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A Mechanistic Comparison Between [2+2] and [4+2] Cycloadditions of Tetracyanoethylene to 2,7-Dimethyl-2,*trans*-4,6-octatriene. A Very Remote Secondary H/D Isotope Effect

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Abstract

Cycloaddition of tetracyanoethylene to 2-methyl-*1',1',1'*-d_3-7-methyl-2,*trans*-4,6-octatriene-*1,1,1*-d_3 (DMOT-d_6) shows a small inverse steric ß-secondary isotope effect for the [4 + 2] path (k_H/k_D=0.95±0.05), which is consonant with a concerted mechanism. On the other hand a substantial remote η-secondary isotope effect (k_H/k_D=0.81±0.05) was measured for the [2 + 2] path. This isotope effect, is the most remote reported in the literature, and it is a result of hyperconjugation in the dipolar intermediate which is formed in the rate determining step for the [2 + 2] path.

Keywords: Cyano compounds; Cycloadditions; Isotope effects; Trienes.

Tetracyanoethylene (TCNE) is a highly electron-deficient (E_{red}=0.15 V vs SCE) [1] and strongly electrophilic reagent [2], because of the electron-withdrawing ability of the four cyano groups on the double bond. It is not only a potent dienophile in Diels-Alder reactions [1, 2], but it gives also thermal zwitterionic [2 + 2] cycloadditions with electron rich alkenes, such as *p*-methoxystyrenes and vinyl ethers [3-5], which are typical electron donor molecules. It has been reported that an electron transfer mechanism is excluded for the zwitterionic cycloadditions of TCNE [6]. A dipolar mechanism proposed earlier, provides satisfactory rationale of previous and recent experimental results. Most of these reactions include the formation of a dipolar intermediate whose intervention has been supported by the strong dependence of the reaction rate on solvent polarity [7], the lack of stereospecifity [8], the nucleophilic trapping of these intermediates [9, 10], and the high negative value of Hammet's ρ = -5 in the reactions with *para* substituted 1,1-diaryl butadiene [11]. TCNE gives to a lesser extent ene reactions [12, 13].

On the other hand, TCNE gives [4+2] adducts, rapidly with the *trans,trans*-2,4-hexadiene isomer, slowly with the *cis,trans*, and no adduct with the *cis,cis*. This [4+2] reaction is stereospecific, leading exclusively to 1,1,2,2-tetracyano-3,6-*cis*-dimethylcyclohexene from

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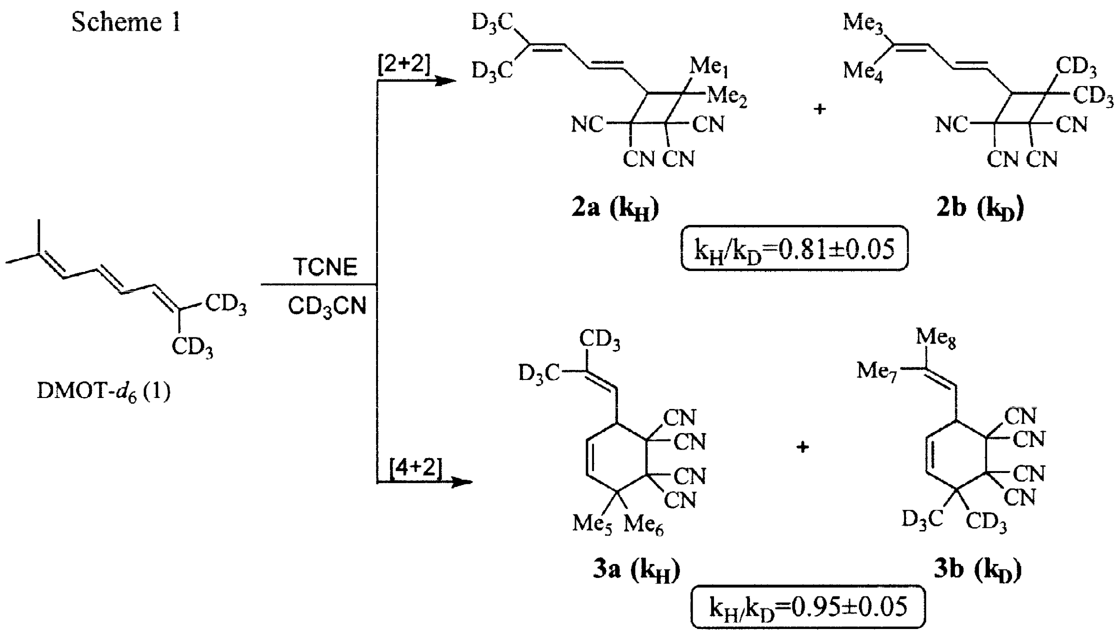
the *trans,trans*-isomer, and exclusively the *trans* [4 + 2] analog from the *cis,trans*-isomer [14]. Reaction of TCNE with 2,5-dimethyl-2,4-hexadiene (DMHD) affords exclusively the [2 + 2] adduct [15]. Generally, the reactions of TCNE with substituted 1,3-butadienes [16, 17] and 1,3,5-hexatrienes [19, 20] occur by the competing [4 + 2] and [2 + 2] cycloadditions. The regiospecificity of the reactions depends on the substitution at both diene termini, as well as on the polarity of the solvent. For example, the addition of TCNE to 2,6-dimethyl-2,*E*-4,*E*-6-octatriene affords a *cis* [4 + 2] adduct on the less substituted triene termini, while addition to 2,6-dimethyl-2,*E*-4,*Z*-6-octatriene affords a *trans* [4 + 2] adduct on the same terminus accompanied by the [2 + 2] adduct in which the cyclobutane ring also closed at the less hindered triene terminus [18]. 2,7-Dimethyl-2,*trans*-4,6-octatriene (DMOT) undergoes quantitative cycloaddition with TCNE to give the [2 + 2] adduct as well as the [4 + 2] adduct [19]. Formation of the [2+2] adduct is favored in more polar solvents. For example, the ratio of [4+2]/[2+2] was reported to be 67:33 in tetrahydrofuran and 50:50 in acetonitrile. We measured a ratio 39:61 in acetone and 37:63 in acetonitrile by ^{1}H-NMR (500 MHz) integration of the appropriate signals.

We report in this study the intramolecular secondary kinetic isotope effects (KIE) of the reaction of 2-methyl-*1',1',1'*-d_3-7-methyl-2,*trans*-4,6-octatriene-*1,1,1*-d_3 (DMOT-d_6)[1] with TCNE. DMOT-d_6 was reacted with TCNE in acetone-d_6 and acetonitrile-d_3, at room temperature, to produce an intense blue charge-transfer complex whose color disappeared completely at the end of the reaction.

Scheme 1

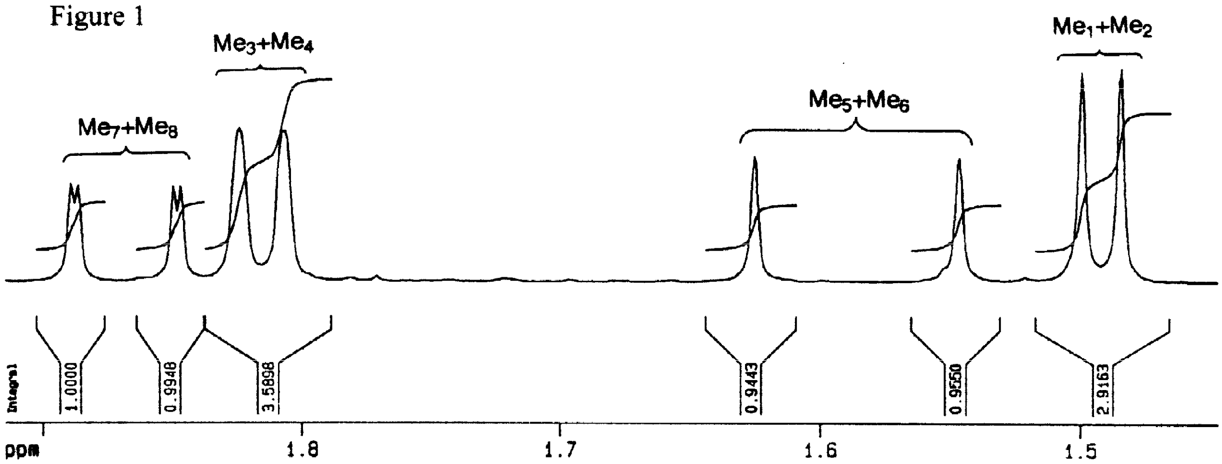


We define as product isotope effects for the [2 + 2] cycloaddition the ratio **2a/2b** and for the [4+2] cycloaddition the ratio **3a/3b**, which are proportional to k_H/k_D (Scheme 1). The secondary intramolecular KIE k_H/k_D for the [2 + 2] pathway was measured by integration of the ^{1}H-NMR

[1] DMOT-d_6 was prepared by Wittig coupling of triphenylphosporanylidene-isopropane-d_6 with 5-methyl-hexadien-trans-2,4-al. ^{1}H-NMR (250 MHz) in $CDCl_3$ d 1.76 (s, 3H), 1.79 (s, 3H), 5.89 (dd, J_1=7.3 Hz, J_2=3.0 Hz, 2H), 6.30 (dd, J_1=7.3 Hz, J_2=3.0 Hz, 2H). MS m/z 142 (M^+, 100).

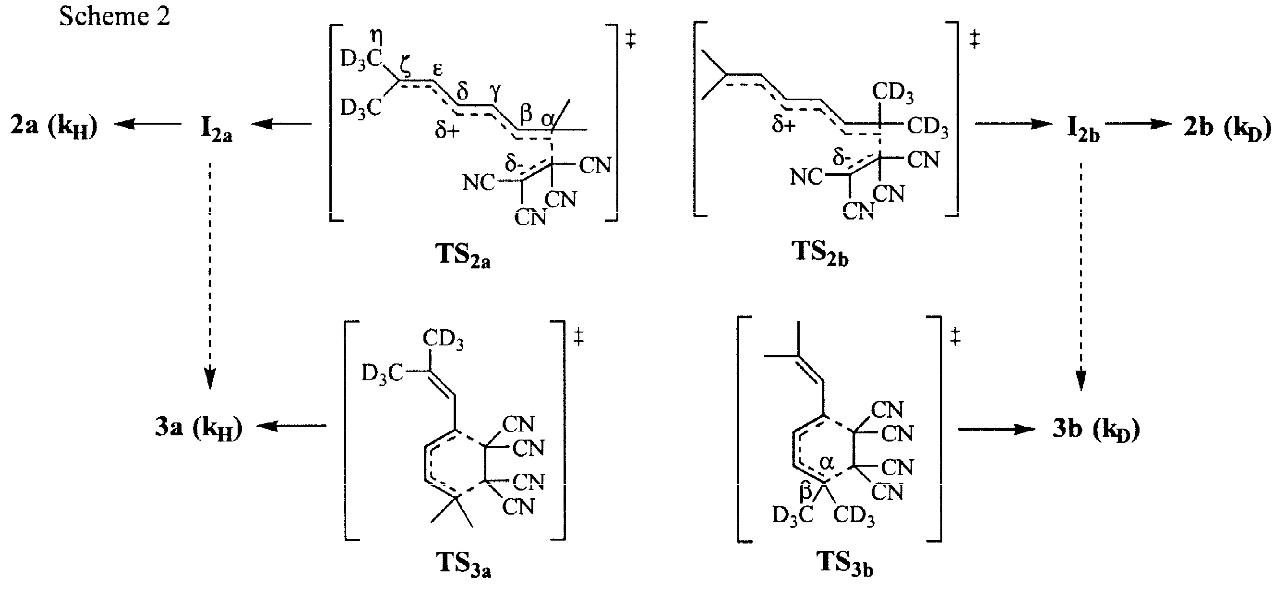
spectrum (Figure 1) at 1.47 and 1.49 ppm (Me_1, Me_2 next to the cyclobutane ring of **2a**) and 1.80 and 1.81 ppm (Me_3, Me_4 of **2b**). It was found to be 0.81±0.05. On the other hand, the isotope effect for the [4 + 2] path was measured by integration of the ^{1}H-NMR spectrum (Figure 1) at 1.53 and 1.61 ppm (Me_5, Me_6 next to the cyclohexenyl ring of **3a**) and 1.84, 1.88 ppm (Me_7 and Me_8 of **3b**), was found to be 0.95±0.05. Thus a significant inverse KIE was found in the [2 + 2] cycloaddition, but a smaller one in the [4 + 2] addition.

Figure 1



We wish to focus attention to the fact that the k_H/k_D is different for the two reactions. This finding excludes the formation of a dipolar intermediate as a common intermediate for both reaction paths. A synchronous mechanism was previously proposed for the [4 + 2] addition, on the basis that the product ratio [4 + 2]/[2 + 2] was affected by solvent polarity. The finding of a small inverse β-secondary k_H/k_D (0.95±0.05) in the [4 + 2] cycloaddition supports a concerted mechanism. Thus, **TS$_{3b}$** is more favored over **TS$_{3a}$**, because of the lesser steric hindrance of the six deuteriums than that of the six protons (Scheme 2).

Scheme 2



Assuming an open intermediate in the [2 + 2] cycloaddition, the k_H/k_D is nominally an η-secondary isotope effect since the isotopic labeling is at the η-position, seven bonds away with respect to the newly formed C-C bond. We attribute this remote η-secondary isotope effect to hyperconjugation (positive charge at the ζ-carbon through conjugation). It is well known that in ordinary systems with hyperconjugation possible, less than 10% of the observed isotope effect is due to nonbonded interactions [20, 21]. Thus $\mathbf{TS_{2b}}$ is favored over $\mathbf{TS_{2a}}$ (Scheme 2). The corresponding zwitterionic intermediates $\mathbf{I_{2b}}$ and $\mathbf{I_{2a}}$ lead exclusively to the formation of the [2 + 2] adducts **2b** and **2a** respectively.

Remote secondary deuterium KIEs can result mainly from hyperconjugative [15, 22, 23] or steric effects [22, 24]. The significant inverse η-secondary KIE is, to our knowledge, unique and therefore worthy of further experimental and theoretical investigation. It is the most remote secondary isotope effect which has been reported in the literature. An ε-secondary isotope effect k_H/k_D=0.72 was reported by us in the [2 + 2] cycloaddition of TCNE to DMHD [15]. The magnitude of the η-secondary KIE is smaller than that of the ε-secondary KIE because of a more effective delocalization of a positive charge into a conjugate trienic system compared with a dienic system. In the [2 + 2] reaction of TCNE with DMHD, the positive charge in the zwitterionic intermediate is delocalized in a secondary and a tertiary carbon. In DMOT however, the positive charge of the zwitterionic intermediate, in the same reaction, is delocalized in two secondary and one tertiary carbon. As a result the hyperconjugative ability is smaller in the case of the most remote η-secondary kinetic isotope effect.

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