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An Addition–Cyclization–Elimination Mechanism for Dehydro Diels–Alder Reactions

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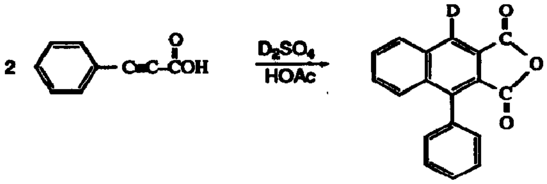
Abstract: Vinylacetylene 1 undergoes reactions with dienophiles by a mechanism involving initial addition of acids to the triple bond, cycloaddition, and elimination of acid.

For more than half a century the fact that vinylacetylenes can undergo cycloaddition reactions with dienophiles ("dehydro Diels–Alder reactions")[1] has puzzled organic chemists. If the mechanisms of the cycloadditions are similar to those of Diels–Alder reactions the initial products would be 1,2-cyclohexadienes or 1,2,4-cyclohexatrienes — highly strained intermediates which are unlikely to be formed under the mild conditions reported for some dehydro Diels–Alder reactions. Furthermore, to yield the observed products these intermediates would have to undergo 1,3-hydrogen shifts, although such shifts are not commonly observed in cyclic allenes.[2]

In the only previous investigation of the mechanisms of dehydro Diels–Alder reactions, Whitlock, Wu, and Whitlock reported that the dimerization of phenylpropiolic acid in acetic acid containing deuterosulfuric acid yielded 1-phenyl-2,3-naphthalenedicarboxylic anhydride substituted with deuterium at C-4 (eq. 1).

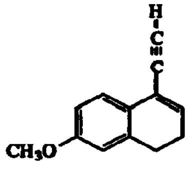
1)



They proposed a mechanism in which protonation of a triple bond at a position adjacent to a phenyl group is concerted with the cycloaddition process.[3]

There are several difficulties with that proposed mechanism: (a) If broken down into individual steps, the mechanism requires that protonation take place at a benzylic position to form an α-carboxy cation in preference to protonation at a position α- to the carboxy group to form a benzylic cation. (b) The presence of deuterium in the product does not demonstrate that the process is acid-catalyzed, since deuterium would appear at the same position if the protonation step took place after the cyclization step (e.g., by protonation of a 1,2-cyclohexadiene intermediate). (c) Dehydro Diels–Alder reactions have been reported to take place in the absence of acid catalysts under mild conditions.[1]

The most dramatic examples of apparently uncatalyzed dehydro Diels–Alder reactions are the reports by Dane and her coworkers that vinylacetylene 1 undergoes cycloaddition reactions with maleic anhydride simply on standing overnight in ether solution at room temperature.[4]



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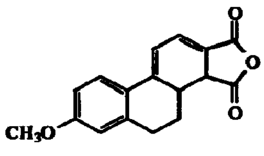

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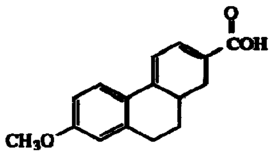
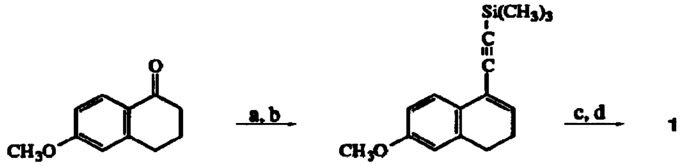


3

We have reexamined the reactions of 1 with dienophiles. This required a convenient source of pure 1. The synthesis shown below was found to be simpler, in practice, than previously reported procedures,[4,5] and yielded 1 in essentially pure form.[6]



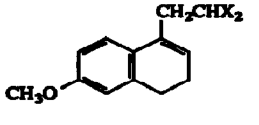
a) $Li{-}C{\equiv}C{-}Si(CH_3)_3$ b) $POCl_3$, C_5H_5N c) $AgNO_3$ d) KCN

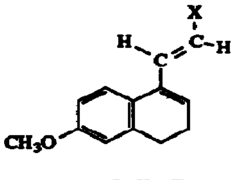
In our hands, pure 1 did not undergo any reaction with maleic anhydride in ether solution even after one week at room temperature, nor did any reaction occur if solutions of 1 and maleic anhydride in ether, benzene, or toluene were heated at reflux for several days. Irradiation of ether solutions with visible light yielded no reaction, while addition of aluminum trichloride, boron trifluoride etherate, or conc. sulfuric acid resulted only in decomposition of 1.

Bubbling rapid streams of hydrogen chloride or hydrogen bromide through ether solutions of 1 and maleic anhydride did not result in formation of cycloaddition products. However, if only ca. 0.5 molar equivalents (compared to 1) of the hydrogen halides were bubbled into the solutions, brownish yellow crystals appeared on the following morning, as described by Dane et al. Purification by the published procedure yielded a bright yellow monoaddition product, mp 200.0–200.5 °C, reported,[4] 200 °C), and a pale yellow adduct of one mole of 1 with two moles of maleic anhydride (mp 263–264 °C, reported,[4] 263 °C), in ratios of ca. 4:1. The structure of the monoaddition product was shown from its spectra[7] to be 2, rather than the structure with a double bond in ring B provisionally assigned by Dane et al.[4] The diadduct appeared from its spectra to be a mixture, and no structural assignments have been made.

The cycloadduct[8] from HBr catalyzed reaction of 1 with acrylic acid in ether similarly was found to have structure 3.[7]

When HCl and HBr were bubbled through solutions of 1 in ether or chloroform the dihalides 4a and 4b[7]


4a, X = Cl
4b, X = Br

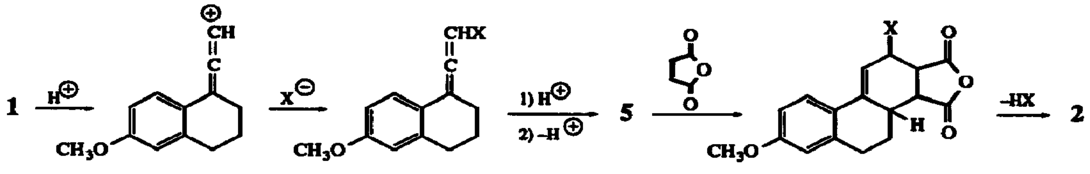

5a, X = Cl
5b, X = Br

were obtained in quantitative yields. Both compounds proved to be extremely sensitive, losing hydrogen halides on contact with the atmosphere to form deep blue, insoluble powders.

Dihalides 4a and 4b seemed unlikely to be intermediates in the cycloaddition reactions of 1 and, indeed, maleic anhydride did not react with either dihalide. Attempts to obtain a monochloride by reaction of 1 with HCl were unsuccessful. Instead, 4a was reacted with one mole of potassium *t*-butoxide. This resulted in loss of one mole of hydrogen chloride to form a product whose ^{1}H NMR spectrum was consistent with that of a ca. 3:1 mixture of 5a and its Z isomer. (When the reaction of 1 with HCl was followed by NMR, small signals attributable to 5a were detectable, together with signals for 1 and 4a.) In contrast to the reaction of 1 with HCl, when HBr was bubbled very cautiously through a solution of 1 in CDCl$_3$ and the reaction monitored by ^{1}H NMR, the monobromide 5b[7] was obtained in apparently pure form. Like 4a and 4b, 5a and 5b proved to be very reactive in air, forming deep blue insoluble products apparently identical with those obtained from 4a and 4b.

Maleic anhydride reacted with 5a and with 5b to form product mixtures essentially identical with those obtained from the hydrogen halide catalyzed reactions of maleic anhydride with 1. *When maleic anhydride reacted with a solution containing 1 and 5a in a 10:1 molar ratio, the molar yield of cycloaddition products was more than seven times as large as the amount of 5a employed.*

Thus, the dehydro Diels–Alder reactions of 1 proceed by addition of acid to 1 to form a halodiene, followed by a normal Diels–Alder cycloaddition step and then by elimination of acid to reform the catalyst.



We suggest that the dimerization of phenylpropiolic acid proceeds by a similar mechanism. While we believe the reaction is indeed acid catalyzed, as proposed by Whitlock's group,[2] this cannot be deduced from deuterium labelling experiments, since the deuterium label remaining in the product would be introduced *after* the rate limiting cycloaddition step.

There thus seems to be little evidence for concerted cycloaddition reactions of vinylacetylenes. However, the "double dehydro Diels–Alder reactions" of divinylacetylenes investigated by Butz and coworkers[9] are difficult to explain by our mechanism. We are presently investigating the mechanisms of those reactions.

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References and Notes

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6. As reported by previous workers,[5b] **1** is extremely sensitive to contact with air and is difficult to store for prolonged periods. In our hands, employing solutions of **1** obtained directly from the desilylation step gave results identical with those obtained using distilled samples of **1**.
7. Partial spectra: **2**, UV(EtOH) λ_{max} 369.5 nm (log ε = 4.69); IR (KBr) 1750, 1812 cm^{-1}; ^1H NMR (acetone–d_6) vinyl protons, δ 6.96 (1 H, dd, J = 5.89, 2.58 Hz), 7.39 (1 H, ddd, J = 5.88, 3.04, 0.76 Hz). **3**, UV(EtOH) λ_{max} 365.5 nm (log ε = 4.25); IR (KBr) 1652 cm^{-1}; ^1H NMR (acetone–d_6) vinyl protons, δ 6.78 (1 H, dd, J = 7.87, 2.71 Hz), 7.31 (1 H, m). **4a**, ^1H NMR ($CDCl_3$) δ 3.27 (2 H, dd, J = 6.66, 0.71 Hz $\underline{CH_2}$–CH), 5.78 (1 H, d, J = 6.66, $\underline{CH}$–CH_2), 5.90 (1 H, dt, J = 6.81, 0.70 Hz, C=C–$\underline{H}$). **4b**, ^1H NMR ($CDCl_3$) δ 3.51 (2 H, dd, J = 6.66, 0.39), 5.71 (1 H, d, J = 6.67), 5.89 (1 H, dt, J = 5.82, 0.40). **5b**, ^1H NMR ($CDCl_3$) vinyl protons δ 6.00 (1 H, t, J = 4.77), 6.53 (1 H, d, J = 13.66), 6.97 (1 H, d, J = 13.66).
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