Synthesis, Characterization, and Intramolecular Diels–Alder Reaction Tandem Dehydroaromatization of a Diene-diyne

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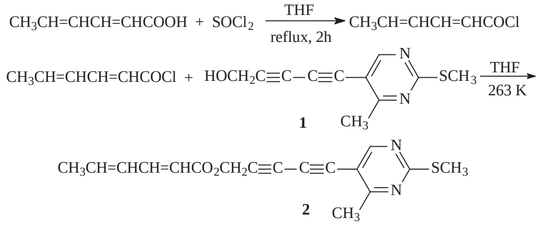
5-(2-Methylthio-4-methyl-5-pyrimidinyl)-2,4-pentadiynyl sorbate **2** was synthesized and characterized. It had two conjugating systems, which made its 5*J* and 6*J* ^{1}H–^{13}C correlating signals be obtained in gHMBC spectra. Intramolecular Diels–Alder reaction tandem dehydroaromatization of diene-diyne **2** under heating and irradiating resulted in formation of benzolactone. The reaction underwent the two steps: thermochemistry and photochemistry. The intermediate was confirmed using C_{60} as an intermediate catcher. This reaction represents a rare example of intramolecular Diels–Alder reaction tandem dehydroaromatization of diene-diyne under mild conditions without catalyst and oxidant.

Intramolecular Diels–Alder reactions were efficient methods for the synthesis of many polycyclic compounds. The methodology was particularly effective for the construction of highly strained bridgehead bicycle[3.*n*.1]alkenes[1] and complex polycyclic molecules.[2] Cycloaromatization of (*Z*)-1,2,4-heptatrien-6-ynes underwent mild thermal cyclization to form the biradical α,3-didehydrotoluene,[3] and some cycloaromatizations[4] and dehydroaromatizations[5] were carried out under the efficient catalysts or oxidants. For example, Shim et al. reported intramolecular ionic Diels–Alder reaction of α-acetylenic acetals under acid catalysts,[6] and the cyclization product bicyclodienal gave an aromatic compound by slow aromatization.

The intramolecular dehydro Diels–Alder reactions between alkynes and arenynes had been well-reported[7] as methods for the synthesis of polycyclic aromatic compounds. These reactions evolved to intermediate 1,2,4-cyclohexatrienes which formed aromatic products by isomerization.[8]

Herein, we reported a novel example of intramolecular Diels–Alder cycloaddition that resulted in formation of a bicycle[4.3.0]diene intermediate, a highly strained class of bridgehead dienes, followed by dehydroaromatization of the intermediate leading to a benzolactone.



Scheme 1.

The diene-diyne precursor **2**, 5-(2-methylthio-4-methyl-5-pyrimidinyl)-2,4-pentadiynyl sorbate, was synthesized as outlined in Scheme 1. 5-(2-Methylthio-4-methyl-5-pyrimidinyl)-2,4-pentadiyn-1-ol **1**[9] reacted with sorbyl chloride in anhydrous THF and resulted in 37% yields of **2**.[10] The ^{1}H–^{1}H gCOSY of **2** gave three correlating signals: δ 1.875 coupling with δ 6.21, δ 7.33 coupling with δ 5.804 and δ 6.21, respectively. Interestingly, diene-diyne **2** had two conjugating systems, which made its 5*J* and 6*J* ^{1}H–^{13}C correlating signals obtained in gHMBC spectra: δ 1.875 coupling with δ 117.39, δ 4.910 coupling with δ 72.39 and δ 111.66 respectively. NMR signals of **2** were assigned on the basis of DEPT, ^{1}H–^{1}H gCOSY, ^{1}H–^{13}C gHSQC, and ^{1}H–^{13}C gHMBC spectra (Figure 1). Efforts to obtain a single crystal suitable for an X-ray crystal structure had not as yet been successful.

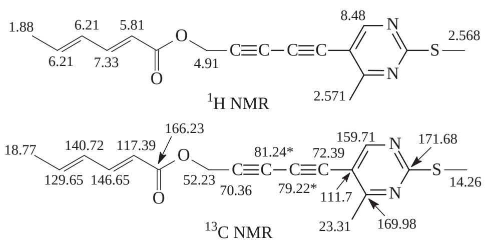
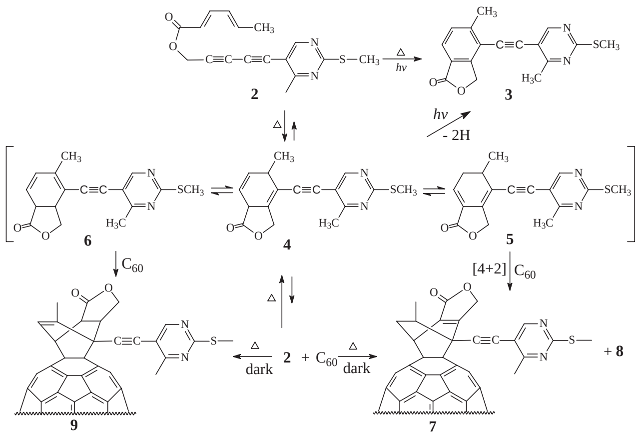


Figure 1. Chemical shifts, peak assignments of **2** in ^{13}C and ^{1}H NMR ($CDCl_3$, TMS). The symbol $*$ denots exchanging of chemical shifts.

Diene-diyne **2** in chlorobenzene, when heated and irradiated, gave **3**[11] as the sole product in 93% yield. A proposed mechanism of producing **3** was shown in Scheme 2. In order to confirm the proposed mechanism, a solution of **2** in chlorobenzene was irradiated at room temperature for 3 days but failed to give any **3**, then the reaction solution was stirred at 398 K in the dark for 48 h resulting in unobserved formation of **3**. It showed that neither heating in the absence of irradiating nor irradiating in the absence of heating resulted in formation of **3**. It suggested that **3** is formed either by the dehydrogenation of intermediate **4** or by a stepwise pathway through **5** or **6** (Scheme 2). The three medium-ring bicyclic lactones containing two bridgehead double bonds were one of the more highly strained representatives of this family of molecules. So they were instable, and none of **4**, **5** and **6** were obtained by column chromatography.

To confirm the presence of the intermediates in the reaction, C_{60}, as an intermediate catcher with 1.1-fold excess, and **2** in chlorobenzene was stirred at 398 K being exposed in room light for several days, but the reaction gave only trace amounts of C_{60} derivative and **3** was isolated as the major product. In contrast, reaction of C_{60} with **2** at 398 K in the dark for 48 h produced **7** in 2% yield and another C_{60} derivative **8** in 15% yield, and no



Scheme 2.

3 was detected by TLC in the reaction mixture. Unfortunately, the structure of **8** is not established for its poor NMR spectra. However, the spectra of **8** suggests that it contains fragments of **2** and C_{60} in 1:1 ratio. The isolation of **7** strongly suggested that the aromatization of **2** occurred via cyclohexadiene **4** or **5**. The reaction conditions for formation of **7** showed that **2** underwent a mild thermal cyclization to form **4** and **5** at 398 K without irradiation, although no intermediate was obtained. Strangely, no **9** was isolated, albeit **6** is supposed to be more stable then **5** due to the lack of bridgehead double bonds.

These results indicated that formation of **3** underwent the two steps: thermochemistry and photochemistry. In the first step, thermolysis of the diene-diyne **2** resulted in intramolecular Diels–Alder reaction to form intermediates **4**, **5**, or **6**. Then, photodehydrogenation of **4**, **5**, or **6** produced benzolactone **3**. The conjugated aromatic diene-diyne system was in favor of absorbing the light, and could lead to a lower barrier to cycloaromatization of **2**. This barrier may be further reduced by N and S atoms with lone-pair electrons contributing to the p system.

This reaction was strongly influenced by temperature, shown in the results as follows: 403 K (93%, 48 h), 398 K (84%, 48 h), 383 K (20%, 48 h), and at 339 K the product was not obtained at all, even after a prolonged reaction time. The reaction proved to be quite luminous sensitive, even under the room light at 398 K, the reaction was carried out easily and gave **3** in modest yield (53%). And the reaction was not affected by aerobic or anaerobic condition.

In conclusion, this reaction apparently represented a rare example of intramolecular Diels–Alder reaction tandem dehydroaromatization of diene-diyne under mild conditions. Dehydroaromatization was accomplished simply by heating and irradiating without catalyst and oxidant. Further investigation of the reaction was in progress.

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10 Synthesis of **2**: To a stirred solution of 5-(2-methylthio-4-methyl-5-pyrimidinyl)-2,4-pentadiyn-1-ol **1** (4.8 g, 22 mmol) in anhydrous THF (50 mL) was added sorbyl chloride (4.0 g, 30.7 mmol) in THF (20 mL) dropwise over 10 min. The mixture was stirred for 6 h at room temperature, then a solution KOH (2.24 g, 40 mmol) in 20 mL water was added dropwise slowly at −10 °C, The cold bath was removed and the solution warmed to room temperature. After stirring for 12 h at room temperature, the mixture was poured into water and filtered. The crude product was purified by column chromatography on silica gel; elution with ethyl acetate–petroleum ether (1:6, $R_f = 0.6$) afforded **2** (2.52 g, 8.08 mmol, 37%) as a white solid.

11 Synthesis of **3**: A solution of diene-diyne **2** (0.25 g) in chlorobenzene (50 mL) was heated under gentle reflux with stirring and was irradiated with a 500 W medium-pressure mercury UV-lamp for 48 h. The reaction mixture was then concentrated and purified by column chromatography on silica gel. Elution with toluene–ethyl acetate (8:1, $R_f = 0.48$) gave **3** (0.23 g, 93%) as a white solid. **3**: ^{1}H NMR ($CDCl_3$, TMS, 500 MHz) δ 8.531 (s, 1H), 7.7955 (d, $J = 8$, 1H), 7.449 (d, $J = 8$, 1H), 5.356 (s, 2H), 2.656 (s, 3H), 2.640 (s, 3H), 2.596 (s, 3H). ^{13}C NMR (CS_2, 125.6 MHz), δ: 14.217, 20.925, 23.341, 69.210, 91.175, 92.751, 112.383, 117.163, 124.028, 125.527, 130.887, 146.692, 148.958, 158.416, 168.156, 170.394, 171.77.

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