Cycloaddition of Acrylonitrile to Allene: Computed Reaction Path (AM1) and Intramolecular Secondary Isotope Effect

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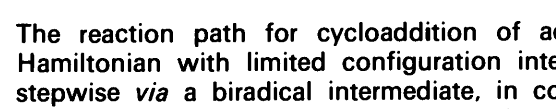
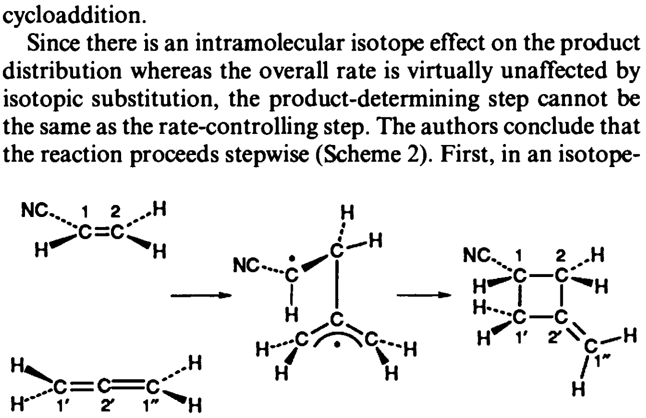
The reaction path for cycloaddition of acrylonitrile to allene was computed using the AM1 Hamiltonian with limited configuration interaction (C.I. = 4). Cycloaddition is found to proceed stepwise *via* a biradical intermediate, in confirmation of the conclusion reached by Dolbier and Dai on the basis of the intramolecular and intermolecular H/D kinetic isotope effects on the reaction. A transition state theory calculation of the ratio of the two isotopomeric products obtained from cycloaddition of acrylonitrile with *gem*-dideuteroallene is in good agreement with the experimental observations. A parallel set of computations on the cycloaddition of fluoroethylene to allene yielded similar results.

Dolbier and Dai[1,2] applied an isotopic criterion to the question of whether [$_{\pi}2 + {}_{\pi}2$]-cycloaddition, being 'forbidden' by non-conservation of orbital symmetry in the face-to-face [s + s] approach, can proceed with concerted formation of the two new σ bonds *via* the presumably 'allowed' [s + a] pathway.[3] They reacted acrylonitrile with *gem*-dideuteroallene in benzene solution between 200 and 225 °C (Scheme 1), and observed a 15–20% preference for incorporation of deuterium in the exocyclic methylene group of the product vinylcyclobutane. In contrast, competition experiments between tetradeuteriated and undeuteriated allene for a limited amount of acrylonitrile showed a negligible intermolecular isotope effect on the rate of cycloaddition.


Scheme 1

Since there is an intramolecular isotope effect on the product distribution whereas the overall rate is virtually unaffected by isotopic substitution, the product-determining step cannot be the same as the rate-controlling step. The authors conclude that the reaction proceeds stepwise (Scheme 2). First, in an isotope-insensitive rate-controlling step, a bond is formed between the unsubstituted carbon atom of acrylonitrile (C_2) and the central carbon atom of allene ($C_{2'}$) to produce a biradical intermediate. The biradical then cyclizes in a more rapid second step, which is subject to the isotope effect that determines the isotopic *exo*/*endo* ratio in the product.


Scheme 2

On the face of it, the direction of the intramolecular isotope effect is unexpected. According to conventional wisdom, closure of a biradical to a four-membered ring should be subject to an inverse isotope effect[4] that would favour incorporation of deuterium in the ring. Following Crawford and Cameron,[5] Dai and Dolbier[2] ascribe the observed normal effect (k_H/k_D) > 1 to slower rotation of the deuterated methylene group before ring-closure. A more usual qualitative explanation in terms of quantum effects on the vibrational partition functions of the respective transition states[6] would deduce that the force constants in the transition state for displacement of the exocyclic methylene hydrogen atoms are higher than for displacement of the H-atoms of the methylene group that is being incorporated in the ring. It was recently suggested by one of us[7] that the direction of the observed isotope effect implies that formation of the exocyclic double bond is nearly complete at the transition state while ring-closure has just begun. Our main purpose in this report is the detailed understanding of the intramolecular isotope effect observed with *gem*-dideuterioallene.

Computational Procedure

Before calculating the isotope effect, it was necessary to map out the pathway to ascertain that it is indeed stepwise, and to characterize the biradical and the transition state between it and the product, 1-vinyl-3-cyanocyclobutane. Since we were dealing with conversion of an open shell intermediate to a closed shell product *via* a transition state lying somewhere in between, it was clear that we would have to use a reasonably high level of configuration interaction. With 36 geometric parameters to optimize, *ab initio* methods seemed to be excessively demanding; so it was decided to use a semi-empirical program. We chose to use the AM1 hamiltonian,[8] which Dewar and Yuan[9] had employed successfully in their computations of isotope effects on elimination reactions. The computational package that we worked with was MOPAC 5.01,*[10] at the C.I. = 4 level, that includes all of the configurations that can be constructed from the two highest occupied and two lowest unoccupied molecular orbitals.

In addition to the title reaction, a parallel set of computations

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* Computations with MOPAC 5.01 were well behaved and yielded results that were virtually identical with those obtained with AMPAC 1.00 or 2.10,[11] whereas those with MOPAC 6.00[12] were not always internally consistent.

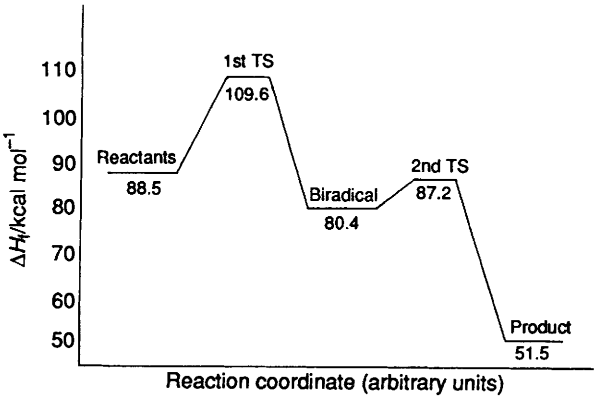

Fig. 1 Schematic reaction profile: acrylonitrile–allene cycloaddition. [The primary energy parameter calculated by MOPAC is called the enthalpy of formation (ΔH_f), the parameters of the method having been chosen so that ΔH_f approximates experimental value of ΔH_f° at 298 K, where available.]

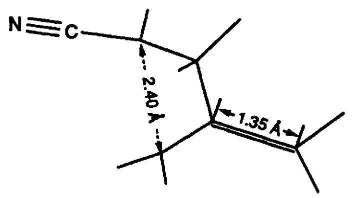

Fig. 2 Second transition state: acrylonitrile–allene cycloaddition

were carried out on the analogous cycloaddition of fluoroethylene to allene. In both cases, extrema were located on the electronic energy surface. First, reaction coordinate calculations were carried out, in which a given internal coordinate is varied systematically while all of the other coordinates are optimized so as to minimize the total electronic energy. Then, these point-by-point calculations were refined to yield both transition states and 'stable' intermediates. Thus, the geometry and electronic structure of the second transition state and the biradical were obtained from a reaction coordinate calculation on the reverse reaction. Starting from the cyclic reaction product, the C_1–$C_{1'}$ bond distance (Scheme 2) was systematically increased until the local minimum on the potential energy surface corresponding to the biradical intermediate was encountered.

In both the acrylonitrile and fluoroethylene reactions, the computations on the reactants, the final products and both transition states were brought to convergence without difficulty with a gradient norm of 0.5 or less, using the subroutines contained in MOPAC. The very flexible biradical—its lowest-lying conformation being one of several separated by low potential barriers—converged with greater difficulty: although its energy remained stable to within ±0.01 kcal mol^{-1},* its gradient norm could not be reduced below 1.6. Moreover, the seven lowest vibrational frequencies were appreciably lower than those calculated for the translations and rotations, the first three of them being essentially zero. Therefore, since the FORCE calculation did not show unequivocally that the biradical has $3N - 6$ real 'genuine' vibrations (which characterize a stable molecule), we were obliged to confirm its characterization as a 'stable' intermediate by a careful mapping of the potential energy surface in the region of the observed local minimum.

Our computations on the second transition state, the only molecular species involved in calculating the intramolecular isotope effect, were refined further by repeated sequential applications of the MOPAC subroutines SIGMA and NLLSQ, with the following results. Second transition state for allene–acrylonitrile cycloaddition: ΔH_f = 87.177 kcal mol^{-1}; gradient norm = 0.121. Second transition state for allene–fluorine cycloaddition: ΔH_f = 1.250 kcal mol^{-1}; gradient norm = 0.112.

In both isotopomers of each transition state, the absolute values of the frequencies for translation were of the order of 1 cm^{-1} or less and the frequencies calculated for rotation were between 15 and 30 cm^{-1}, whereas the lowest real frequency calculated in any of the four transition states was 85 cm^{-1}. It should be noted that isotope effects are dominated by the high frequency vibrations, specifically those involving appreciable motion of isotopic hydrogen atoms, so the contribution of the lower frequency modes is negligible.†

Results and Discussion

Geometry and Energy Along the Stepwise Pathway.—The schematic reaction profile for the cycloaddition of acrylonitrile to allene is shown in Fig. 1. The qualitative features of the mechanism proposed by Dai and Dolbier are borne out in full. The enthalpy of activation for formation of the biradical (21.1 kcal mol^{-1}) is much higher than for its closure (6.8 kcal mol^{-1}), ensuring that the first step is essentially irreversible and rate-controlling.

While the energy, geometry and force constant parameters at the first transition state were sufficiently well determined to yield the mechanistic information in Fig. 1, these parameters were not sufficiently well refined in the present study to enable the calculation of isotope effects on the first step in the reaction mechanism; the evaluation of these parameters will be the subject of a future investigation. As shown below, the careful characterization of the second transition state yields the parameters needed for calculating the intramolecular isotope effect.

As predicted,[7] the exocyclic bond (1.35 Å) in the second transition state (Fig. 2) is only slightly longer than the fully formed double bond in the product (1.33 Å), whereas the length of the new single bond is 2.40 Å, *i.e.* the two carbon atoms between which it is being formed are still essentially radical centres.

The Exclusion of Competitive Pathways.—In the course of the computations described above, as well as those on the analogous cycloaddition of fluoroethylene to allene that will be summarized briefly below, there were no indications of a tendency to depart from the stepwise pathway depicted in Scheme 2. Nevertheless, we felt obliged to ascertain whether there are other reaction paths that can compete with it, in particular whether there might be a competitive mechanism in which concerted formation of bonds C_1–$C_{1'}$ and C_2–$C_{2'}$ occurs in a single step. A number of computational tests were designed to address this point.

(1) Allene and fluoroethylene were set up in a coplanar geometry, in which internuclear distances C_1–$C_{1'}$ and C_2–$C_{2'}$ are long (5 Å) and equal, and then gradually brought closer to each other. One internuclear distance, chosen to serve as the nominal reaction coordinate, was gradually reduced, all of the remain-

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* 1 cal = 4.184 J.

† It might be pointed out in this connection that even if the lower real frequencies did turn out to be of the same order of magnitude as those calculated for the molecular rotations, the latter are prevented from mixing with them by the MOPAC procedure. The force constants for translational and rotational motions are temporarily augmented during the calculation of the internal frequencies in such a way that the six translational/rotational 'frequencies' are by far the largest normal mode frequencies of the system.

It should be noted that the calculated internal frequencies, including the imaginary frequency $\nu_{\mathrm{L}}^{\ddagger}$, of both isotopomers of the second transition state satisfied the Teller-Redlich product rule[6] to a few tenths of one percent in both reactions.

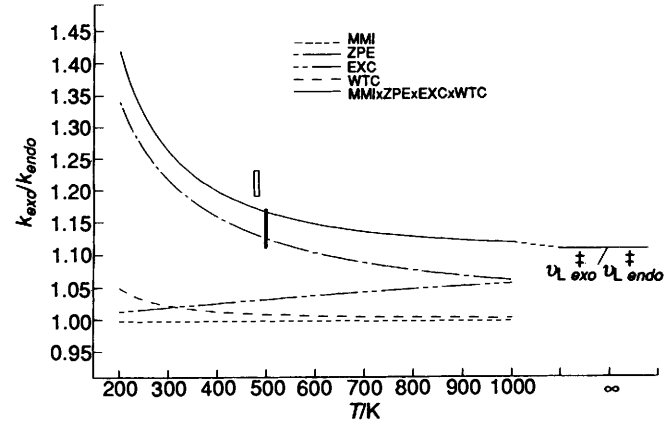

Fig. 3 Intramolecular isotope effect on acrylonitrile–allene cycloaddition. (The two experimental values[2] are indicated by rectangles; their dimensions reflect the cited experimental errors.)

ing 35 geometric parameters being optimized at each step. Whichever of several choices of 'reaction coordinate' was made, the reactants eventually adopted a mutual orientation suitable for formation of a biradical analogous to the one depicted in Scheme 2.

(2) Two tests were performed on the reverse reaction: cycloreversion of the product, 1-vinyl-3-cyanocyclobutane: (a) bond C_2–$C_{2'}$ was elongated gradually and all of the other geometric parameters were optimized at each step. At $r_{22'} \approx 2.6$ Å, a biradical is formed in which the radical centres are C_2 and $C_{2'}$. This second biradical, which is not stabilized by an electronegative substituent at either radical centre, lies approximately 20 kcal mol^{-1} above the first, too high to be an intermediate in a mechanism competitive with that shown in Scheme 2. It was therefore not investigated in detail. Along the entire pathway, $r_{11'}$ remained within less than 0.2 Å of 1.55 Å, suggesting strongly that there is no tendency to move toward a transition state for concerted rupture of both bonds.

(b) Bonds C_1–$C_{1'}$ and C_2–$C_{2'}$ of the cyclic product were assigned an equal length of 1.54 Å (intermediate between their respective lengths, 1.56 and 1.52 Å); the effect on the energy was negligible. The two bonds were then stretched together and the remaining 34 parameters optimized at each step. The calculated energy rose smoothly, peaking at a value of $\Delta H_f \approx 157$ kcal mol^{-1}, when the two bonds were 2.2 Å long. There was no significant departure from coplanarity towards the off-orthogonal [2a + 2s] orientation,[3] that would presumably 'allow' concerted cycloaddition. Even when it is recognized that the two bonds being ruptured need not have exactly the same length in the hypothetical transition state for concerted cycloreversion (and cycloaddition), the calculated energy is so much higher than that of the two transition states in the stepwise reaction (Fig. 1) that we feel justified in discounting the possibility of a competitive one-step mechanism.

Isotope Effect.—Within the framework of transition state theory, the H/D isotope effect for the rate constant of cyclization of the all-protio biradical to 1-vinyl-3-cyanocyclobutane *vs.* the corresponding rate constant for cyclization of the biradical formed from *gem*-dideuterioallene to the product deuteriated in its exocyclic methylene group is given[6] by eqn. (1)

$$\frac{k_H}{k_{exo}} = \left(\frac{Q_{gem}/Q_H}{Q'^{\ddagger}_{exo}/Q^{\ddagger}_H}\right) \times \mathrm{WTC}(\mathrm{H}/exo) \qquad (1)$$

Here, $Q'^{\ddagger}$ refers to the partition function of the relevant transition state whereas Q refers to the partition function of the biradical. The symbol WTC represents the Wigner tunnel correction, which can be calculated from a knowledge of the imaginary frequencies at the protio- and *exo*-D_2 transition states.[6] A similar equation may be written for k_H/k_{endo}. It is obvious that the intramolecular isotope effect k_{exo}/k_{endo} can be obtained by taking the ratio of these two expressions, and that the intramolecular isotope effect involves no reference to either the all-protio or *gem*-dideuteriated biradical, [(eqns. (2)–(4)].

$$\frac{k_{exo}}{k_{endo}} = (Q'^{\ddagger}_{exo}/Q'^{\ddagger}_{endo}) \times \mathrm{WTC}(exo/endo) \qquad (2)$$

$$= \mathrm{MMI} \times \mathrm{ZPE} \times \mathrm{EXC} \times \mathrm{WTC} \qquad (3)$$

$$= [\nu^{\ddagger}_{L\,exo}/\nu^{\ddagger}_{L\,endo}](s_2/s_1)f^{\ddagger}(exo/endo)\mathrm{WTC} \qquad (4)$$

Here eqn. (2) follows directly from the form of eqn. (1). In eqn. (3), MMI is the 'mass-moment of inertia' factor, which for an intramolecular isotope effect reduces to:[6,13]

$$\left[\frac{(I_A I_B I_C)^{\ddagger}_{exo}}{(I_A I_B I_C)^{\ddagger}_{endo}}\right]^{3/2}$$

where I refers to the relevant principal moment of inertia; ZPE is the isotope effect from the zero-point energy in the transition state:

$$\exp\left\{-\frac{h}{2kT}\sum_{i}^{3n-7} \nu^{\ddagger}_i(exo) - \nu^{\ddagger}_i(endo)\right\},$$

where n is the number of atoms in the transition state; EXC is the isotope effect from vibrational excitation in the transition state:

$$\prod_{i}^{3n-7} \frac{1 - \exp\{-h\nu^{\ddagger}_i(endo)/kT\}}{1 - \exp\{-h\nu^{\ddagger}_i(exo)/kT\}};$$

and WTC [or WTC $(exo)/(endo)$] is the Wigner tunnelling correction:

$$\left(1 + \frac{1}{24}\frac{|h\nu^{\ddagger}_{L\,exo}|^2}{kT)^2}\right) \Big/ \left(1 + \frac{1}{24}\frac{|h\nu^{\ddagger}_{L\,endo}|^2}{(kT)^2}\right),$$

in which $\nu^{\ddagger}_{L\,exo}$ and $\nu^{\ddagger}_{L\,endo}$ are the imaginary frequencies at the transition states for closure to the *exo*- and *endo*-deuteriated product respectively. Eqn. (4) is the expression for the rate constant ratio in terms of the transition state (isotopic partition function ratio $[(s_2/s_1)f^{\ddagger}]$ of Bigeleisen and Mayer,[6,14] which goes to unity at high temperature. As is well known,[6] eqns. (3) and (4) are completely equivalent and are connected by the Teller–Redlich product rule. Eqn. (4) demonstrates that the high temperature limit of the isotope effect reduces to the ratio of the imaginary frequencies $\nu^{\ddagger}_L$. One notes that $(s_2/s_1)f^{\ddagger}$ is independent of symmetry numbers and that there is no symmetry number factor in eqn. (4), since the symmetry numbers of both transition states are unity.

The above development is based on the assumption that the biradical intermediate exists in a single stable conformation. The present state of our MOPAC calculations leaves open the possibility that it can have several locally stable conformations of similar energy, in some of which the two methylene groups are not geometrically equivalent. As long as the different conformers of the biradical are in rapid equilibrium with one another and are in quasi-equilibrium with the same transition state, eqns. (2)–(4) are still completely valid.

The isotope effect is plotted as a function of temperature in Fig. 3. Closure at the undeuteriated end to produce the *exo*-

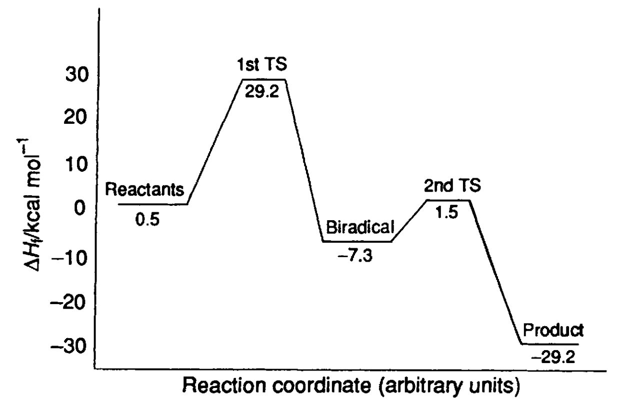

Fig. 4 Schematic reaction profile: fluoroethylene–allene cycloaddition

deuteriated product is favoured, in agreement with experiment.[2] The mass-moment of inertia factor (MMI) is close to unity and its effect is negligible. The effects due to the zero point energy difference between the two transition states (ZPE) and the Wigner tunnelling correction (WTC), both of which decrease with temperature, are augmented by the effect of vibrational excitation (EXC), that increases with temperature. At 490 K, the approximate midpoint of the range covered experimentally, the overall preference for exocyclic closure of the deuteriated methylene group (the product of the four factors enumerated above) is $k_{exo}/k_{endo} = 1.166$, in good agreement with Dolbier's two experimental values, which are plotted in Fig. 3.

The asymptotic value of the isotope effect at the high temperature limit, $(k_{exo}/k_{endo})_{T\to\infty} = 1.108$, is particularly instructive. The reduced partition function ratio and the tunnelling corrections tend to unity as the temperature increases, so the isotope effect approaches its 'classical limit', $\nu^{\ddagger}_{\mathrm{L}exo}/\nu^{\ddagger}_{\mathrm{L}endo}$, the ratio of the imaginary frequencies in the two transition states. The imaginary frequency for closure at undeuteriated $C_{1'}$ (Scheme 1) is $\nu^{\ddagger}_{\mathrm{L}exo} = 351.4i$ cm^{-1}, nearly identical with the corresponding value for the transition state of the reaction with completely undeuteriated allene (352.5i cm^{-1}). This result is consistent with our conclusion that the exocyclic methylene group is already essentially vinylic at the transition state; its two hydrogen atoms are no longer moving at the transition state, so it makes very little difference to the reaction coordinate whether it is a CH_2 or a CD_2 group. In contrast, $\nu^{\ddagger}_{\mathrm{L}endo}$, for closure at deuteriated $C_{1''}$ is a very much lower 317.2i cm^{-1}. The *exo/endo* ratio of $\nu^{\ddagger}_{\mathrm{L}}$, 1.108, is surprisingly large for a secondary isotope effect and is a major contributing factor to it. The reaction coordinate has been reduced at the transition state largely to closure of the long C_1–$C_{1'}$ (or C_1–$C_{1''}$) bond and associated readjustment of the bond- and dihedral angles at that end. When we recall that the imaginary frequency is inversely proportional to the square root of the effective mass for motion along the transition coordinate, we have to concede that Dai and Dolbier were not far off the mark when, following Crawford and Cameron,[5] they ascribed their unexpected isotope effect to slower rotation of the heavier CD_2 group as it approaches the transition state.

Allene–Fluoroethylene Cycloaddition.—To our knowledge, the analogous cycloaddition of fluoroethylene to allene has not been investigated experimentally. The results of our computations on this reaction are qualitatively very similar to those described above for acrylonitrile–allene cycloaddition. The enthalpy of activation for the first step, $\Delta H^{\ddagger} = 28.7$ kcal mol^{-1}, is substantially higher, and would require the reaction to be carried out at an appreciably higher temperature. The reaction profile, shown in Fig. 4, is similar and the isotope effect is even larger in the high temperature limit: $(k_{exo}/k_{endo})_{T\to\infty} = 1.138$.

Acknowledgements

The authors gratefully acknowledge grants of computer time from the San Diego Supercomputer Center (SDSC) and from the Office of Academic Computing at the University of California, Irvine.

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Paper 3/00457K
Received 25th *January* 1993
Accepted 23rd *April* 1993