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Substituent Effect on Stereospecificity and Energy of Concert of the Retro-Diels−Alder Reaction of Isopropylidenenorbornene

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The synchronous concerted and stepwise diradical pathways of the retro-Diels−Alder reaction of isopropylidenenorbornene have been studied theoretically at the B3LYP/6-31G* level. The effect of the isopropylidene substituent on the competition between the two mechanisms was determined by comparing these results to those obtained earlier with norbornene. The ease of internal rotation of the methylene radical center relative to the C−C bond cleavage in the diradical intermediate is compared with experimental data on stereoselectivity in the retro-Diels−Alder reaction of stereospecifically dideuterated isopropylidenenorbornene. Experimental and theoretical evidence indicates that the lifetime of the diradical is long enough for the stereochemical scrambling in the thermal retro-Diels−Alder reaction.

Introduction

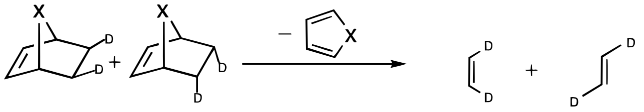
The mechanism of the Diels−Alder reaction and the reverse process has been the subject of intense interest for 60 years.[1] The stereospecificity of addition to cis or trans alkenes has been a key piece of evidence; it has been assumed that internal rotation in a diradical intermediate would result in a loss of stereochemistry and prove the presence of the intermediate.

The experimental study of the parent Diels−Alder reaction of butadiene plus cis and trans dideuterioethylene by Houk, Lin, and Brown showed that the reaction is stereospecific.[2] This was taken as evidence for a concerted mechanism of the butadiene/ethylene Diels−Alder reaction. High-level quantum mechanical calculations on the parent Diels−Alder reaction predict that the concerted mechanism is favored over the stepwise mechanisms, in accord with the stereospecificity of the reaction.[3]

Recently, Zewail has questioned whether the internal rotation of the diradical intermediate can occur during the lifetime of this species.[4] Zewail and co-workers reported a femtosecond-resolved study of the retro-Diels−Alder reaction of norbornene initiated by two-photon laser excitation. They suggested that the lifetime of the diradical intermediate (160 fs) is so short that it will not permit the internal rotation of the methylene radical center about C−C bond in this diradical intermediate: consequently, both stepwise and concerted mechanisms will produce stereochemical retention. However, in the Zewail experiment, the reaction is initiated from an excited state. The mechanism may differ from that of the thermal reactions.[5]

Klärner et al. have studied the stereoselectivity of several thermal retro-Diels−Alder reactions.[6] The retro-Diels−Alder reactions of stereospecifically deuterium-labeled norbornene (NB) and isopropylidenenorbornene (IPNB) were investigated. While the retro-Diels−Alder reaction of norbornene is stereospecific, the retro-Diels−Alder reaction of IPNB is not (Scheme 1).

SCHEME 1. Experimental Stereospecificity in the Retro-Diels−Alder Reactions of Norbornene and Isopropylidenenorbornene[6]



		T (K)	% cis	% trans
X:	$C{=}C(CH_3)_2$	483	94	6
		663	87	13
	CH_2	593	>97	<3

We have explored the potential-energy surface for the retro-Diels−Alder reaction of IPNB using density functional theory calculations with the B3LYP functional, which has proven to be very reliable for both concerted and stepwise pathways for the cyclohexene[3a] and norbornene[7] retro-Diels−Alder reactions and for related pericyclic reactions.[8] We computed the relative energies of the concerted and stepwise pathways and have compared these results to those obtained for cyclohexene[3a] and norbornene.[7] The stereospecificity predicted on the basis of these results is compared to the experimental results.

Computational Methodology

Calculations were performed with Gaussian 94[9] using the B3LYP hybrid HF-DFT method[10] with the 6-31G* basis set. Full geometry optimizations were carried out with restricted B3LYP/6-31G* calculations for closed-shell species: isopropylidenenorbornene (**1**), dimethylfulvene (**3**), ethylene (**4**), and the concerted transition structure (**2**). Open-shell species (**5**−**12**) on the diradical potential-energy surfaces were calculated at the unrestricted B3LYP/6-31G* level. Harmonic vibrational frequency analyses were performed for all the stationary points. Zero-point vibrational energies (ZPE) were obtained and are included in all the energy discussions. Thermodynamical properties at different temperatures were calculated with standard formulas.[9]

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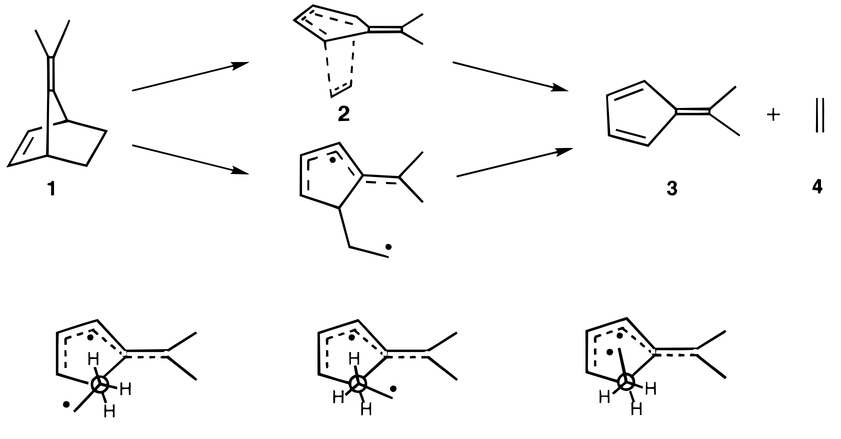

(a) gauche-out (b) anti (c) gauche-in

Figure 1. Concerted and stepwise pathways for the retro-Diels–Alder reaction of isopropylidenenorbornene.

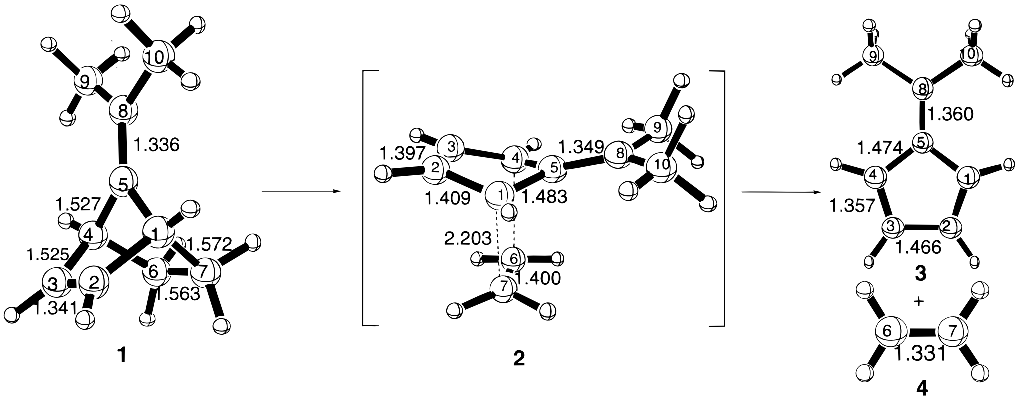

Figure 2. RB3LYP/6-31G*-optimized geometries of the reactant (**1**), concerted transition structure (**2**), and products (**3** and **4**) of the retro-Diels–Alder reaction of isopropylidenenorbornene. Bond lengths are in angstroms.

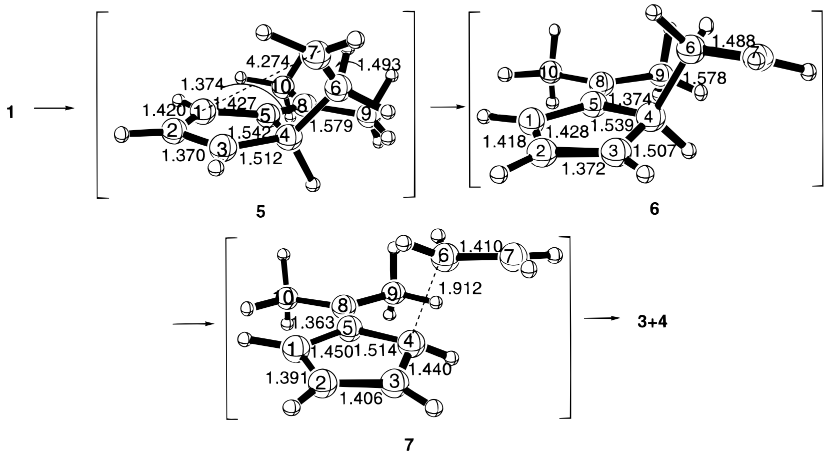

Figure 3. UB3LYP/6-31G* geometries of the stepwise gauche-out transition state (**5** and **7**) and intermediate (**6**). Bond lengths are in angstroms.

Results and Discussion

Figure 1 shows the concerted and stepwise mechanisms for the retro-Diels–Alder reaction of IPNB. The three conceivable conformers of the diradical intermediate on the gauche-out, anti, and gauche-in stepwise paths are shown.

Figure 2 shows the optimized geometries of isopropylidenenorbornene (**1**), the concerted transition structure (**2**), dimethylfulvene (**3**), and ethylene (**4**). The structures are similar to those found for the norbornene reaction, with differences expected as a result of isopropylidene conjugation. Comparing the concerted transition structure (**2**) with that of the norbornene,[7] the C1–C5 and C4–C5 bonds are both shortened by 0.03 Å, indicating conjugation of the C5–C8 π orbital with the newly forming π orbital at C2–C1 and C3–C4. This conjugation also results in a shortening of 0.04 Å for the C1–C7 and C4–C6 bonds. The isopropylidene substituent stabilizes the concerted path (Figure 5) by 5.6 kcal/mol compared with that of norbornene.[7]

Figures 3 and 4 list the geometries of the transition structures and intermediates located for the paths involving the gauche-out (**6**) and anti (**9**) diradical intermediates. Attempts to locate a gauche-in cleavage transition structure for IPNB always lead to the concerted transition structure (**2**). The potential gauche-in transition structure has a structure very close to the concerted

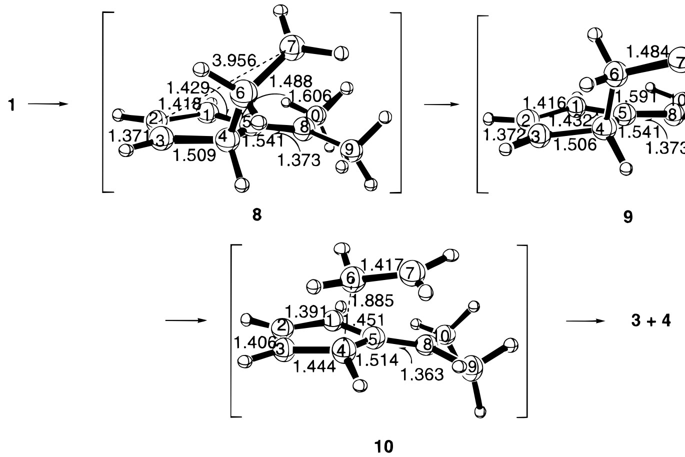

Figure 4. UB3LYP/6-31G* geometries of the stepwise anti diradical transition state (**8** and **10**) and intermediate (**9**). Bond lengths are in angstroms.

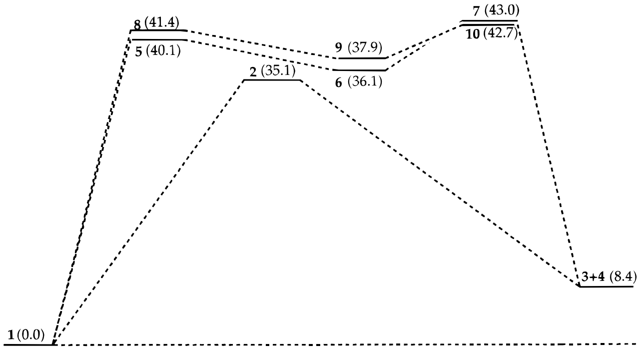

Figure 5. B3LYP/6-31G* energy profile (Δ*E* + ZPE) for the retro-Diels−Alder reaction of isopropylidenenorbornene. Energies are in kcal/mol.

transition structure, and exploration of this region of the potential energy gave the concerted transition state as the only stationary point in this region of the surface.[3] The gauche-out and anti diradicals involve more than ±120° rotation about the C4−C6 bond as the C1−C7 bond cleavage occurs (Figures 3 and 4). This causes the radical centers at C1 and C7 to move apart, and once rotation through the eclipsed conformer occurs, the stationary diradical intermediates are formed.

The species on the diradical paths of IPNB (**5**−**10**) are stabilized by a pentadienyl resonance instead of the allyl resonance in those species on the diradical paths of norbornene. The shortening of 0.06−0.1 Å for the C1−C5 bond in structures **5**−**10** reflects conjugation in the pentadienyl diradical. The energy of diradical **9** from IPNB is 10.2 kcal/mol lower than that from norbornene. Doering et al. report that the pentadienyl is 9.7 kcal/mol more stable than allyl.[11] The isopropylidene substituent lowers the activation energies for the diradical transition structures (**5**, **7**, **8**, **10**) (Figure 5) by 11−13 kcal/mol compared with those of norbornene.

Figure 5 summarizes the energetics of these reactions. At this level, the concerted path is favored by 5.0 kcal/mol relative to the first step of the diradical mechanism and by 7.6 kcal/mol relative to the second step. This is in the range of Doering's energy of concert of 2−7 kcal/mol based upon thermochemical analysis.[12] Figures 6 and 7 list the relative free energies of the retro-Diels−Alder reaction and its reverse process at 483 and 663 K, respectively. Since the diradical structures have higher entropies than the concerted structure, the free energy differences between the stepwise and concerted mechanisms decrease as the temperature increases.

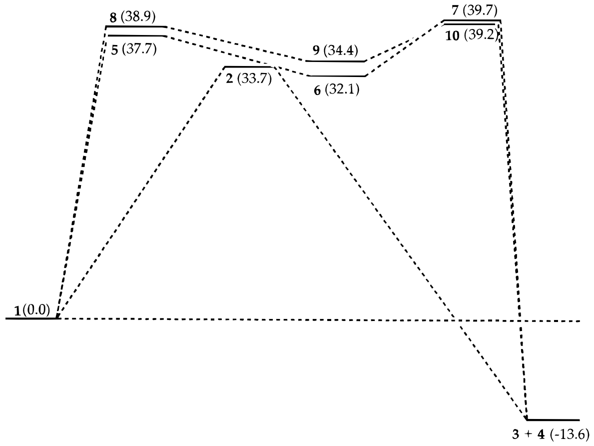

Figure 6. B3LYP/6-31G* Gibbs free-energy profile (483 K) for the retro-Diels−Alder reaction of isopropylidenenorbornene. Energies are in kcal/mol.

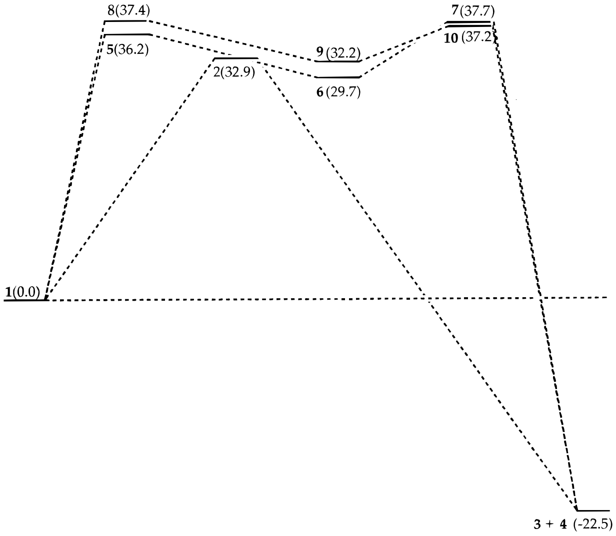

Figure 7. B3LYP/6-31G* Gibbs free-energy profile (663 K) for the retro-Diels−Alder reaction of isopropylidenenorbornene. Energies are in kcal/mol.

The experimental and B3LYP/6-31G* calculated energies, enthalpies, entropies, and free energies at 484 K are listed in Table 1. Since the Diels−Alder reactions are relatively insensitive to solvent polarity,[13] the gas-phase calculations match well with the experimental results in solution.[3] The calculated results are generally in harmony with the experimental results, although

TABLE 1: Experimental[6] and B3LYP/6-31G* Calculated Energies and Thermodynamical Parameters at 484 K, Relative to Isopropylidenenorbornene, for the Stationary Points of the Retro-Diels−Alder Reaction Potential-Energy Surface

structure	$\Delta E^\ddagger$ (kcal/mol)	$\Delta H^\ddagger$ (kcal/mol)	$\Delta S^\ddagger$ (cal/mol·K)	$\Delta G^\ddagger$ (kcal/mol)
concerted T S (**2**)	36.0	36.0	4.7	33.7
gauche-out TS (**5**)	41.8	41.8	8.4	37.7
anti TS (**8**)	42.8	42.8	8.1	38.9
experimental[6]	40.24 ± 0.21	39.28 ± 0.21	5.63 ± 0.43	36.52 ± 0.21

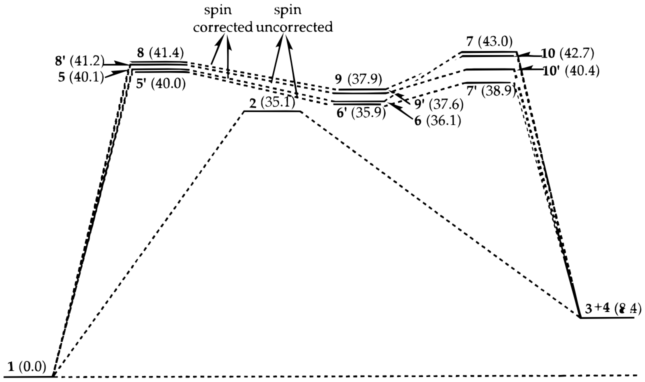

Figure 8. B3LYP/6-31G* energy profile (ΔE + ZPE) for the spin-uncorrected **5**, **6**, and **7**) and spin-corrected **5′**, **6′**, and **7′**) gauche-out diradical paths; the spin-uncorrected (**8**, **9**, and **10**) and spin-corrected (**8′**, **9′** and **10′**) anti diradical paths for retro-Diels−Alder reaction of isopropylidenenorbornene. Energies are in kcal/mol.

B3LYP/6-31G* calculations underestimate the stability of IPNB and norbornene by 2−3 kcal/mol relative to the reaction products.

The calculations presented involve unrestricted B3LYP calculations, which yield wave functions that are a mixture of singlet and triplet states for open-shell diradical species. We tested the effect of spin projection on the energetics of the two diradical paths (Figure 8). Spin-projected energies were calculated with the following approximate spin correction procedure:[3a,14a,b]

$$\Psi_{(\mathrm{UB})} = C_{\mathrm{S}}{}^{1}\Phi + C_{\mathrm{T}}{}^{3}\Phi$$

$${}^{1}E_{(\mathrm{SC})} = {}^{1}E_{(\mathrm{UB})} + f_{(\mathrm{SC})}[{}^{1}E_{(\mathrm{UB})} - {}^{3}E_{(\mathrm{UB})}]$$

$$f_{(\mathrm{SC})} = \frac{C_{\mathrm{T}}{}^{2}}{1 - C_{\mathrm{S}}{}^{2}} \approx \frac{{}^{1}\langle S^2\rangle}{{}^{3}\langle S^2\rangle - {}^{1}\langle S^2\rangle}$$

The $\langle S^2\rangle$ values of the transition structure for cleavage of the first bond and for the diradical intermediate (**5**, **6**, **8**, **9**) are all around 1; these structures are true diradicals with wave functions composed of an equal mixture of singlet and triplet spin states. The differences between the energies of the contaminated singlet and the triplet at the same geometry are very small. The spin-projected energy is lower than the contaminated singlet energy by only 0.1−0.3 kcal/mol (Figure 8), within the expected range of error. The cleavage transition structures (**7**, **10**) have less triplet mixing ($\langle S^2\rangle$ is around 0.6), and the difference in energy between the contaminated singlet and triplet states is bigger. The spin-projected singlet energy is 2−4 kcal/mol below the mixed state (Figure 8). The wisdom of using spin projection to obtain the energetics of density functional wave functions has been discussed.[3a,14c] Our experience is that experimental results on related systems are generally intermediate between the spin-contaminated and spin-projected results.[3a]

To explore whether scrambling of the stereochemistry is likely to occur in the diradical, transition structures were calculated for the rotation about the single bond to the radical center in the diradical intermediates. Barriers were obtained for rotation in the gauche-out diradical intermediate structure (**6**) via **11** and for the anti diradical intermediate structure (**9**) via **12** (Figure 9). These rotational barriers determine how readily scrambling of the stereochemistry will occur relative to bond cleavage or reclosure to reactant. If the rotation is faster than the bond cleavage in the retro-Diels−Alder reaction, a loss of stereoselectivity in the product should be observed via this mechanism.

As shown in Figure 9, B3LYP/6-31G* calculations show the rotational barrier for the gauche-out diradical (**6**) is negligible; the rotation is essentially free. This is in accord with other experimental and calculated results on alkyl radicals.[15] Since the bond-cleavage barrier is 3.0−6.9 kcal/mol (Figure 8), the internal rotation and loss of stereoselectivity is competitive with the cleavage of the diradical. In the case of the anti diradical intermediate, the steric repulsion between the isopropylidene substituent and the methylene radical center causes the methylene radical center to move away from the isopropylidene substituent during internal rotation. The rotation barrier is 0.8 kcal/mol, much lower than the bond-cleavage barrier of 2.8−4.8 kcal/mol.

The relative rates of the diradical and concerted paths were estimated by the following equation:[16]

$$\frac{k_1}{k_2} = \frac{g_1}{g_2}\exp\left(-\frac{\Delta\Delta G^\ddagger}{RT}\right)$$

$\Delta\Delta G^\ddagger$ is the difference between the activation free energy of the diradical transition structure (**5** or **8**) and that of the concerted transition structure (**2**); g_1 and g_2 are the reaction path degeneracy for the diradical and concerted paths, respectively. The path degeneracy "g" refers to the number of equivalent reaction paths leading from the reactant to transition state and, therefore, depends on the symmetry properties of both the reactant and the transition state.[16] Since the IPNB reactant (**1**) is C_s symmetric while the diradical transition state (**5** or **8**) is asymmetric, the diradical path degeneracy (g) is 2. The concerted transition state (**2**) is C_s symmetric, so that the degeneracy of the concerted reaction path is 1.

The internal rotation of the methylene radical center about the C6−C7 bond in the diradical intermediates is nearly free, while the barriers of both cleavage and closure are significant. Reaction by the diradical pathway should produce approximately 50% *cis*- and 50% *trans*-dideuterioethylene.[10] The experimental and computational stereospecificities for the retro-Diels−Alder reactions of isopropylidenenorbornene and norbornene are listed in Table 2. The yield of the scrambling product of the stepwise path, *trans*-dideuterioethylene, is predicted to be 2% and 10% at 483 and 663 K, respectively, as compared to the experimental results of 6% and 13% at the same temperatures. The theoretical and experimental results are in excellent agreement. For comparison, in the retro-Diels−Alder reaction of norbornene at 593 K, the experimental stereospecificity is greater than 97%[6] and the calculations estimate it to be greater than 99.99%. The concerted mechanism is predominant in this retro-Diels−Alder reaction.

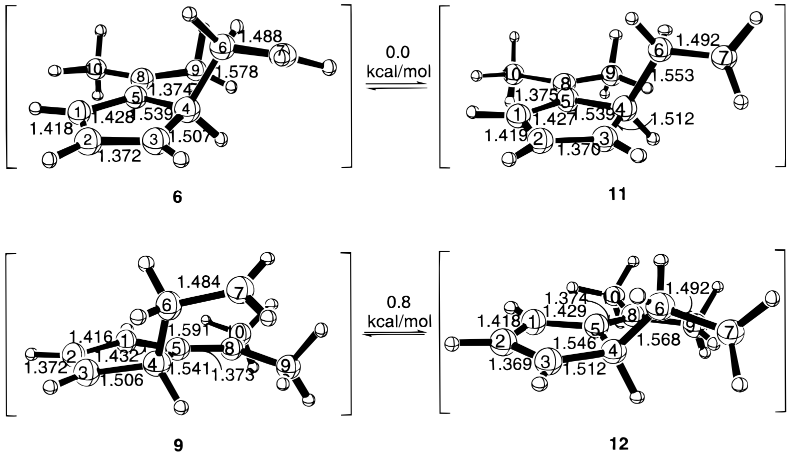

Figure 9. UB3LYP/6-31G*-optimized geometry of the internal rotation transition structure (**11**) of the intermediate (**6**) in the gauche-out diradical pathway and the internal rotation transition structure (**12**) of the intermediate (**9**) in the anti diradical pathway of the retro-Diels−Alder reaction for isopropylidenenorbornene. Bond lengths are in angstroms.

TABLE 2: Experimental[6] and Computational Stereospecificity in the Retro-Diels−Alder Reactions of Isopropylidenenorbornene and Norbornene, Beginning from *cis*-Dideutero Reactants

molecule	method	*T* (K)	% *cis*-dideuterioethylene	% *trans*-dideuterioethylene
isopropylidenenorbornene	experimental[6]	483	94	6
	computational	483	98	2
	experimental[6]	663	87	13
	computational	663	90	10
norbornene	experimental[6]	593	>97	<3
	computational	593	>99.99	<0.01

The activation barriers of the diradical for closures of diradicals **6** or **9** back to **1** are 4.0−4.1 and 3.5−3.6 kcal/mol. These barriers are close to the bond-cleavage barriers 3.0−6.9 and 2.8−4.8 kcal/mol (Figure 8) of diradicals **6** or **9** leading to products. Partial scrambling of the deuterium labels of the starting material **1**, reisolated after incomplete reaction, is expected to occur to a small or large extent depending upon the actual value of the reclosure barriers. In the flow thermolysis of **1**, a conversion up to 60% of **1** was observed, while the ^{1}H NMR spectrum of reisolated **1** was unchanged.[17] These experimental results indicate that there is not a great deal of reversion of **6** or **9** to **1**, but a longer conversion time and greater detection precision could be required to detect a small amount of reversion.

The computational study rationalizes the experimental results and supports the observed stereochemical scrambling results from the diradical pathway. The intermediate in the thermal experiments of IPNB clearly gives the internal rotation products, in contrast to the observation that the lifetime of the diradical intermediate generated photochemically is too short to allow scrambling of stereochemistry[4] in the retro-Diels−Alder reaction. It is likely that the species observed in these experiments is not the same as the diradicals involved in the thermal retro-Diels−Alder reaction.[7]

Conclusion

The concerted mechanism is predicted to be predominant in the retro-Diels−Alder reaction of isopropylidenenorbornene, but pentadienyl resonance stabilizes the stepwise pathway sufficiently to make it detectable experimentally. The free internal rotation in the diradical intermediate indicates that there will invariably be loss of stereochemistry in the stepwise mechanism. The lifetime of the diradical intermediate is predicted to be sufficiently long for the occurrence of internal rotation in the thermal Diels−Alder reaction.

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