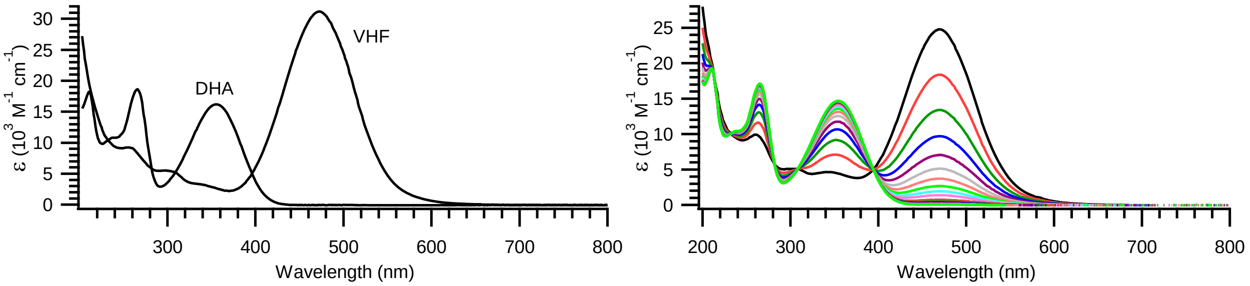


Figure 7. Absorption spectra of DHA **1** and its corresponding VHF **9** in MeCN (left). Absorption spectra for the thermal ring-closure (VHF→DHA) measured every minute at 60 °C in MeCN (right).

The rate constant at 25 °C was generally calculated by extrapolation from an Arrhenius plot or directly measured and for a series of solvents the activation energy and the pre-exponential factor was calculated using the Arrhenius equation. The data are collected in Table 2. In accordance to Daub's findings,[7] the back-reaction was faster in polar solvents than in non-polar solvents. In fact we found that the rate constant of the back-reaction was 12 times larger in the polar solvent EtOH than in the non-polar solvent cyclohexane. As shown in Figure 8 a linear trend was observed when plotting $\ln(k_{25°C})$ against the $E_T(30)$ value[17] of the solvent. This trend supports a mechanism via a zwitterionic structure as suggested previously by Daub and co-workers.[18] Interestingly, the activation energy is only affected to a small degree by the solvent polarity (Table 2), which is, however, somewhat in disagreement with previously reported data.[7] Instead, our data show that it is mainly the pre-exponential factor that causes the variation in the rate constant (*i.e.*, an entropy effect). Thus, in a polar solvent there are smaller entropy constraints for the proper reaction geometry (more successful encounters). This is likely explained by the fact that electrostatic attraction between opposite charges in a zwitterionic structure (already promoted to some degree in the ground state by a polar solvent) results in some degree of preorganization (ion-pairing) for intramolecular cyclization.

Table 2. Absorption maxima for DHA **1** and its corresponding VHF **9**, and kinetic data for the thermal back-reaction in different solvents. Where E_a and A are left out, the rate constant was only measured at 25 °C

Solvent	λ_{DHA} (nm)	λ_{VHF} (nm)	$k_{25°C}$ (s^{-1})	$t_{½\ 25°C}$ (min)	E_a (kJ/mol)	A (s^{-1})	φ^a	$E_T(30)^b$ (kcal/mol)
EtOH	354	471	$5.72 \times 10^{-5\ c)}$	202	95.5 ± 0.2	$3.05 \cdot 10^{12}$	0.5	51.9
MeCN	353	470	$5.36 \times 10^{-5\ c)}$	218	91.8 ± 0.2	$6.35 \cdot 10^{11}$	0.55	45.6
CH_2Cl_2	357	475	$2.12 \times 10^{-5\ c)}$	545	-	-	-	40.7
EtOAc	355	463	$1.28 \times 10^{-5\ c)}$	903	94.2 ± 0.1	$4.13 \cdot 10^{11}$	-	38.1
THF	357	467	$9.8 \pm 0.3 \times 10^{-6}$	1096	-	-	-	37.4
Et_2O	354	456	-	-	-	-	-	-
Toluene	360	464	$7.8 \pm 0.04 \times 10^{-6}$	1474	93.2 ± 0.5	$1.65 \cdot 10^{11}$	0.6	33.9
c-hexane	354	446	$4.95 \pm 0.03 \times 10^{-6}$	2333	92.1 ± 0.5	$6.65 \cdot 10^{10}$	-	30.9

[a]Quantum yields of light-induced ring-opening taken from Ref. 7. [b]Ref. 17. [b]Uncertainty less than ± 0.004.

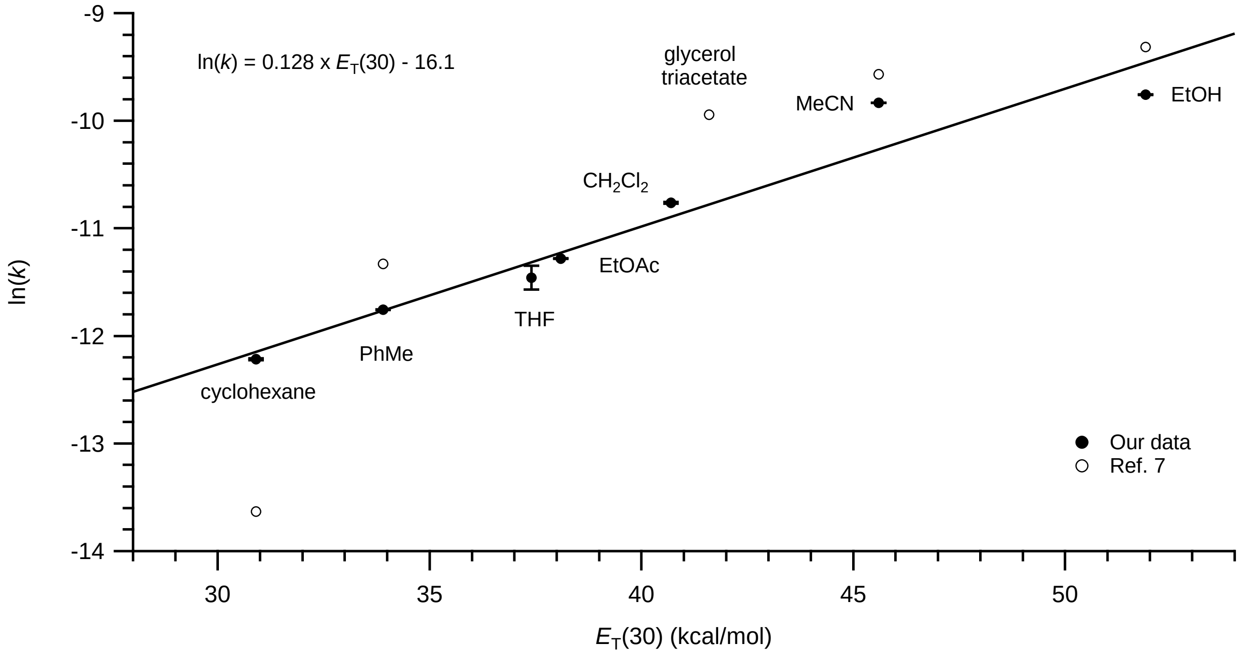


Figure 8. Rate constant dependency on solvent polarity; ln($k_{25°C}$) plotted against $E_T(30)$. The best straight line describing our data is inserted (*i.e.*, data from Ref. 7 are not included).

Another experiment was conducted by following the VHF conversion by ^{1}H-NMR spectroscopy. By plotting the change in the relative integral of a specific VHF-signal against time, the rate constant was measured in CD_3CN. At 25°C, this rate constant ($k_{25°C} = 5.39 \times 10^{-5}\ s^{-1}$) was almost identical to that measured by UV-Vis spectroscopy ($k_{25°C} = 5.36 \times 10^{-5}\ s^{-1}$). The rate constant was also measured in C_6D_6 at 40°C and the NMR-spectra are showed in Figure 9. A series of other control experiments were conducted, and a selection of these is explained in the experimental section.

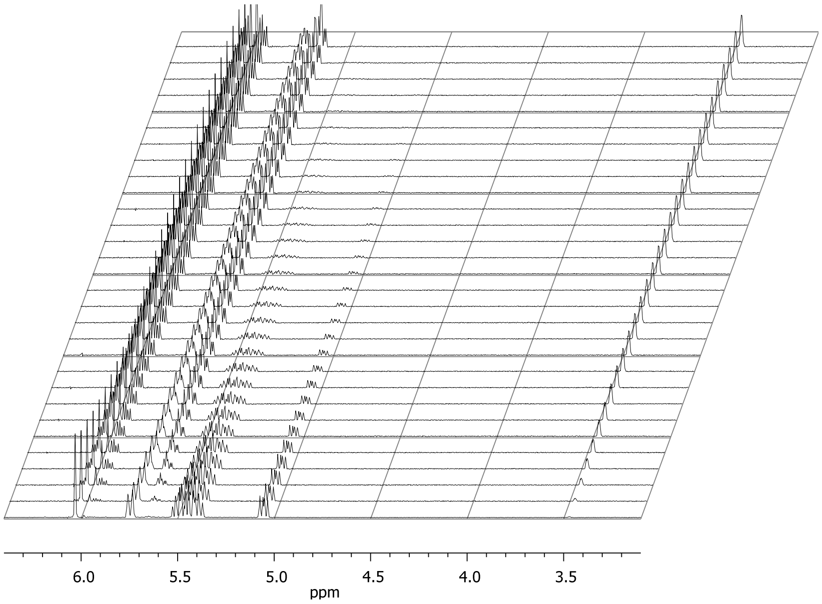


Figure 9. Stacked ^{1}H-NMR spectra of the thermal conversion from VHF to DHA acquired in benzene-d_6 at 40 °C (showed with 40 minutes interval). Note the decay of VHF signals at δ = 5.55 – 5.37, 5.06 ppm and rise of DHA signal at δ = 3.45 ppm.

Conclusions

In conclusion, we have developed a high-yielding route with easy work-up procedures for the preparation of 2-phenyl-1,8a-dihydroazulene-1,1-dicarbonitrile. This optimization is important as the compound serves as the parent compound for direct incorporation of a functional group in the seven-membered ring of DHA, using an earlier developed regioselective bromination – elimination – cross-coupling protocol. Both this compound and its crotononitrile precursor were subjected to detailed NMR and X-ray crystallographic analyses. In this way, all NMR signals for the ring-protons were unambiguously assigned. The influence of solvent polarity on the thermal ring-closure of VHF was investigated in relation to solvent parameters, providing a linear correlation with the $E_T(30)$ parameter. Moreover, it is an increase in the Arrhenius pre-exponential factor that first of all causes fast ring-closure in polar solvents; this observation implies that entropy effects are in play.

Experimental Section

General. NMR spectra were measured on 300 or 500 MHz (with cryoprobe) instruments. All chemical shift values are referenced to the solvent. Chloroform ($CDCl_3$) δ = 7.26 and δ = 77.16 ppm. Acetonitrile (CD_3CN) δ = 1.94 and δ = 1.32 ppm. Benzene (C_6D_6) δ = 7.16 and 128 ppm. Thin Layer Chromatography (TLC) was carried out on commercially available precoated plates (silica 60) with fluorescence indicator. For column chromatographic purification of DHA, the column was covered by an aluminum foil to exclude light. All isolated fractions were kept in the dark. All melting points are uncorrected. All spectroscopic measurements (including photolysis) were performed in a 1-cm path length cuvette. UV-Vis absorption spectra were obtained by scanning the wavelength from 800 to 200 nm. Photoswitching experiments were performed using a 150 W xenon arc lamp equipped with a monochromator; the DHA absorption maximum for each individual species was chosen as the wavelength of irradiation (line width 2.5 nm). The thermal ring-closure was performed by heating the sample (cuvette) by a Peltier unit in the UV-Vis spectrophotometer.

2-(1-Phenylethylidene)malononitrile (**6**). Acetophenone (18.5 g, 154 mmol) and malononitrile (28.4 g, 430 mmol) were dissolved in toluene (500 mL). NH_4OAc (40 g, 519 mmol) dissolved in AcOH (60 mL, 1 mol) was added, the flask was equipped with a Dean-Stark apparatus and the reaction mixture was heated to reflux and stirred for 2 h (oil temperature: 180 °C). After cooling the reaction mixture, it was diluted with diethylether (300 mL), washed with water (2 x 300 mL), brine (300 mL), and dried with $MgSO_4$. Evaporation of the solvents gave **6** (25.4 g, 151 mmol, 98 %) as pale yellow crystals. Recrystallization from boiling heptanes (1400 mL) gave **6** (24.1 g, 143 mmol, 93 %) as colorless crystals. Mp. 94.0 – 94.5 °C (heptanes). Litt: 94.5 - 95.5 (ethanol).[19] ^1H NMR (300 MHz, $CDCl_3$) δ 7.66 – 7.44 (m, 5H), 2.64 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.6, 136.0, 132.4, 129.3, 127.5, 112.9, 112.9, 84.8, 24.4 ppm. MS (ESP+): *m*/*z* = 169.1 [MH^+], calc. for $C_{11}H_9N_2$: *m*/*z* = 169.1.

Tropylium tetrafluoroborate (**5**). Triphenylmethanol (40.2 g, 154 mmol) was dissolved in warm acetic anhydride (500 mL) under argon atmosphere. After cooling to 20 °C, tetrafluoroboric acid – diethyl ether complex (25.0 mL, 210 mmol, 52 %) was added in portions of approx. 1 mL over 1 h, while keeping the temperate below 25 °C. The color changed to dark yellow. The temperature was decreased to 0 °C and freshly distilled (113 – 116 °C) cycloheptatriene (16.0 mL, 154 mmol) was added, until the characteristic yellow color of the tritylium ion had vanished and precipitation of the colorless tropylium tetrafluoroborate had begun. Ice cold, dry diethylether (600 mL) was added and the reaction mixture was cooled for an additional 30 min, which gave **5** (19.2 g, 108 mmol, 70 %) as a colorless powder. The powder was collected on a very fine funnel and washed with ice cold ether (2 x 100 mL). ^1H NMR (300 MHz, CD_3CN) δ 9.25 ppm. ^{13}C NMR (75 MHz, CD_3CN) δ 156.3 ppm. $C_7H_7BF_4$ (177.94): C 47.25 %, H 3.97 %, found: C 47.18 %, H 3.89 %.

2-(Cyclohepta-2,4,6-trienyl-1-phenylethylidene)malononitrile (**7**). Tropylium tetrafluoroborate **5** (16.0 g, 90 mmol) and the crotononitrile **6** (12.6 g, 75 mmol) were suspended in dry CH_2Cl_2 (1000 mL) by ultrasound sonication (30 min) under argon atmosphere. The reaction mixture was cooled to – 78 °C and Et_3N (11.5 mL, 82.5 mmol) was added dropwise over 1 h. The solution was stirred for 10 min and aqueous 2 M HCl (25 mL) was added. The organic phase was washed with water (2 x 250 mL) and dried with $MgSO_4$. Evaporation of the solvents gave **7** (19.4 g, 75 mmol, > 99 %) as a dark oil. For characterization a sample was crystallized from heptanes and crystals suitable for X-ray crystallography were grown from heptanes. Mp. 81.0 – 82.5 °C (heptanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55 – 7.40 (m, 5 H), 6.60 (t, ^3J = 6.4 Hz, 2 H), 6.22 (t, ^3J = 6.4 Hz, 1 H), 6.19 (t, ^3J = 6.4 Hz, 1 H), 5.17 (d, ^3J = 6.4 Hz, 1 H), 5.14 (d, ^3J = 6.4 Hz, 1 H), 3.19 (d, ^3J = 8.0 Hz, 2 H), 1.99 (p, ^3J = 8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.4 (C2), 134.8 (C2), 132.1 (Ph), 131.3 (C6), 129.4 (Ph), 127.5 (Ph), 126.6 (C5), 123.1 (C4), 112.8 (CN), 112.7 (CN), 86.8 (C1), 39.1 (C3), 37.9 (C3a) ppm. MS (ESP+): *m/z* = 259.1 [MH^+]; calc. for $C_{18}H_{15}N_2$: *m/z* = 259.1.

Tritylium tetrafluoroborate (**8**). Triphenylmethanol (45.0 g, 173 mmol) was dissolved in warm propionic anhydride (450 mL) under argon atmosphere. After cooling to 20 °C tetrafluoroboric acid – diethylether complex (42 mL, 380 mmol, 52 %) was added in portions of approx. 1 mL over 1 h, while keeping the temperature between 15 and 25 °C. After addition of ca. 12 mL of acid, the precipitation began and the reaction mixture took a red to yellow color. Cooling to 0 °C for 30 min gave **8** (39.9 g, 121 mmol, 71 %) as a curry yellow powder, which was washed with ice cold diethylether (4 x 50 mL) until the fractions were colorless. $C_{16}H_{15}BF_4$ (330.12): C 69.13 %, H 4.58 %, found: C 68.96 %, H 4.47 %.

2-Phenyl-1,8a-dihydroazulene-1,1-dicarbonitrile (**1**). The cotononitrile **7** (19.4 g, 75.0 mmol) and tritylium tetrafluoroborate (27.0 g, 81.8 mmol) were dissolved in dichloroethane (500 mL) under an argon atmosphere. The reaction mixture was stirred at 80 °C for 2 h after which it was diluted with toluene (250 mL) and cooled to 0 °C. Et_3N (15 mL, 10.9 g, 108 mmol) was added over 1 h. The reaction mixture was then excluded from light and heated at 80 °C for 1 h and the solvents were evaporated in *vacuo*. Purification by dry column chromatography (SiO_2, 113 cm^2, 0 % - 70 % CH_2Cl_2 / heptanes, 5 % steps, 150 mL fractions) followed by recrystallization from heptanes gave **1** (14.8 g, 57.8 mmol, 77 %) as yellow crystals. Crystals suitable for X-ray crystallography were grown from chloroform / heptanes. TLC, $CHCl_3$ / heptanes (4:6 v/v), R_f = 0.32 (yellow to red). Mp. 134.0 – 136.0 °C (heptanes). Litt: 128.0 (methanol).[6] IR (KBr, cm^{-1}): 3073w, 3055w, 3008w, 2893w, 2245w (CN), 1491m, 1446m, 1378m, 1221m, 1182m, 1111m, 1076m, 937m, 908s, 897s, 803s, 770s, 758s, 709s, 690m, 671m, 588m. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 – 7.72 (m, 2H), 7.53 – 7.39 (m, 3H), 6.89 (s, 1H), 6.58 (dd, *J* = 11.2, 6.2 Hz, 1H), 6.48 (dd, *J* = 11.2, 6.2 Hz, 1H), 6.34 (d, *J* = 6.2 Hz, 1H), 6.31 (ddd, *J* = 10.0, 5.8, 2.0 Hz, 1H), 5.82 (dd, *J* = 10.0, 3.8 Hz, 1H), 3.79 (dt, *J* = 3.8, 2.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.3, 138.8, 132.5, 131.0 (2 signals), 130.6, 130.2, 129.4, 127.8, 126.4, 121.1, 119.6, 115.3, 112.9, 51.3, 45.4 ppm. ^{1}H NMR (500 MHz, CD_3CN) δ 7.89 – 7.79 (m, 2H), 7.61 – 7.46 (m, 3H), 7.18 (s, 1H), 6.64 (dd, *J* = 11.3, 6.4 Hz, 1H), 6.53 (dd, *J* = 11.3, 6.1 Hz, 1H), 6.47 (dd, *J* = 6.2, 1.4 Hz, 1H), 6.37 (ddd, J = 10.3, 6.2, 2.1 Hz, 1H), 5.82 (dd, J = 10.3, 3.8 Hz, 1H), 3.90 (dt, J = 3.8, 2.1 Hz, 1H). $C_{18}H_{12}N_2$ (256.30): C: 84.35 % H: 4.72 % N: 10.93 %, found: C: 84.07 % H: 4.63 % N: 10.89 %. MS (ESP+): m/z = 257.1 [MH^+], calc. for ($C_{18}H_{13}N_2$): m/z = 257.1

2-(2-(2,4,6-Cycloheptatriene-1-ylidene)-1-phenylethylidene)malononitrile (9). The DHA **1** (2.5 mg, 9.8 μmol) was dissolved in C_6D_6 (0.6 mL). The solution was irradiated with light (350 nm) for 12 h at ambient temperature. The formation of VHF **9** is accompanied by change of color from yellow to dark red. ^{1}H NMR (500 MHz, C_6D_6) δ 6.98 – 6.89 (m, 5H), 6.06 (s, 1H), 5.73 (d, J = 11.4 Hz, 1H), 5.55 – 5.37 (m, 4H), 5.06 (dd, J = 12.0, 7.8 Hz, 1H) ppm. ^{13}C NMR (125 MHz, C_6D_6) δ 168.0, 152.8, 142.3 (C4), 135.4, 135.0 (C5), 134.8, 134.2 (C8), 133.3, 132.7 (C8a), 130.7 (Ph), 129.5 (Ph), 128.4 (Ph), 119.7 (C3), 115.0 (CN), 114.9 (CN), 78.8 (C1) ppm.

The extinction coefficients for the DHA **1** and VHF **9** measured at the absorption maxima (see Table 2) are provided in Table 3.

Table 3. Extinction coefficient (10^4 M^{-1} cm^{-1}) of DHA **1** and its corresponding VHF **9** in selected solvents at the absorption maxima provided in Table 2

	CH_2Cl_2	Et_2O	Toluene	MeCN	EtOH	THF	*c*-hexane	EtOAc
1	1.08	1.28	1.58	1.79	1.39	-	1.36	1.66
9	2.00	2.50	2.93	3.44	1.82	-	2.46	3.17

Kinetic studies

A stock solution of DHA **1** was prepared by dissolving a sample in the given solvent (*cf.*, Table 2). This stock solution was then further diluted until the absorption level was within the limits of the instrument. The sample was then irradiated with light at the DHA absorption maximum in the given solvent until no change in the absorption spectrum was observed. The sample was then heated and an absorption spectrum was measured against time (Figure 7) using a kinetics program, until at least three half-lives had passed. The cycle was repeated for at least four different temperatures. The change in absorption at the VHF absorption maximum was plotted against time, and the rate constant for the back-reaction at each different temperature was calculated (first-order kinetics). From an Arrhenius plot (shown in Figure 10 based on data given in Table 4), the activation energy E_a, the pre-exponential factor A, and the rate constant at 25 °C were calculated (if not measured directly at this temperature).

We note that the small light irradiation from the UV-Vis apparatus (causing reformation of VHF) can be neglected. Thus, a series of control experiments were conducted in order to confirm that our setup did not tamper with the reaction conditions. The thermal back-reaction was followed by scanning both the VHF absorption decrease and the DHA absorption appearance by UV-Vis spectroscopy. Thus the calculated rate constant at 25 °C in acetonitrile (obtained at normal procedure, by extrapolation with an Arrhenius plot) was compared to the measured value (without scanning the DHA-absorption). No difference was found. In addition two almost identical experiments were conducted in toluene at 40 °C (scanning every 10 minutes), with and without scanning the DHA absorption region. This experiment showed only a small difference in the measured rate constant ($k_{40°C} = 4.00 \times 10^{-5}$ s^{-1} compared to $k_{40°C} = 3.89 \times 10^{-5}$ s^{-1}).

Table 4. Measured rate constants (x 10^{-5} s^{-1}) for the back-reaction in different solvents, on which the Arrhenius plots are based

Solvent	$k_{100°C}$	$k_{90°C}$	$k_{80°C}$	$k_{75°C}$	$k_{70°C}$	$k_{65°C}$	$k_{60°C}$	$k_{50°C}$	$k_{45°C}$	$k_{40°C}$	$k_{35°C}$	$k_{25°C}$
EtOH					795	546	326	113	64.2	36.2		
MeCN					681		261	95.0		31.7		5.31
CH_2Cl_2												2.12
EtOAc					189		69.3	24.2				1.26
THF												1.05
Toluene	1367	654	275		108					4.04		
c-hexane				112	64.3	39.8	20.0		5.09			

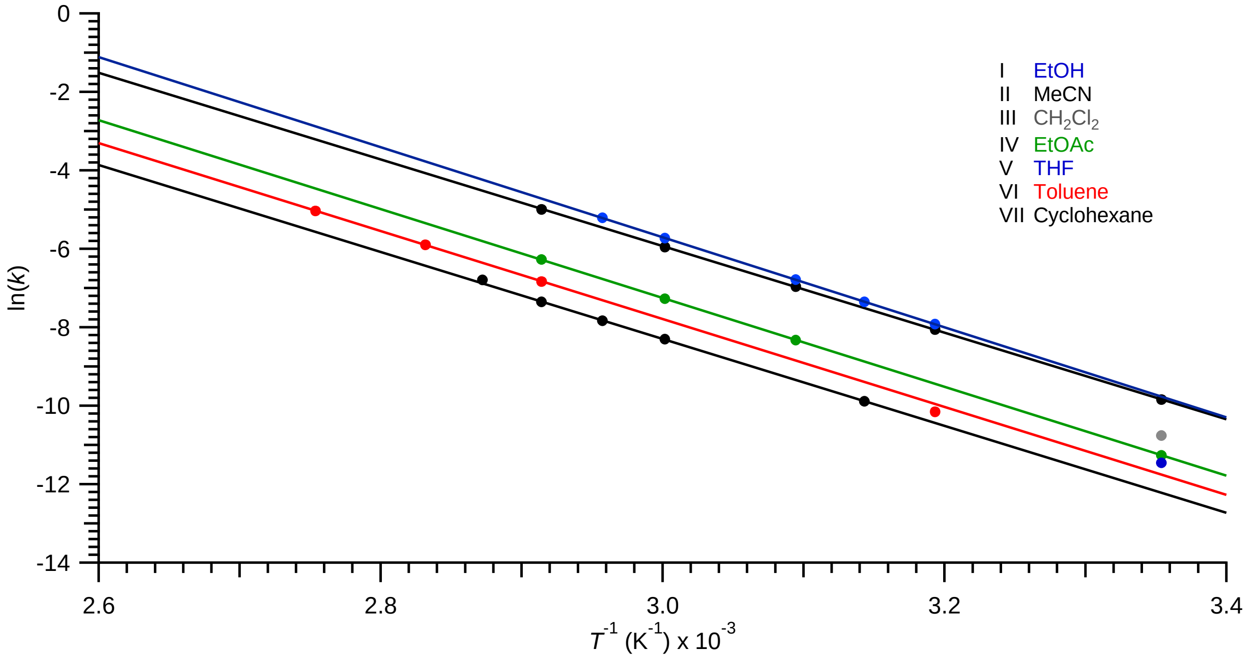


Figure 10. Arrhenius plot (ln(*k*) *vs.* T^{-1}) based on different solvents. EtOH, MeCN, CH_2Cl_2, EtOAc, THF, toluene, cyclohexane.

X-Ray crystallography

A list of C-C and C-N bond lengths (except for the phenyl ring) for DHA **1** is provided in Table 5.

Table 5. List of DHA bond lengths for **1** (C-H and phenyl C-C / C-H not listed). For atom labeling, see Figure 1

Bond	C1-C2	C1-C8a	C1-C9	C1-C10	C2-C3
Length (Å)	1.542(2)	1.575(1)	1.480(2)	1.477(2)	1.344(2)
Bond	C3-C3a	C3a-C4	C3a-C8a	C4-C5	C5-C6
Length (Å)	1.436(2)	1.349(2)	1.509(2)	1.439(2)	1.353(2)
Bond	C6-C7	C7-C8	C8-C8a	C9-N1	C10-N2
Length (Å)	1.446(2)	1.342(2)	1.501(2)	1.145(2)	1.141(2)

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References

1. (a) Balzani, V.; Gómez-López, M.; Stoddart, J. F. *Acc. Chem. Res.* **1998**, *31*, 405. (b) *Molecular Switches* Feringa, B. L. Wiley-VCH: Weinheim, Germany, **2001.** (c) Weibel, N.; Grunder, S.; Mayor, M. *Org. Biomol. Chem.* **2007**, *5*, 2343. (d) Berg, T. *Angew. Chem. Int. Ed.* **2009**, *48*, 3218.
2. (a) Irie, M. *Chem. Rev.* **2000**, *100*, 1685. (b) Kawata, S.; Kawata, Y. *Chem. Rev.* **2000**, *100*, 1777. (c) Tian, H.; Yang, S. J. *Chem. Soc. Rev.* **2004**, *33*, 85. (d) Raymo, F. M.; Tomasulo, M. *Chem. Soc. Rev.* **2005**, *34*, 327.
3. (a) *Chem. Rev.* **2000**, *100*, issue 5. (b) K. Matsuda, H. Yamaguchi, T. Sakano, M. Ikeda, N. Tanifuji, M. Irie, *J. Phys. Chem. C.* **2008**, *112*, 17005. (c) J. Areephog, W. R. Browne, N. Katsonis, B. L. Feringa, *Chem. Commun.* **2006**, 3920. (c) M. R. Banghart, A. Mourot, D. L. Fortin, J. Z. Yao, R. H. Kramer, D. Trauner, *Angew. Chem. Int. Ed.* **2009**, *48*, 9097.
4. (a) Kumar, A. S.; Ye, T.; Takami, T.; Yu, B. C.; Flatt, A. K. Tour, J. M.; Weiss, P. S. *Nano Lett.* **2008**, *8*, 1644. (b) Nozaki D.; Cuniberti G. *Nano Research* **2009**, *2*, 648. (c) Smaali, K.; Lenfant, S. Karpe, S.; Oçafrain, M.; Blanchard, P.; Deresmes, D.; Godey, S.; Rochefort, A.; Roncali, J.; Vuillaume, D. *ACS Nano* **2010**, *4*, 2411.
5. (a) Browne, W. R.; Kudernac, T.; Katsonis, N.; Areephong, J.; Hielm, J.; Feringa, B. L. *J. Phys. Chem. C* **2008**, *112*, 1183. (b) Zhuang M.; Ernzerhof M. *J. Chem. Phys.* **2009**, *130*, 114704.

6. Daub, J.; Knöchel, T.; Mannschreck, A. *Angew. Chem. Int. Ed.* **1984**, *23*, 960.
7. Görner H.; Fischer C.; Gierisch S.; Daub J. *J. Phys. Chem.* **1993**, *97*, 4110.
8. (a) Petersen, M. Å.; Broman, S. L.; Kadziola, A.; Kilså, K.; Nielsen, M. B. *Eur. J. Org. Chem.* **2009**, 2733. (b) Broman, S. L.; Petersen, M. Å.; Tortzen, C. G.; Kadziola, A.; Kilså, K.; Nielsen, M. B. *J. Am. Chem. Soc.* **2010**, *132*, 9165.
9. (a) Achatz, J.; Fischer, C.; Salbeck, J.; Daub, J. *J. Chem. Soc. Commun.* **1991**, 504. (b) Daub, J.; Gierisch, S.; Salbeck, J. *Tetrahedron Lett.* **1990**, *31*, 3113. (c) Petersen, M. Å.; Zhu, L.; Jensen, S. H.; Anderson, A. S.; Kadziola, A.; Kilså, K.; Nielsen, M. B. *Adv. Funct. Mater.* **2007,** *17*, 797.
10. (a) Bäumer, A.; Daub, J.; Pickl, W.; Rieger, W. *Chem. Ber.* **1985**, *118*, 1857. (b) Daub, J.; Gierisch, S.; Klement, U.; Knöchel, T.; Maas, G.; Seitz, U. *Chem. Ber.* **1986**, *119*, 2631. (c) Daub, J.; Gierisch, S.; Knöchel, T.; Salbeck, E. *Z. Naturforsch.* **1986**, *41b*, 1151.
11. Gierisch, S.; Daub, J. *Chem. Ber.* **1989**, *122*, 69.
12. Gobbi, L.; Seiler, P.; Diederich, F. *Helv. Chim. Acta* **2001**, *84*, 743.
13. (a) Finkelstein, M. *Chem. Ber.* **1957**, *90*, 2097. (b) Cope, A. C.; Nelson, N. A.; Smith, D. S. *J. Am. Chem. Soc.* **1979**, *101*, 251.
14. Fry, J. *Org. Lett.* **2007**, *9*, 1671.
15. Dauben, Jr., H. Honnen, L.; Harmon, K.; *J. Org. Chem.* **1960**, *25*, 1442.
16. For the technique of dry column chromatography, see: Rosenbohm C., Pedersen D. S. *Synthesis* **2001**, 2431.
17. Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, VCH: Weinheim, 1988.
18. Spreitzer, H.; Daub, J. *Liebigs Ann.* **1995**, 1637.
19. Barnes, D. M.; David, M.; Haight, A. R.; Harneury, T.; McLaughlin, M. A.; Jianzhang, M.; Tedrow, J. S.; Toma, J. D. R. *Tetrahedron* **2006**, *62*, 11311.