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Photocyclization of a naphthyl substituted Y-enyne†,‡

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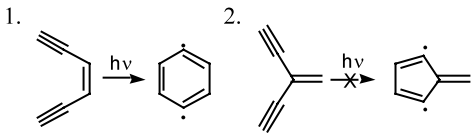
Abstract—Y-enyne **1** undergoes electrocyclic ring closure, via a cumulene intermediate **2**, to photoproduct **3** upon irradiation at 350 nm in the presence/absence of air. In non-polar solvents, a [1,5] H-shift affords the photoproduct. In MeOX (X=H/D), protonation/deuteration of the central allenic carbon in **2** occurs. The X-ray structure of **3**, the photoproduct upon irradiation of **1** in benzene, is reported.

Interest in antitumoral activity of enediynes has increased recently and calicheamicin and esperamicin have been tested clinically.[1] Bergman[2] cyclization of enediynes (**A**) was reported to play a key role in such enediyne antitumor drugs.[3] After a trigger reaction (cyclization is not spontaneous) brings the edges of the enediyne with its six conjugated π electrons into sufficient proximity, cyclization takes place in vivo forming active diyl radicals, which subsequently interact with macromolecule targets.[4]



A B

Unlike linear enediynes, cross-conjugated enediynes (Y-enynes), **B** cannot undergo Bergman cycloaromatization because five carbon atoms with only five π electrons are involved, and this is insufficient for aromatization. However, under reductive conditions cyclization may be possible generating a product with a Hückel number of $(2n+2)$ π electrons.[5]

Tinnemans and Laarhoven first reported the photocyclization of enynes[6] proposing a radical mechanism[7] in non-polar solvents (hexane and benzene) and an ionic mechanism in methanol. In a subsequent paper in the series, Van Arendonk[8] et al. proposed a 1,2,4-cyclohexatriene derivative formed from the singlet-excited *cis*-1,4-diaryl-butenyne as the primary reaction intermediate. This led to a product either via a radical intermediate, an ionic intermediate or under an argon atmosphere directly by intramolecular hydrogen shift. Previously, we reported that photocyclization occurred when the Y-enyne was substituted with a naphthyl group (Scheme 1).[9] We suggested photocyclization of **1** occurred entirely via an intermediate cumulene, **2**, in methanol, hexane and benzene under both argon and air (Scheme 1).[9]

The photoreaction of **1** in C_6D_6 was followed by ^1H NMR (Fig. 1). The starting material **1** shows two distinct peaks (Fig. 1a). The most downfield peak, a broad singlet due to *meta* coupling with H_c, is assigned to H_a. H_c is a doublet of doublets (*ortho* coupled to H_d and *meta* coupled to H_a; $J_{meta}=1.4$ Hz). Irradiation at 350 nm in benzene caused four new peaks to appear (Fig. 1b). Eventually, the two peaks corresponding to the starting material disappeared affording photoproduct **3** (Fig. 1c). In **3**, H_b and H_e are *meta* coupled ($J_{meta}=1.4$ Hz), while H_c is coupled to H_d and is therefore a doublet. Similar results were observed when **1** was irradiated in C_6H_6, C_6D_6, C_6H_{14}, and C_6D_{14}, indicating that these solvents are not involved in the photoreaction. Irradiation of **1** in CH_3OD led to deuterium incorporation. The H_b peak in the photoproduct observed upon irradiation in CH_3OH, a doublet *meta* coupled with H_e (same as in Fig. 1c), became a singlet

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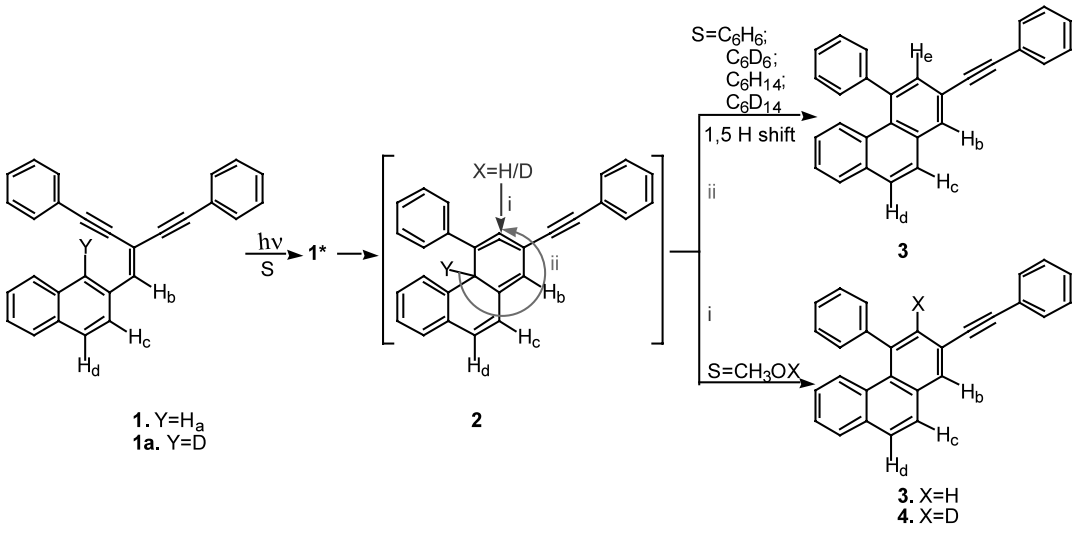
upon irradiation of **1** in CH_3OD (photoproduct **4**). This was accompanied by the disappearance of the H_e peak (Fig. 1d). GC/MS (DIP) indicated a MW of 355 (MW of **3** is 354). No deuteration was observed when irradiation was carried out in CD_3OH. In MeOX (X = H/D), protonation/deuteration of the central allenic carbon in **2** afforded the photoproduct **3**/**4** (path i of Scheme 1). In non-polar solvents, a [1,5] H-shift afforded the photoproduct (path ii of Scheme 1). Irradiation of **1a** (>95% D incorporation) in hexane led exclusively to **4** (>95% D incorporation).[10] This confirmed the proposed [1,5] H-shift via the cumulene intermediate **2**.[9] The photocyclization formed phenanthrene rather than anthracene (Fig. 2a). MOPAC and SPARTAN calculations showed the absence of electron density over the γ position of the naphthalene (Fig. 2b) in **1** in both the HOMO (highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital), explain-



Scheme 1. Proposed mechanism for photocyclization of **1**.

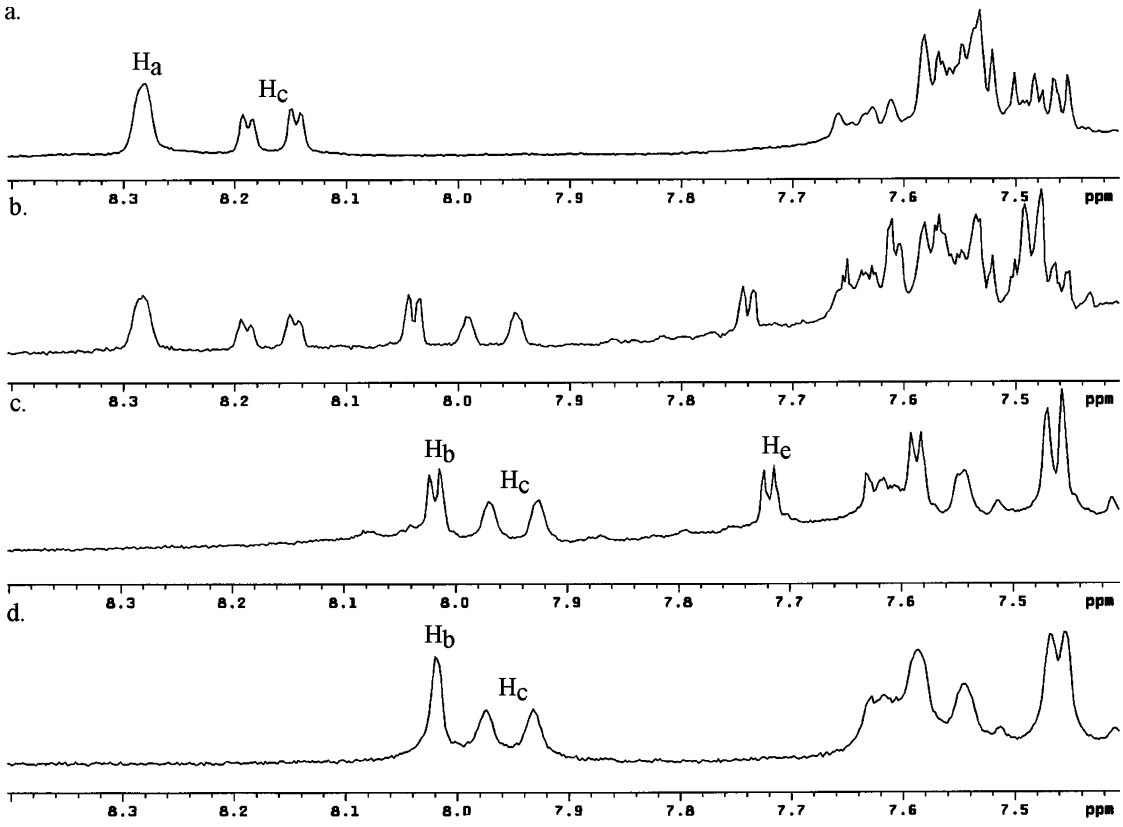


Figure 1. ^1H NMR (200 MHz) spectra of **1** in C_6D_6 upon 350 nm irradiations. Irradiation time is (a) 0 h, (b) 13 h, (c) 32 h (photoproduct **3**). (d) ^1H NMR spectrum of **4** dissolved in C_6D_6.

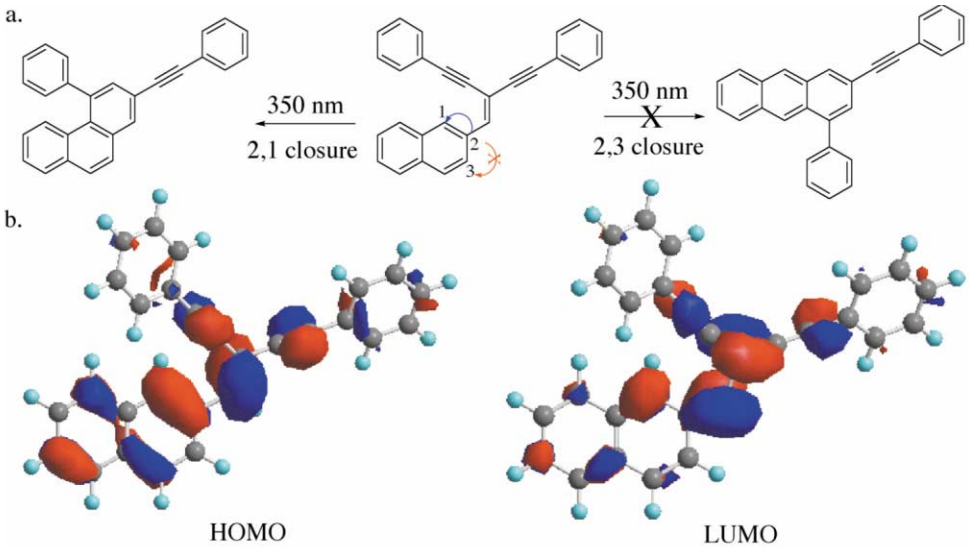


Figure 2. (a) Specificity of the photoreaction. (b) HOMO and LUMO of **1**.

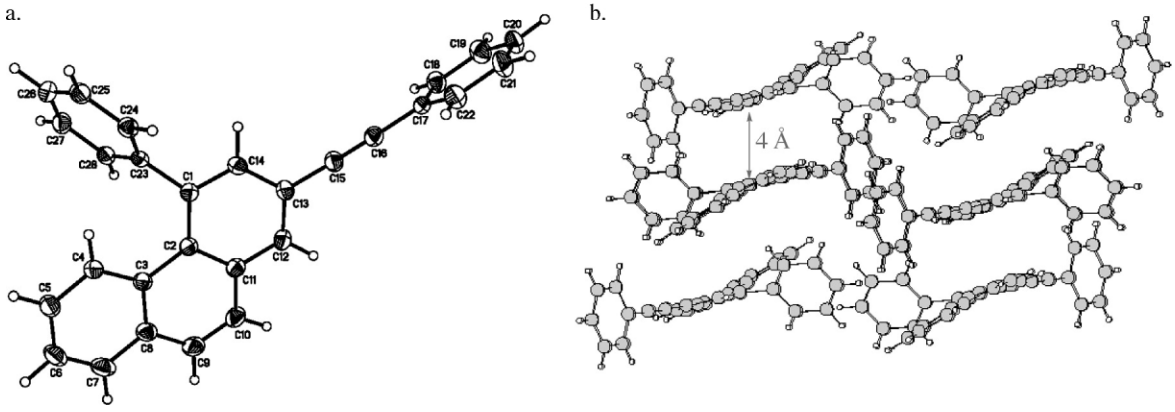


Figure 3. (a) ORTEP of **3** at 150 K (ellipsoids at 50% probability). (b) Stacking of **3**.

ing the specifity of this photoreaction. α-Cyclization[11] in naphthalene substituted ethylenes was supported by molecular orbital calculations.

X-Ray[12] analysis of **3**, the photoproduct formed upon irradiation of **1** at 350 nm in benzene, confirms its chemical structure (Fig. 3a). We noticed that **3** molecules pack along the *b* axis of the unit cell where they appear as ribbons of molecules, separated by 4 Å (intermolecular π–π interactions between the phenanthryl rings) (Fig. 3b).

Acknowledgements

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