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Stereochemistry and Mechanisms of Thermal Cycloaddition Reactions of Conjugated Enynes. The Stereospecific Formation of Six Tetrahedral Centers in a Single Reaction.

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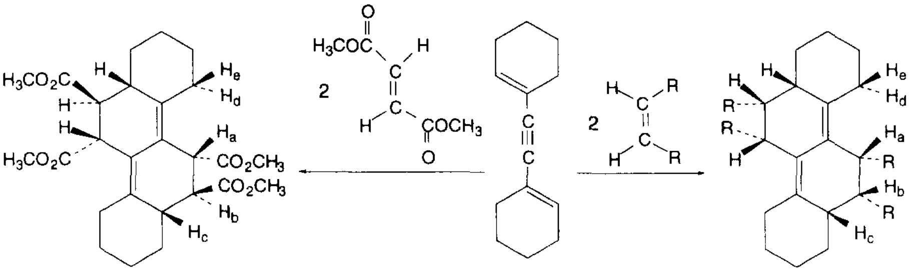
Abstract: Thermal condensations of penta-1,5-dien-3-ynes with two molecules of olefinic dienophiles proceed stereospecifically with retention of the configurations of the dienophiles, and with both molecules of the dienophile in each reaction adding to the same face of the dienyne.

For a century[1] it has been reported that triple bonds can add to conjugated enynes (vinylacetylenes) to form aromatic rings.[2] While these reactions (sometimes called dehydro Diels-Alder reactions[4]) are strongly catalyzed by protic[2,4] or Lewis[3,5] acids, there is strong evidence that they can also proceed under purely thermal conditions.[3,6]

Although a variety of possibilities, including ionic,[7] free radical,[3,6b] and concerted[3] processes have been proposed to account for thermal cycloadditions of enynes with triple bonds, very little is actually known about the mechanisms of these reactions. A major problem is that there are no verified examples of cycloaddition reactions of simple enynes with double bonds under thermal conditions. (Putative thermal cycloadditions of enynes to olefinic dienophiles[8] have been shown to proceed by initial addition of acids to the enynes.[9]) Thus, it has not been possible to investigate the stereochemistry of dehydro Diels-Alder reactions.

Although thermal cycloaddition reactions of monoenynes with olefinic reagents are unknown, L. W. Butz and his coworkers in the 1940's reported that conjugated *di*enynes (1,5–dien–3–ynes) react with olefinic dienophiles at temperatures of 130–220°C to form products incorporating one molecule of the dienyne and two molecules of the dienophile.[10] They were able to establish that each reaction resulted in formation of two new six-membered rings, but, given the limitations of the available technology, could not determine the geometries of the products. Their work appears to have been ignored for half a century.

We have now confirmed that reactions of dienyne **1** with dimethyl fumarate at 180°C,[10d] and with maleic anhydride at 140°C,[10a] yield a single condensation product in each case, with the carbon skeletons shown in structures **2** and **3**, respectively. Thus, each reaction results in the stereospecific formation of six tetrahedral centers!



2 **1**

3, R,R = $-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-$

4, R = CN

The geometries of **2** and **3** have been established by X-ray crystallography.[11] In each reaction both molecules of the dienophile added from the same face of the dienyne. Maleic anhydride added in the (double) *endo* sense, while dimethyl fumarate added with carbomethoxy groups *endo* to the triple bond and *exo* to the double bonds.

No reaction took place between **1** and dimethyl maleate, even after prolonged reaction times at high temperatures. However, **1** did react with maleonitrile at 180°C, again yielding a single product, (m.p. 318–320°C (dec.). These crystals were not suitable for X-ray structure determination. However, the ^{1}H NMR spectrum of the product (see Table) strongly support structure **4**.

TABLE. ^{1}H NMR PEAKS [a]

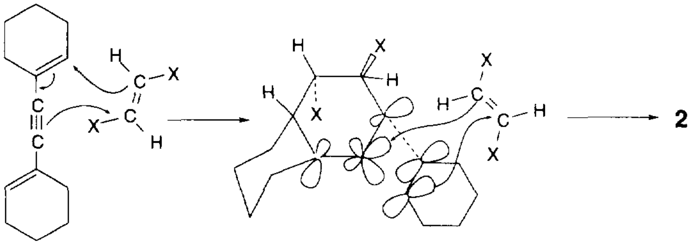
Values of d in ppm (J in Hz)

H_a	(d, 1.9)	(d, 8.7)	(d, 4.8)
H_b	3.18[b] (d, 1.8)	(dd,[c] 8.7, 7.8)	(dd, 6.2, 4.8)
H_c	(dd, 12.8, 3.3)	(ddd, 10.4, 7.8, 3.4)	(ddd, 10.3, 6.1, 3.4)
H_d	(broad d, 13.9)	(dt, 13.7, 3.5)	(dt, 13.9, 3.7)
H_e	ca. 1.8	ca. 2.1	ca. 2.1

[a] Taken on a 500 MHz instrument. Assignments confirmed by COSY or NOESY.
[b] Apparent singlet, analyzed as a doublet (0.75 Lorentzian, 0.25 Gaussian).
[c] Apparent triplet, analyzed as a doublet of doublets.

Of particular significance is the fact that H_a and H_d show strong NOESY coupling in the spectra of **4** (as they do in the spectra of **2** and **3**). This demonstrates that H_a is in a pseudoequitorial position in **4**. H_a and H_b must therefore be *cis* to each other, since they would otherwise show only very small coupling constants, as in the spectrum of **2**. Furthermore, the value of the H_b–H_c coupling constant requires that H_b and H_c also be *cis* to each other. Thus, *the addition of maleonitrile to 1 proceeds with retention of configuration*. Addition of both molecules again proceeds in the *endo* sense. The spectrum of **4** cannot conclusively distinguish between structures in which the maleonitrile units are *cis* or *trans* to each other. However, the very close similarity between the spectra of **3** and **4** suggests that both molecules of maleonitrile again add from the same face of the dienyne, resulting in the formation of **4**.

The stereospecific course of cycloadditions of dienynes to double bonds (which may be called *double dehydro Diels-Alder reactions*) strongly indicates that the reactions proceed by concerted processes. We suggest that initial formation of 1,2-cyclohexadiene intermediates (first "considered" by Butz[10a]) is readily



5 $\left(X = -\overset{O}{\overset{\|}{C}}OCH_3\right)$

reversible at the high temperatures of these reactions, so that no stable products are formed from reactions of monoenynes with olefinic reagents. In contrast, the intermediates formed from cycloadditions of dienynes can be trapped in Diels-Alder reactions, while the 1,2,4–cyclohexatrienes which would be formed from reactions of enynes with dienophiles containing triple bonds could undergo [1,5] hydrogen migrations to form aromatic products.[3] Addition of the second molecule of dienophile from the "outside" face of cup-shaped intermediates, such as **5**, would result in the observed addition of both molecules of dienophile to the same face of **1**.

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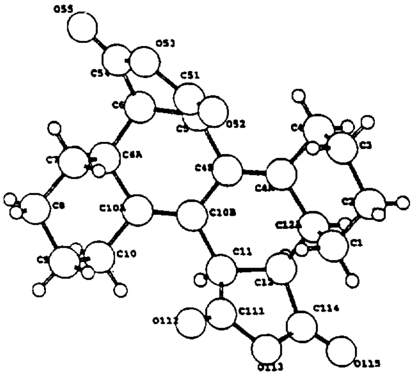
11. A PLUTO drawing of the structure of adduct **3** is shown below. Further details of the crystal structure investigation may be obtained from the Director of the Cambridge Crystallographic Data Centre, 12 Union Road, GB–Cambridge CB21EZ (UK) on quoting the full journal citation.



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