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[4 + 2] Cycloadditions of Rigid s-*cis* Dienes to C_{60}. A Synchronous Diels–Alder Reaction

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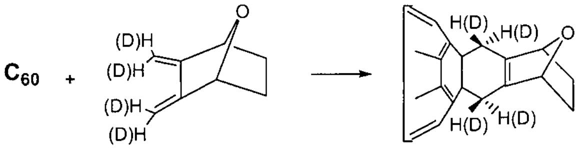
ABSTRACT



$k_H/k_D = 0.61 \pm 0.03$

The Diels–Alder reaction of rigid s-*cis* dienes with C_{60} occurs by a concerted mechanism, via a symmetrical transition state.

Among the functionalizations of C_{60}, the Diels−Alder reactions with rigid s-*cis* dienes are particularly useful, since they usually provide thermally stable adducts.[1] However, the mechanism of this reaction still remains unexplored.[2]

Following our recent studies on the [2 + 2][3] and the ene[4] reactions of [60]fullerene, we present here a mechanistic study of the [4 + 2] cycloaddition reaction of rigid s-*cis* dienes to C_{60}. For this purpose, α-secondary kinetic isotope effects (KIEs) were used in order to determine whether the mechanism is concerted or stepwise. 2,3-Dimethylene-7-oxabicyclo[2.2.1]heptane (**1-d$_0$**) and its deuterated analogues **1-d$_2$** and **1-d$_4$** were chosen as the appropriate reactive substrates. The synthesis of compounds **1-d$_0$**, **1-d$_2$**, and **1-d$_4$** is shown in Scheme 1.

A 10-fold molar excess of the conjugated diene **1-d$_0$** reacted smoothly with C_{60} at 80 °C, in a toluene solution. No multiadducts were detected by HPLC, and the Diels−Alder adduct **2-d$_0$** was remarkably stable at the reaction temperature. The isolated adduct **2-d$_0$** was stable even after prolonged heating in toluene, at 80 °C. Under these conditions not even traces of retro Diels−Alder products were detected by HPLC and ^{1}H NMR spectroscopy. In the ^{1}H NMR spectrum of the adduct **2-d$_0$** at 298 K (Figure 1), the diastereotopic methylene hydrogens H_a and H_b of the cyclohexene ring absorb at 4.15 ppm and appear as a sharp AB system. In addition, the methine hydrogens H_c appear as a singlet absorption at 5.20 ppm and the four methylene hydrogens H_d and H_e are represented by two multiplet absorptions at 2.06 and 1.77 ppm, respectively.

The cyclohexene ring of **2-d$_0$** can adopt two nondegenerate boat conformations, namely, a folded one and an extended one. To verify the stability of the two conformers, we used ab initio calculations. The two geometries were fully optimized at the HF/3-21G level of theory, and the local minima were found to be almost isoenergetic. In particular,

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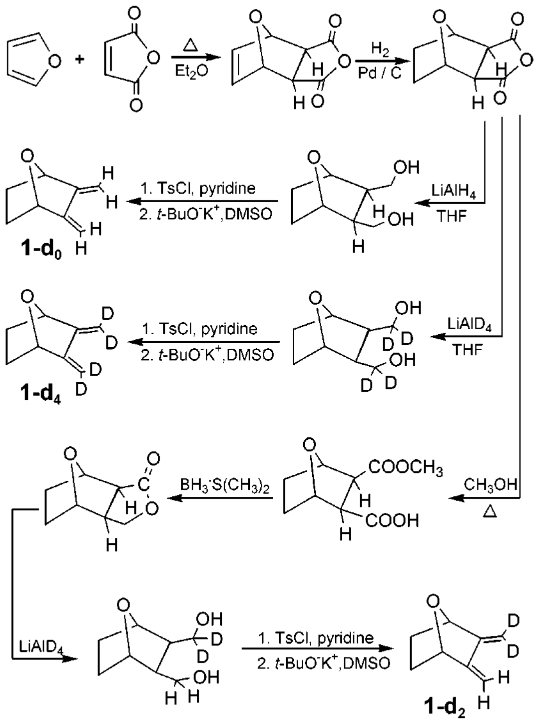
Scheme 1. Synthesis of the Rigid s-*cis* Dienes **1-d$_0$**, **1-d$_2$**, and **1-d$_4$**



the folded conformation is more stable than the extended one by 0.5 kcal/mol. All the computations were performed with the GAUSSIAN 94 program package.[5]

The dynamic behavior of cycloadduct **2-d$_0$** was investigated by using variable-temperature ^{1}H NMR experiments. No change of the sharp AB system at 4.15 ppm was observed at different temperatures, ranging from −40 to +74.3 °C. This indicates that the boat-to-boat inversion of the cyclohexene ring connecting the C_{60} cage to the organic addend has a high activation energy. The fast flipping motion of the cyclohexene ring has already been reported for other organofullerenes.[6]

Along with the M^+ ion of C_{60} at 720, the MALDI-TOF MS of **2-d$_0$** gave the M − 28 ion at 814, which indicates the loss of a $-CH_2-CH_2-$ fragment under the spectrometric conditions.

To determine the intermolecular α-secondary isotope effect $k_H/k_{D(4D)}$, a mixture of C_{60} and a 10-fold excess of an equimolar mixture of **1-d$_0$**/**1-d$_4$** was dissolved in deoxygenated toluene and heated at 80 °C. The reaction was followed by HPLC equipped with a Cosmosil 5C18-MS reversed phase column. A 45% yield of the Diels−Alder monoadducts was obtained after 4 h, based on the recovered C_{60}. The fullerene cycloadducts **2-d$_0$** and **2-d$_4$** (Figure 2) were purified by flash column chromatography (SiO_2, C_{60}: hexane/CH_2Cl_2 = 1/1; **2-d$_0$**, **2-d$_4$**: hexane/CH_2Cl_2 = 1/3) and characterized by ^{1}H NMR spectroscopy and MALDI-TOF mass spectrometry [**2-d$_0$**: *m/z* (M − 28) 814; **2-d$_4$**: *m/z* (M − 28) 818]. The isotope effect $k_H/k_{D(4D)}$ is proportional to the ratio of the **2-d$_0$**/**2-d$_4$** adducts and was measured by the integration of the signals of the methylene hydrogens (AB system at 4.16 ppm) and the signal of the methine hydrogens H_c and $H_{c'}$ at 5.21 ppm (Figure 2). The average value of the intermolecular α-deuterium isotope effect was found to be $k_H/k_{D(4D)} = 0.61 \pm 0.03$ [$k_H/k_{D(4D)} = 0.88 \pm 0.03$ per D atom].

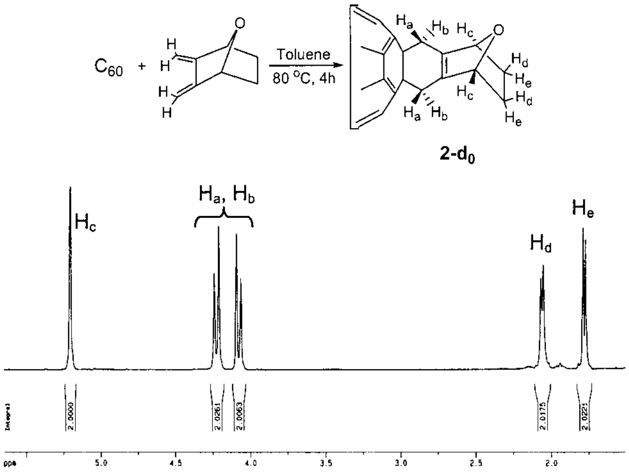


Figure 1. Diels−Alder reaction of **1-d$_0$** with C_{60}.

The origin of α-secondary isotope effects is due to changes in the force constants upon going from reactants to the transition state at the rate-determining step. In a concerted mechanism, the force constants[7] for the bonds C_α−H(D) are greater in the transition state than in the reactant, because the out-of-plane bending vibrations increase upon conversion of the reaction centers from sp^2 to sp^3. Thus, the isotope effect is expected to be inverse. The large inverse value of the α-secondary isotope effect that was measured here strongly supports a one-step mechanism (Scheme 2, case B or C) for the Diels−Alder reaction. In the case of a stepwise mechanism (Scheme 2, case A) the α-secondary isotope effect should have been close to one.[8] These effects (inverse α-secondary isotope effects) are comparable to previously calculated[8] or measured[9] isotope effects for other Diels−Alder reactions, which were interpreted as supporting a concerted mechanism.

It is interesting to note here that for the [4 + 2] cycloadditions substantial differences between calculated isotope effects for the "inside" and "outside" hydrogens on the diene terminal double bonds have been also reported.[10] These isotope effect patterns were attributed to steric and electronic interactions for the concerted Diels−Alder reactions and provide a sensitive probe of the transition state geometry.

In the present study, the averaged secondary kinetic isotope effects of the "inside" and "outside" terminal double bond hydrogens of the diene were measured experimentally. Furthermore, by using "Thornton analysis" [11] a better inside of the transition state geometry was obtained. For example, in the concerted Diels−Alder reaction of rigid s-*cis* dienes with C_{60}, the transition state may be either symmetrical—both bonds formed to the same extent—or unsymmetrical—

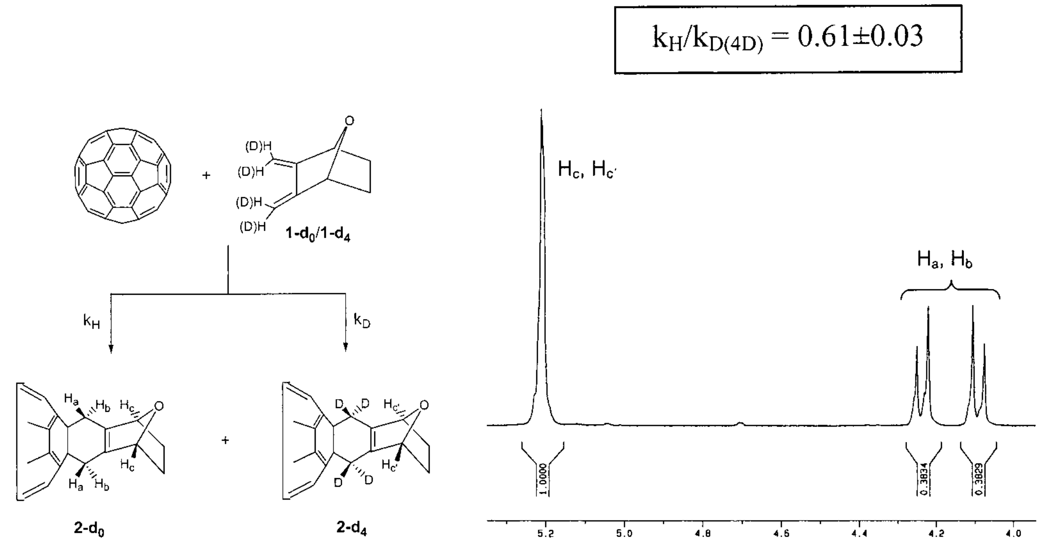


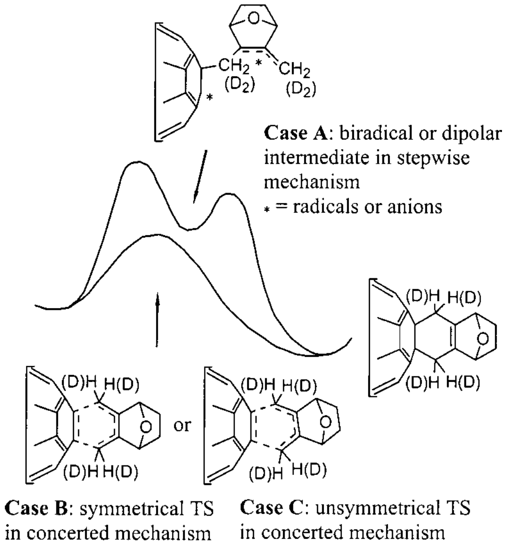
Figure 2. Determination of the intermolecular α-secondary isotope effect in the Diels−Alder reaction of **1-d$_0$**/**1-d$_4$** with C_{60} by ^{1}H NMR spectroscopy.

one bond stronger than the other—(Scheme 2, cases B and C correspondingly).

The transition-state structure was subjected to the "Thornton analysis", which provides a general method to visualize the symmetry of the transition state. For this purpose, the magnitude of the secondary deuterium isotope effect $k_H/k_{D(2D)}$ between **1-d$_0$** and **1-d$_2$** with C_{60} was measured and compared with that derived from the intermolecular competition between **1-d$_0$** vs **1-d$_4$** and C_{60}. It should be noted that k_H, $k_{D(2D)}$, and $k_{D(4D)}$ are the rate constants for the formation of Diels−Alder cycloadducts between **1-d$_0$**, **1-d$_2$**, **1-d$_4$**, and C_{60}, respectively.

As a typical procedure, a mixture of C_{60} and a 10-fold excess of an equimolar mixture of **1-d$_0$**/**1-d$_2$** was dissolved in deoxygenated toluene and heated at 80 °C. The fullerene cycloadducts **2-d$_0$** and **2-d$_2$** were purified by flash column chromatography and characterized by ^{1}H NMR spectroscopy and MALDI-TOF MS [**2-d$_0$**: *m/z* (M − 28) 814; **2-d$_2$**: *m/z* (M − 28) 816]. The value of the α-secondary isotope effect $k_H/k_{D(2D)}$ is proportional to the adduct ratio **2-d$_0$**/**2-d$_2$** and was measured by ^{1}H NMR integration of the appropriate signals.

Scheme 2. Energy versus Reaction Coordinate Diagrams for the Concerted and Stepwise Mechanisms of the Diels−Alder Reaction



It is interesting to note that hydrogen atoms H_a and $H_{a'}$ as well as H_b and $H_{b'}$ have different chemical shifts in the ^{1}H NMR spectrum (CS_2/C_6D_6 as solvent). As a result, these protons appear as two AB quartets, separated by 0.013 ppm (Figure 3). Apparently, the homoallylic location of the methylene deuterium atoms in adduct **2-d$_2$** affects the chemical shift of $H_{a'}$ and $H_{b'}$ to an extent sufficient to distinguish them from H_a and H_b.

The α-secondary isotope effect was measured by integration of the absorption of the methylene hydrogens at 4.17 ppm $[4k_H + 2k_{D(2D)}]$ and the absorption of the methine hydrogens H_c, $H_{c'}$ at 5.21 ppm $[2k_H + 2k_{D(2D)}]$. The average value of the intermolecular α-deuterium isotope effect was found to be $k_H/k_{D(2D)} = 0.78 \pm 0.03$ $[k_H/k_{D(2D)} = 0.88 \pm 0.03$ per D atom]. The results are summarized in Table 1.

The measured $k_H/k_{D(4D)}$ and $k_H/k_{D(2D)}$ values shown in Table

Table 1. α-Secondary Isotope Effects for the Diels−Alder Cycloaddition Reaction of 2,3-Dimethylene-7-oxabicyclo[2.2.1]-heptane with C_{60}

substr	solvent	*t* (h)	convn (%)[a]	*T* (°C)	k_H/k_D (av)[b]	k_H/k_D (per D)
1-d$_0$/1-d$_4$	toluene	4	45	80	0.61 ± 0.03	0.88 ± 0.03
1-d$_0$/1-d$_2$	toluene	4	45	80	0.78 ± 0.03	0.88 ± 0.03

[a] On the basis of recovered C_{60}. [b] Determined by ^{1}H NMR integration of the appropriate signals. The error was ± 4%.

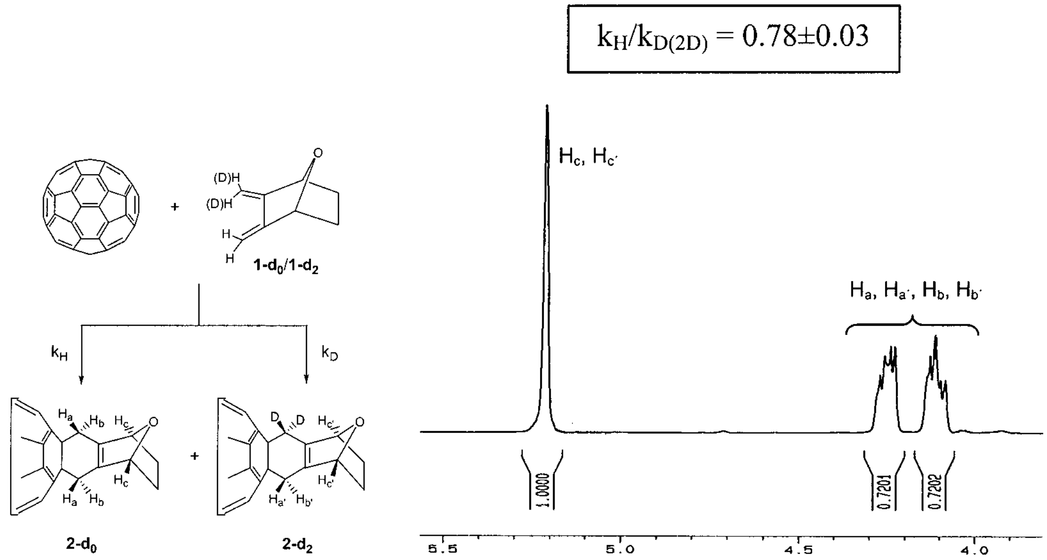
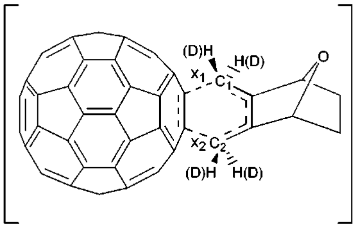


Figure 3. Determination of the α-secondary isotope effect in the Diels−Alder reaction of **1-d_0/1-d_2** with C_{60} by ^1H NMR spectroscopy.

1 were in good agreement with the mechanistic predictions of the "Thornton analysis".

In the case of a symmetrical, concerted mechanism, the new bonds x_1 and x_2 (Scheme 3) are formed at the same extent in the transition state, leading to the same extent of rehybridization (from sp^2 to sp^3) of the reaction centers C_1 and C_2. Consequently, deuterium substitution of C_1 or C_2 carbon atoms would lead to the same α-deuterium isotope effect per deuterium atom and $[k_H/k_{D(2D)}]^2$ should be exactly equal to $k_H/k_{D(4D)}$. The measured isotope effect values verify eq 1 and support a symmetrical transition state.

Scheme 3. Synchronous Transition State in the Concerted Diels−Alder Cycloaddition of Rigid s-*cis* Dienes to C_{60}



$$[k_H/k_{D(2D)}]^2 = (0.78)^2 = 0.61 = k_H/k_{D(4D)} \qquad (1)$$

In conclusion, the measured values of the α-secondary isotope effects are consistent with a concerted mechanism of the Diels−Alder reaction of rigid s-*cis* dienes with C_{60}. Comparison of the $k_H/k_{D(4D)}$ and $[k_H/k_{D(2D)}]^2$ values, applying the "Thornton analysis", supports a symmetrical transition state.

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Supporting Information Available: ^1H NMR and ^{13}C NMR spectra and GC MS for **1-d_0**, **1-d_2**, and **1-d_4**; ^1H NMR and ^{13}C NMR spectra and MALDI-TOF MS of **2-d_0**; ^1H NMR and MALDI-TOF MS of **2-d_0/2-d_2** and **2-d_0/2-d_4**; ab initio theoretical calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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