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Remote ε- Secondary Isotope Effect in the Reaction of Tetracyanoethylene with 2,5-Dimethyl-2,4-hexadiene. A Step-Wise Mechanism.

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Abstract: Cycloaddition of TCNE to 2-methyl-1',1',1'-d3-5-methyl-2,4-hexadiene-1,1,1-d3 (DMHD-d6) shows a substantial secondary isotope effect, which depends on solvent polarity. This remote ε-secondary isotope effect is a result of hyperconjugation in the dipolar intermediate which is formed in the rate determining step. Copyright © 1996 Elsevier Science Ltd

Tetracyanoethylene (TCNE) is a powerful electrophile, which gives[1] with olefins and dienes a variety of cycloadditions and to a lesser extent ene reactions. It is well documented[2] that TCNE affords [2+2] or [4+2] cycloadditions with electron rich alkenes such as p-methoxy styrene and methyl vinyl ether. These reactions proceed through a dipolar intermediate, whose intervention has been supported by a) the strong dependence of the reaction rate on solvent polarity;[3] b) the lack of stereospecificity;[4] c) the nucleophilic trapping of the intermediates;[5] and d) the high negative value of Hammet's $\varrho = -5$ in the reactions with 1,1-diaryl butadiene.[6]

The reaction of TCNE with the isomeric 2, 4-hexadienes has been studied previously by Foote and O'Shea.[7] The reaction gives stereospesifically [4+2] adducts as the only products. The least hindered (E, E)-isomer reacts fast, while with (E, Z)- isomer (more hindered) reacts very slow only at elevated temperatures. The most hindered (Z, Z)- isomer is unreactive. The authors suggested that there is no direct evidence for any intermediate other than the charge transfer complex in the reactions of the isomeric dienes with TCNE.

We report in this study, remote secondary isotope effects of the reaction of TCNE with 2-methyl-1',1',1'-d3-5-methyl-2,4-hexadiene-1,1,1-d3 (DMHD-d6, 1)[8] that indicate the formation of a dipolar intermediate in the rate determining step of this reaction.

DMHD-d6 reacted with TCNE in polar solvents at 25°C to yield the [2+2] adduct quantitatively. Upon addition of the diene, the solution instantaneously turned dark blue[9] and after several hours faded to yellow.

The reaction mixture was free of [4+2] adduct. It is rather expected that the s-cis conformation of the diene, required for the Diels-Alder cycloaddition, is prevented due to severe steric interactions of the four terminal methyl groups of the diene.

The secondary intramolecular isotope effect k_H/k_D was measured by integration of the ^1H NMR spectrum at 1.47 and 1.49 ppm (two methyl groups next to the cyclobutyl ring of **1a**) and 1.77 and 1.85 ppm (two geminal methyl groups of **1b**), Figure 1.
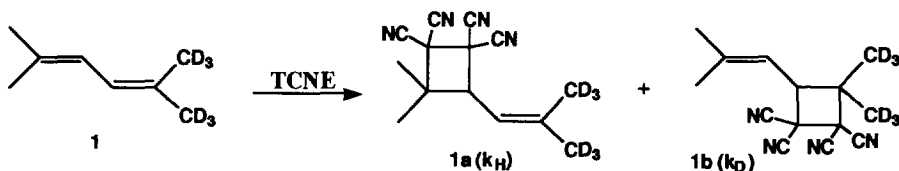
We define as product isotope effect the ratio **1a/1b** of the adducts which is propotional to k_H/k_D. The results are shown in Table 1.

Table 1. Intramolecular ε-Secondary Isotope Effect of the Cycloaddition of TCNE to **1**

| Solvent	t, hrs	Conversion %	k_H/k_D [a]
acetone-d_6	180	100	0.77±0.04
" "	120	80	0.75±0.04
acetonitrile-d_3	15	100	0.72±0.04

[a]Determined by ^1H NMR integration of the proper peaks.

A substantial inverse secondary isotope effect was found in the intramolecular competition between the double bonds of the diene. The new C-C bond between TCNE and diene is preferentially formed by 1.3 times more at the carbon which bears the geminal -CD_3 methyl groups. This result shows an inverse k_H/k_D=0.77 isotope effect when the reaction takes place in acetone-d_6. In acetonitrile the reaction occured 12 times faster than in the less polar acetone, while the value k_H/k_D =0.72 in acetonitrile, was found to be less than in acetone (Table 1)

Figure 1. Determination of k_H/k_D by ^1H NMR integration of the proper peaks of the products **1a** and **1b**.
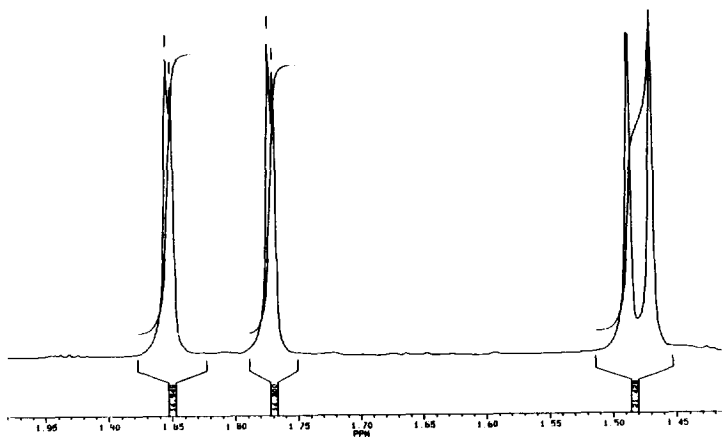
Examination of the possible transition states TS_I and TS_{II} leading to the [2+2] adducts, provides an insight into the observed inverse isotope effect. It is expected that the TS_{II} transition state will have lower energy than TS_I, because the developing positive charge is stabilized better in TS_{II} by hyperconjugation from the six hydrogens of the two methyl groups than in TS_I by the six deuteriums of the two deuterated methyls.
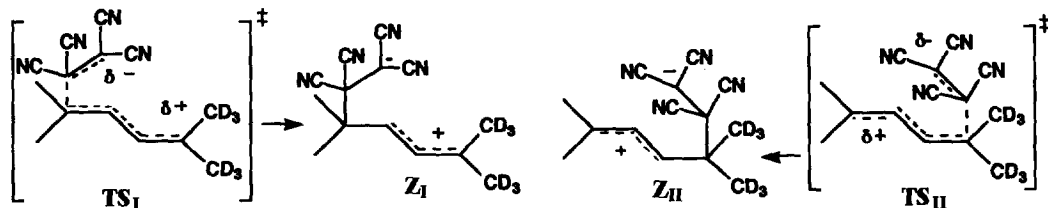
These results are consonant with the formation of an open dipolar intermediate with the positive charge distributed through the conjugated diene system and stabilized better by hydrogens than deuterium atoms.

When the reaction of TCNE with DMHD-d_6 was carried out in methanol at 5°C, the only isolated products were the methoxy adducts[10]derived from methanol trapping of the dipolar intermediates Z_I and Z_{II}. The values of k_H/k_D were determined by the integration of peaks at δ 1.56 ppm (6H, geminal methyls next to TCNEH of 2a) and 1.31 ppm (6H, geminal methyls next to -OMe of 2b), Figure 2. It is remarkable to note that the value k_H/k_D= 0.77 found for the methanol trapping experiment, is identical with the k_H/k_D =0.77 found for the [2+2] cycloaddition of TCNE to DMHD-d_6. These results indicate that both the methanol and
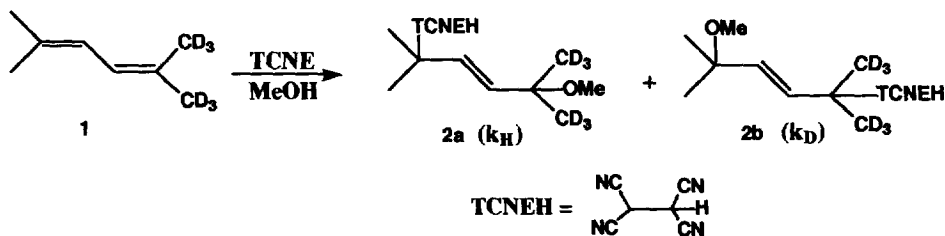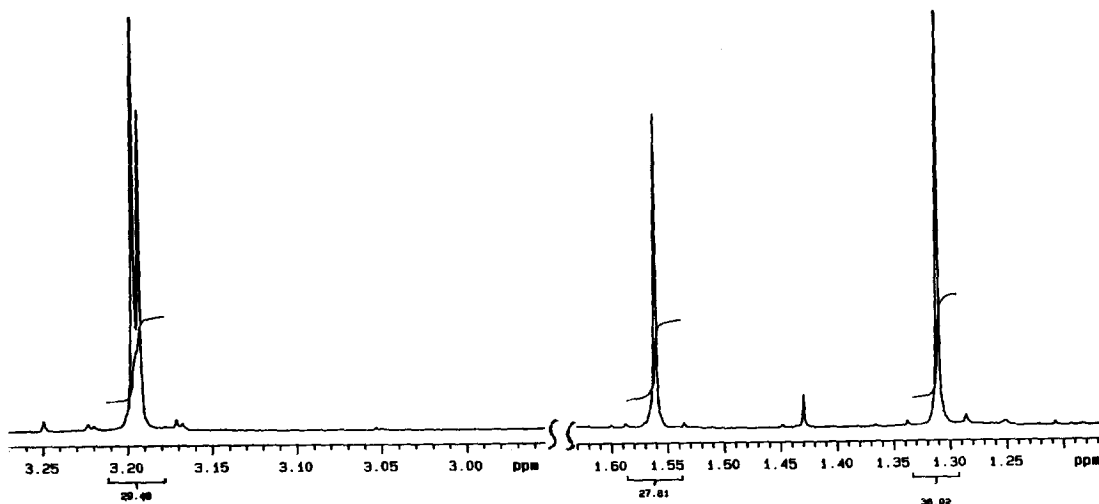

Figure 2. ^{1}H NMR spectrum of methanol adducts **2a** and **2b**.

the [2+2] adducts are produced from the common dipolar intermediates Z_I and Z_{II} in a fast step. It is worthwhile to note here that the absorption of the two -OMe functionalities of **2a** , upfield, and **2b**, downfield, are distinguishable by 0.004 ppm in a 500 MHz spectrometer (Figure 2). It is obvious that the uniqual size of the above peaks is due to the remote ε-secontary isotope effect.

It is interesting to note that the observed secondary isotope effect occurs at the (ε) position with respect to the newly formed C-C bond. Remote isotope effects are caused mainly from differences in steric interactions.[11,12] To the best of our knowledge, no such a remote kinetic secondary isotope effect, due to hyperconjugation interaction has been reported in the past. Shiner and Kritz[13] have reported a similar but nominally δ secondary isotope effect in the solvolysis of 4-chloro-4-methyl-2-pentyne.

In conclusion, the observed ε-secondary isotope effect in the cycloaddition of TCNE to DMHD-d_6 is consonant with the formation of a dipolar intermediate in the rate determining step of this reaction. The ratio of the methanol trapping adducts **2a/2b** of TCNE with DMHD-d_6 is the same with the value of k_H/k_D found in the cycloaddition reaction, indicating also the formation of a common zwitterionic intermediate in a rate determining step.

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