

Transition Structures, Energetics, and Secondary Kinetic Isotope Effects for Cope Rearrangements of *cis*-1,2-Divinylcyclobutane and *cis*-1,2-Divinylcyclopropane: A DFT Study

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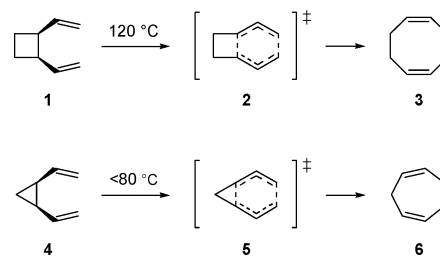
The minimum energy reaction paths and secondary kinetic isotope effects (KIE) for the Cope rearrangements of *cis*-1,2-divinylcyclobutane and *cis*-1,2-divinylcyclopropane obtained by (U)B3LYP calculations are reported. Both reactions proceed through endo-boatlike reaction paths, and have aromatic transition states. The predicted activation energies are in agreement with the experimental data. The reaction paths of the rearrangements are intervened by enantiomerization saddle points of the products (and the reactant in the case of divinylcyclobutane). The calculated KIEs are similar in the two systems, and consistent with the geometries of the transition structures. There is computational evidence that the isotope effect associated with the conversion of a pure sp^2 C–H bond into a pure sp^3 one might be the same in all molecules. The predicted KIEs agree with experiment for divinylcyclopropane, but not for divinylcyclobutane.

Introduction

The facile thermal $\sigma^2s+\pi^2s+\pi^2s$ (Cope) rearrangement of *cis*-1,2-alkenylcycloalkanes represents a very rapid entry into *cis,cis*-cycloalkadienes.¹ As illustrated in Scheme 1, *cis*-1,2-divinylcyclobutane-to-*cis,cis*-1,5-cyclooctadiene (**1** to **3**)² and *cis*-1,2-divinylcyclopropane-to-*cis,cis*-1,4-cycloheptadiene (**4** to **6**)³ rearrangements are the most known and studied examples of these types of reactions. Particularly since 1980, synthetic applications of these reactions have been explored and studies have shown that these rearrangements provide a versatile, effective method for the construction of functionalized cyclic compounds.^{1–3}

The thermal rearrangements of divinylcyclobutane **1**⁴ and divinylcyclopropane **4**⁵ were first reported by Vogel in 1958 and 1960, respectively, and these rearrangements were studied extensively from a mechanistic point of view.^{3,6,7} Driven by the release of ring strain, the Cope rearrangements of both **1** and **4**, particularly that of **4**, often proceed at significantly lower temperatures than analogous reactions involving acyclic 1,5-dienes.^{5c,8} In his experiments, Vogel did not isolate **4**, since, under the conditions of its formation, it rearranges rapidly to **6**.⁵

SCHEME 1



Indeed, it was not until more than a decade later that divinylcyclopropane **4** was isolated and shown to rearrange to cycloheptadiene **6** with half-lives of approximately 90 s and 25 min at 35 °C and 11 °C, respectively.⁹ It should be noted that charged-accelerated versions of these reactions proceed under unusually mild conditions.¹⁰ Subsequent physical organic studies elucidated the important mechanistic features of these reactions.^{3,6,7}

The mechanism of the Cope rearrangement has been the subject of intense experimental and theoretical investigations.^{1,11–13} Two reaction paths have been established for the rearrangement of the parent 1,5-hexadiene system: (i) a “chairlike” path in which the molecule maintains a chairlike (C_{2h}) geometry and (ii) a “boatlike” path along which the molecule has a boatlike C_{2v} symmetry. In the parent molecule, the chairlike path has an experimental activation enthalpy of 33.5 kcal/mol whereas the boatlike path has a higher activation en-

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thalpy estimated to be about 11.2 kcal/mol larger than that of the chairlike path. Along each path, one may conceive three types of stationary points corresponding to qualitatively different molecular structures based on the magnitude, R , of the forming–breaking bond lengths (C1–C6 and C3–C4 bonds). They will be referred to as: (i) “tight” ($R < 1.8$ Å; the 1,4-diyl structure), (ii) “aromatic” ($R \approx 1.9$ – 2.3 Å), and (iii) “loose” ($R \geq 2.5$ Å; the bis-allyl structure). The minimum energy path of 1,5-hexadiene is the chairlike path passing through a single (aromatic) transition state of C_{2h} symmetry.^{11d,e}

Reactions of substituted 1,5-hexadienes are generally faster than the parent reaction, implying that substituents lower the activation enthalpy below 33.5 kcal/mol. Substituents may reduce the symmetry, but the chairlike and boatlike paths survive. For the majority of substituents, the chairlike path is lower in energy^{11b} and, hence, is the minimum energy path as in the parent molecule. Chemical intuition suggests that switching between the two reaction paths may be realized by simultaneous control of sites 3 and 4 of the parent molecule. From this point of view, divinylcyclopropane **4** and divinylcyclobutane **1** molecules may be regarded as the simplest substituted 1,5-hexadienes fulfilling this requirement. The rigidity imposed on the carbon chain by fusing a cyclopropane or a cyclobutane ring at the 3,4 positions may be sufficient to reverse the usual order of the chairlike and boatlike pathways.

It appears to be well accepted that the rearrangements of both **1**^{6,7} and **4**^{3,8c,13} proceed in a concerted fashion via boatlike transition states, in which the vinyl groups lie over the four- and three-membered rings to afford cyclooctadiene **3** and cycloheptadiene **6** (Scheme 1). The energy of activation E_a for the rearrangements of **1** into **3** and **4** into **6** has been reported to be about 24.0^{7a,b} and 19.0–20.0^{9a,d,14} kcal/mol, respectively. The activation energy for the rearrangement of **4** into **6** is approximately 4.0–5.0 kcal/mol lower than that of **1** into **3**. To explore differences in the transition structures (TS) for the 3,3-sigmatropic shift of **4** relative to that of **1**, Gajewski measured the secondary deuterium kinetic isotope effects

(KIE) at the vinyl termini of both materials.¹⁵ For the cyclopropane derivative, k_H/k_{D4} was 0.78(± 0.09) at 10 °C in deuteriochloroform. For the cyclobutane derivative, k_H/k_{D4} was 0.96(± 0.02) at 77.7 °C in hexachlorobutadiene solvent. In light of these KIEs, Gajewski concluded that there is more bonding at the terminal carbons in the TS for the rearrangement of the cyclopropane analogue and relatively little bonding at the termini in the rearrangement of cyclobutane material.¹⁵

Recently, Cope rearrangement of divinylcyclobutane **1** has been theoretically studied at the levels of RHF/6-31G* and MP2(full)/6-31G**/RHF/6-31G*¹⁶ and B3LYP/6-31G*.¹⁷ Although activation energies calculated at the RHF/6-31G* level were quite high as compared with the experimental values, the pathway through the boatlike transition state had the lowest activation barrier. On the other hand, single-point MP2 calculations at the RHF/6-31G* geometries predicted activation energies closer to the experimental value but, within the limitations of MP2 method employed, the chairlike transition state was favored over the boatlike transition state by 1.1 kcal/mol,¹⁶ in contrast with the experimental findings. Formation of *trans,trans*-1,5-cyclooctadiene from divinylcyclobutane **1** has been recently investigated at the B3LYP/6-31G* level, and the activation barrier for this rearrangement has been calculated to be 31.4 kcal/mol.¹⁸ Cope rearrangement of divinylcyclopropane **4** has been theoretically studied as well.^{19,20} The calculated activation enthalpy of 19.7 kcal/mol¹⁹ at the B3LYP/6-31G* level is in good agreement with the experimentally derived value of 19–20 kcal/mol.^{9a,d,14} Moreover, the reaction enthalpy for this rearrangement was calculated to be –20.1 kcal/mol at the same level of theory.

The mechanisms and activation barriers of pericyclic reactions are a subject of continuing interest. The aim of this study is to contribute to a better understanding of such processes.^{11c,21} We report herein a detailed study of the Cope rearrangements of *cis*-1,2-divinylcyclobutane (**1**) and *cis*-1,2-divinylcyclopropane (**4**) at the (U)B3LYP level, and explore properties of the TSs in the Cope rearrangements of **1** and **4**, particularly via secondary KIEs.

Computational Methods

Calculations were performed mainly at the Density Functional Theory (DFT) level by using the Gaussian 98 program package.²² Becke's three-parameter exchange functional (B3)²³ in conjunction with the Lee–Yang–Parr correlation functional

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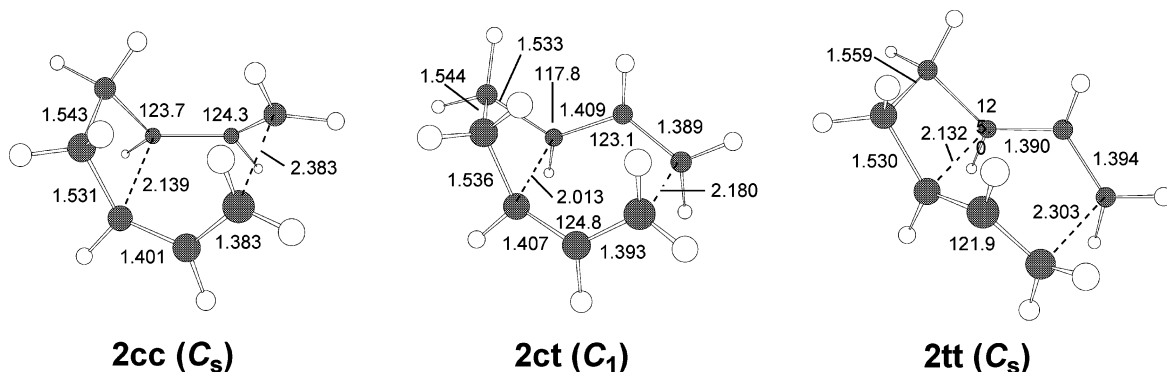


FIGURE 1. Selected interatomic distances (Å), bond angles (deg), and point groups (in parentheses) for transition structures shown in Scheme 2.

(LYP)²⁴ was employed as implemented in Gaussian 98.²² The majority of geometry optimizations employed Pople's 6-31G* split valence basis set.²⁵ The advantages and disadvantages of the (U)B3LYP/6-31G* method have been assessed by Houk and co-workers.^{11c,12,26} Very recently, (U)B3LYP/6-31G* calculations have been successfully used in the calculation of TSs and reaction parameters for similar pericyclic rearrangements.¹² Some of the optimizations were repeated with larger basis sets, and also with *ab initio* methods as indicated below.

In all regions of the potential energy surfaces explored in this work, the spin-restricted DFT was stable with respect to spin-symmetry breaking (i.e. $\langle S^2 \rangle = 0$ with UB3LYP, using the "guess=(mix,always)" option). Geometries were optimized without constraint. Vibrational frequencies were computed to characterize each stationary structure as a minimum or TS, via the number of imaginary frequencies (zero for minima and one for saddle points, respectively). After locating a TS, intrinsic reaction coordinate (IRC)²⁷ calculation was carried out to identify its respective reactant and product. All results reported in this work refer to such completely verified reactant–TS–product triples.

Electronic energies and zero-point vibrational energies (ZPVE) of the reactants, TSs, and products for Cope rearrangements of divinylcyclobutane **1** and divinylcyclopropane **4** are given in the Supporting Information. Designations of the species involved and their relative energies including ZPVE are given in Schemes 2 and 3. For the reactants and TSs, **c** denotes a vinyl group in the endo orientation while **t** shows that in the exo orientation. For the products, **c** denotes a cis

double bond while **t** shows a trans one. Secondary KIEs were calculated at the same level of theory (B3LYP/6-31G*) from free energies of activation, as will be discussed later, and no scaling factor was applied.

Results and Discussion

Divinylcyclobutane. Initially, the Cope rearrangement of divinylcyclobutane **1** to cyclooctadiene **3** was studied as shown in Scheme 2. The computed geometries of TSs are depicted in Figure 1. Depending upon the orientation of vinyl groups, three distinct conformations of **1** were located. These conformers are easily interconvertible isomers due to small activation barriers. The conformational barrier from **1tt** to **1ct** is 1.7 kcal/mol and that from **1ct** to **1cc** is 3.6 kcal/mol. No direct pathway between **1tt** and **1cc** could be located. In all conformers the four-membered ring is slightly folded, which gives partial relief from the eclipsing of bonds. We located three aromatic TSs, two of them (**2cc** and **2tt**) are boatlike and one (**2ct**) is chairlike. The former can be classified as endo- (**2cc**) and exo-boatlike (**2tt**) TSs based on the orientation of the four-membered ring relative to vinyl groups. The endo-boatlike TS (**2cc**) is lowest in energy with the chairlike TS (**2ct**) lying between **2cc** and **2tt**. Hence, the rearrangement of **1** is predicted to take place along the endo-boatlike path passing through **2cc**. Four-membered rings in the boatlike TSs **2cc** and **2tt** adopt a planar structure, and moreover the forming and breaking bonds in both TSs are eclipsed. Thus boatlike TSs appear to suffer from the slightly worse eclipsing interactions. However, the four-membered ring in the chairlike TS is folded, and the forming and breaking bonds in this structure are somewhat staggered, which partially reduces the eclipsing of bonds. It should be noted that endo- and exo-boatlike TSs **2cc** and **2tt** are looser than the chairlike TS **2ct** since the forming (2.383 and 2.303 Å) and breaking bonds (2.139 and 2.132 Å) in the boatlike TSs are slightly longer than the forming (2.180 Å) and breaking bonds (2.013 Å) in the chairlike TS. The length of the breaking bond in the chairlike TS, **2ct**, is the same as that in the parent 1,5-hexadiene, but the forming bond is almost as long as that (2.210 Å) in the boatlike TS of the parent. The predicted activation barriers are 25.0, 26.9, and 31.4 kcal/mol for the three possible Cope rearrangements in Scheme 2, the lowest of which is in good agreement with the experimentally derived E_a of

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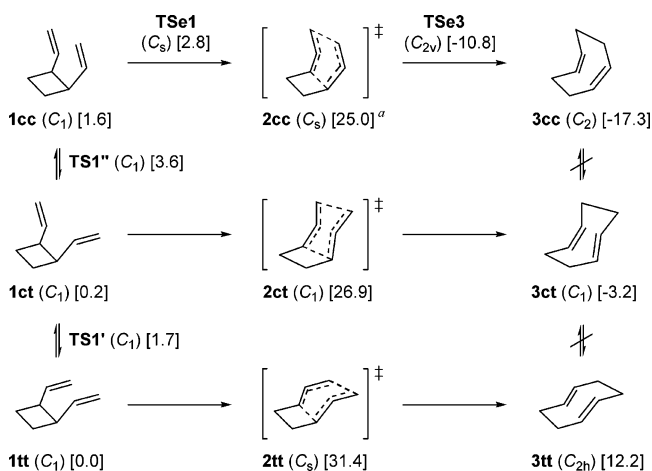
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SCHEME 2. Point groups in Parentheses and Energies, Including ZPVE (kcal/mol), in Brackets Relative to Those of 1tt


^a 24.2 kcal/mol at the UB3LYP/6-311G+(d,p) level.

24.0 kcal/mol.^{7a,b} The energy of chairlike TS **2ct** is comparable to that of endo-boatlike TS **2cc**; this may be due to smaller amount of eclipsing interaction in the former, as noted before. Compared to the Cope rearrangement of 1,5-hexadiene (barriers of 34.0 kcal/mol for chairlike rearrangement and 42.0 kcal/mol for boatlike rearrangement at the same level of theory),^{11c,28} the barriers for the rearrangement of divinylcyclobutane **1** are reduced by 7.1, 17.0, and 10.6 kcal/mol for the chairlike, endo-boatlike, and exo-boatlike rearrangements, respectively. The largest effect occurs in the TS **2cc**, making the endo-boatlike path the least energy path.

The minimum energy path, or simply the reaction path, connecting **1cc** (reactant) and **3cc** (product) through **2cc** (TS) deserves further consideration. The TS has C_s symmetry whereas **1cc** is unsymmetrical, and **3cc** has C_2 symmetry; the symmetry of **2cc** is broken on both sides of the saddle point before reaching the stable species. To explore the details of the path, IRC calculations (initiated from **2cc**) were carried out (see path A in Figure 2). At **2cc**, the vibration with imaginary frequency (the “ts mode”) is totally symmetric, and as a result, the reaction path initially maintains the C_s symmetry on both sides of **2cc**. It smoothly joins the saddle points labeled as **TSe1** and **TSe3** in Figure 2. They are TSs for enantiomerization of **1cc** and **3cc**, respectively. The barrier for the passage of **1cc** to its enantiomer through **TSe1** is only 1.1 kcal/mol so that **1cc** has effectively C_s symmetry. There is no such enantiomerization saddle point in the case of divinylcyclopropane (see path B in Figure 2) as the C_s -symmetric **4cc** is stable. The small enantiomerization energy, 1.1 kcal/mol, of **1cc** may be ascribed to the difference between the ring strains of **1cc** and **4cc**. The barrier for the enantiomerization of **3cc** through **TS3e** is 6.5 kcal/mol. The symmetry of the molecule at **TSe1** is C_s , and that of **TSe2** is C_{2v} , the latter corresponding to the symmetrical *cis,cis*-1,5-cyclooctadiene structure (**3cc**). The ts modes at both **TSe1** and **TSe3** are nontotally symmetric (a'' of

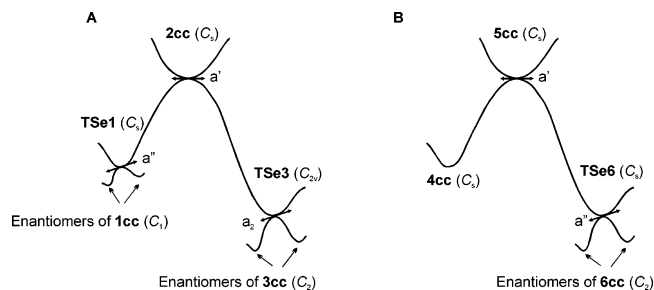


FIGURE 2. Qualitative features of the reaction paths: (A) divinylcyclobutane and (B) Divinylcyclopropane. Double-headed arrows show the vibrational modes with imaginary frequencies; symmetry species of the modes are also indicated.

C_s and a_2 of C_{2v} groups, respectively), and therefore, symmetry of the reaction path coming from **2cc** is broken at these points. Actually, of course, the reaction path turns into a ridge before reaching these points. Summarizing, the reaction path starting from **2cc** bifurcates upon reaching the ridge near **TSe1** on the **1cc** side, or **TSe3** on the **3cc** side, and ends up with an enantiomer of **1cc** or **3cc**, respectively. It is interesting that three consecutive saddle points occur along the path connecting **1cc** to **3cc**. Examples of such sequential TSs without intervening intermediates are known.²⁹

The formation of cyclooctadiene **3cc** is quite exothermic, but that of cyclooctadiene **3ct** is slightly exothermic due to the larger ring strain present in the latter. Cyclooctadiene **3cc** is twisted in such a manner as to bring the neighboring methylene units into a staggered conformation. Although this causes a transannular steric repulsion between cross methylene hydrogens which are only 1.978 Å apart (Figure S1), the relief from eclipsing bonds for **3cc** is apparently more important than that from transannular interactions. Indeed, the eclipsed, C_s symmetric structure is **TSe3**, which lies 6.5 kcal/mol above **3cc**, as stated before. In fact, for most rings, there is no escape from at least one of these types of strain. Similarly, methylene carbons in **3ct** are staggered. Cyclooctadiene **3ct** is less stable than **3cc** by 14.1 kcal/mol. This may be taken as the amount of ring strain caused by the change of one *cis* double bond in **3cc** with a *trans* one. An independent synthesis of **3ct** has shown that it is thermodynamically unstable with respect to the *cis*-*cis* isomer **3cc**, and it easily converts to **3cc** when treated with iodine.³⁰ As expected, formation of cyclooctadiene **3tt** is not energetically favorable since the presence of two *trans* double bonds as well as eclipsing interactions between methylene carbons increase the strain by 29.5 kcal/mol in comparison to its *cis,cis* analogue, **3cc**. The

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(30) (a) Cope, A. C.; Howell, C. F.; Knowles, A. *J. Am. Chem. Soc.* **1962**, *84*, 3190. (b) Cope, A. C.; Ganellic, C. R.; Johnson, H. W. *J. Am. Chem. Soc.* **1962**, *84*, 3191. (c) Cope, A. C.; Howell, C. F.; Bowers, J.; Lord, R. C.; Whitesides, G. M. *J. Am. Chem. Soc.* **1967**, *89*, 4024.

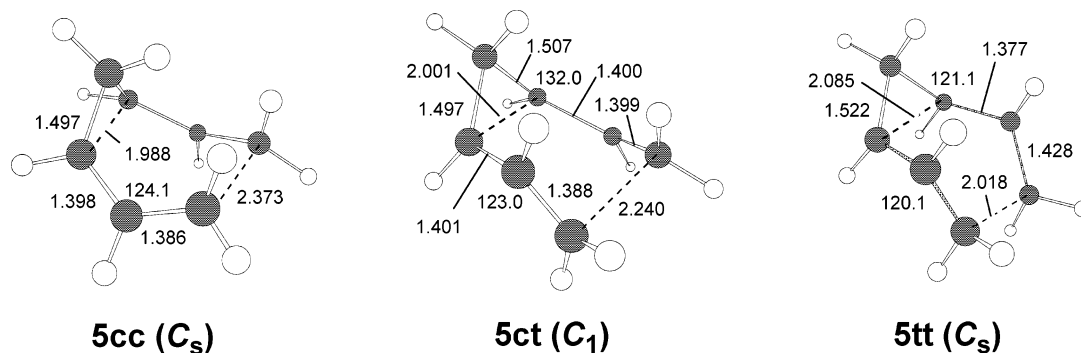
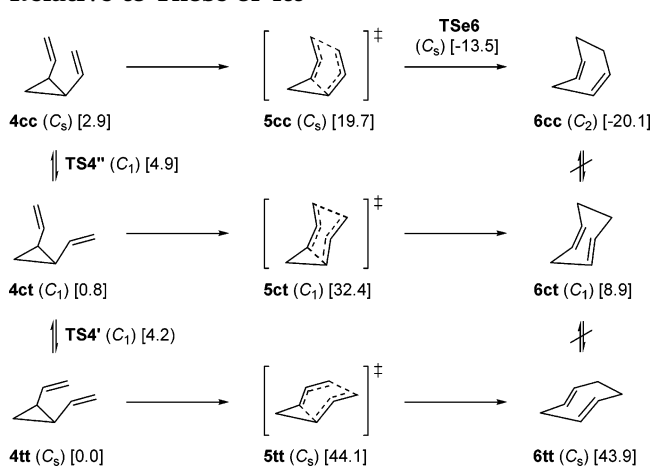


FIGURE 3. Selected interatomic distances (Å), bond angles (deg), and point groups (in parentheses) for transition structures shown in Scheme 3.

bond distance between adjacent methylene carbons is slightly longer (1.622 Å) for a C–C single bond, most likely as a result of the strain present in this compound. The structure of **3tt** was further verified by using (U)-B3LYP/6-311+G* with the “tight” convergence criteria. No significant change in geometries was observed. Synthetic studies have shown that cyclooctadiene **3tt** is very sensitive to traces of oxygen or acid and it polymerized explosively on the addition of solvent that had not been deoxygenated.³¹ However, it is stable while frozen at –78 °C under an inert atmosphere or when kept in a dilute solution of degassed aprotic solvents.³¹ The ring strains and eclipsing interactions associated with 1,5-cyclooctadienes seem to be reflected inversely in the exothermicities of the rearrangements to some extent. Although cyclooctadienes **3cc**,^{4,7} **3ct**,³⁰ and **3tt**³¹ are all known compounds, the Cope rearrangement of *cis*-1,2-divinylcyclobutane (**1**) is well-known to produce only *cis*,*cis*-1,5-cyclooctadiene (**3cc**). Formation of a *cis*,*trans*-1,5-cyclooctadiene derivative from the Cope rearrangement of *trans*-1,2-*cis*,*cis*-dipropenylcyclobutane, however, was proposed but as an intermediate.⁷ To the best of our knowledge, there is no report regarding the formation of a *trans*,*trans*-1,5-cyclooctadiene derivative from these types of rearrangements. The direct interconversion of cyclooctadienes **3cc**, **3ct**, and **3tt** is most unlikely since a formal *cis*/*trans* alkene isomerization of this type could occur only by a stepwise mechanism.¹² It should be noted that the reaction pathway connecting **1tt** to **3tt** via **2tt** was studied previously at the same level of theory, which is consistent with our current results.^{17,18}

Divinylcyclopropane. Cope rearrangement of divinylcyclopropane **4** to cycloheptadiene **6** was next investigated as exemplified in Scheme 3. The computed geometries of TSs are depicted in Figure 3. Although the rearrangement of **4** was previously studied in part,^{19,20} we investigated this rearrangement in more detail to compare it against its four-membered-ring analogue **1**. We first located three distinct conformations of **4**, which are easily interconvertible due to low activation barriers. The conformational energy barrier is 4.2 kcal/mol from **4tt** to **4ct** and 4.9 kcal/mol from **4ct** to **4cc**. No direct pathway between **4tt** and **4cc** could be located (Scheme 3), as in the case of conversion of **1tt** to **1cc** (Scheme 2).

SCHEME 3. Point groups in Parentheses and Energies, Including ZPVE (kcal/mol), in Brackets Relative to Those of **4tt**



The calculated pathways into cycloheptadienes **6cc**, **6ct**, and **6tt** involve endo-boatlike **5cc**, chairlike **5ct**, and exo-boatlike **5tt** TSs with barriers of 19.7, 32.4, and 44.1 kcal/mol, respectively. The forming and breaking bonds are eclipsed in the endo- and exo-boatlike TSs **5cc** and **5tt**, while they are staggered in the chairlike TS **5ct**. The barrier of 19.7 kcal/mol for **5cc** is in good agreement with the experimentally derived E_a of 19–20 kcal/mol.^{9a,d,14} As in the **3cc** case, the eclipsed C_s symmetric configuration derived from **6cc** is a TS between the two enantiomers of **6cc** (**TS6** in Figure 2B). The barrier is 6.6 kcal/mol, similar to that in **3cc**. **TS6** lies on the reaction path between **5cc** and **6cc** near which the path bifurcates. The endo- and exo-boatlike TSs suffer from the slightly worse eclipsing interactions. The breaking bond in all TSs is roughly the same and around 2 Å. However, the forming bond (2.373, 2.240, and 2.018 Å for **5cc**, **5ct**, and **5tt**, respectively) shows a decrease in the order of **5cc**, **5ct**, and **5tt**. Clearly, endo-boatlike TS **5cc** is looser than chairlike and exo-boatlike TSs **5ct** and **5tt**, and it is energetically most favored, giving rise to formation of cycloheptadiene **6cc**. Adjacent methylene carbons in **6cc** are staggered, which reduces the eclipsing of bonds.

Formation of cycloheptadiene **6cc** is quite exothermic but formation of **6ct** and **6tt**, especially the latter, is not energetically favorable due to increasing ring strain. Cycloheptadienes **6cc** and **6ct** are relatively free of eclipsing interactions since adjacent methylene carbons in them are staggered. However, cycloheptadiene **6tt**

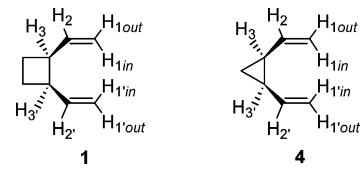
(31) (a) Whitesides, G. M.; Goe, G. L.; Cope, A. C. *J. Am. Chem. Soc.* **1967**, *89*, 7136. (b) Whitesides, G. M.; Goe, G. L.; Cope, A. C. *J. Am. Chem. Soc.* **1969**, *91*, 2608. (c) Boeckh, D.; Huisgen, R.; Noth, H. *J. Am. Chem. Soc.* **1987**, *109*, 1248.

experiences slightly worse eclipsing interactions due to eclipsed methylene carbons. Cycloheptadienes **6ct** and **6tt** are less stable than their cis,cis analogue, **6cc**, by 29.0 and 64.0 kcal/mol, respectively. Apparently, replacement of a cis double bond in a cycloheptadiene system with a trans one increases the ring strain by approximately 29.0–32.0 kcal/mol, which is roughly twice that (14.1–15.2 kcal/mol) in a cyclooctadiene system. It should be noted that due to severe ring strain the bond distance between adjacent methylene carbons in **6tt** is lengthened to 1.751 Å, which is very long for a C–C single bond. Since work by Zavitsas³² appears to have placed an upper limit of 1.75 Å for a C–C bond, it became necessary to explore the geometry of **6tt** in further detail. This species was reoptimized by using a larger basis with UB3LYP, and also by Møller–Plesset³³ (MP2) and CASSCF methods. The UB3LYP method with the triple-split valence basis, 6-311G(d,p),³⁴ elongated the bond slightly to 1.760 Å, and there was no spin contamination.³⁵ The spin-restricted MP2/6-31G(d) wave function was unstable toward spin symmetry breaking, and the unrestricted UMP2(full)/6-31G(d) optimization reduced the aforementioned bond length to 1.666 Å at the expense of a large spin contamination ($\langle S^2 \rangle = 1.04$).³⁶ A four-electron, four-orbital, (4e,4o) CASSCF/6-31G(d) calculation predicted an even smaller bond length of 1.629 Å (nearly the same as the B3LYP/6-31G(d) value in **3tt**). The true bond length probably lies near the latter value in agreement with Zavitsas. Since **6tt** is not expected to have any significant stability, it was not investigated further. To the best of our knowledge, cycloheptadienes **6ct** and **6tt** are unknown compounds.

Kinetic Isotope Effects. We have also calculated the secondary KIEs at various positions using the definition, $KIE = k_H/k_D = \exp(-\delta\Delta G^\ddagger/RT)$, where $\delta\Delta G^\ddagger = \Delta G_H^\ddagger - \Delta G_D^\ddagger$, with ΔG_H^\ddagger and ΔG_D^\ddagger being the activation free energies of the protonated and the deuterated species, respectively.^{37–39} A value of KIE = 1 means no isotope effect whereas KIE > 1 and KIE < 1 indicate a *normal* and an *inverse* isotope effect, respectively. The computed secondary KIEs at 25 °C are presented in Table 1.

The behavior of KIEs at the terminal “in” and “out” positions is markedly different, with the “in” positions displaying a larger effect.^{11c,39} Note that KIE at the “out”

TABLE 1. B3LYP/6-31G* Calculated Secondary KIEs at 25 °C



deuterium position	divinylcyclobutane (1) 1tt → 2cc	divinylcyclopropane (4) 4tt → 5cc
1in	0.934	0.911
1out	0.977	0.992
2	0.978	0.994
3,3'	1.230	1.163
1in,1'in	0.832 (0.869, 0.892) ^a	0.816 (0.801) ^c
1out,1'out	(0.96 ± 0.02) ^b	(0.78 ± 0.09) ^d

^a Calculated at 77.7 °C. The second value refers to the B3LYP/6-311+G(d,p) result. ^b Experimental value at 77.7 °C reported by Gajewski (ref 15). ^c Calculated at 10 °C. ^d Experimental value at 10 °C reported by Gajewski (ref 15).

position is almost identical with that at position 2, in both systems. It appears that the local force fields⁴⁰ of these hydrogens in the TS are quite similar. The effect at the “in” position of divinylcyclopropane is significantly more than that in divinylcyclobutane. But the opposite is true for the “out” positions so that full deuteration at the terminal (1,1') positions of both systems show similar KIEs. On the basis of the values of the KIEs, we may conclude that both TSs are more “reactant-like” in their bond-making centers. This conclusion is consistent with the calculated geometries where the forming bond is rather long, 2.37–2.38 Å, in both TSs. The calculated equilibrium isotope effect (EIE) at 25 °C for the (1in,1out) substitution in both systems is near 0.73–0.74. The experimental value in the parent 1,5-hexadiene (at 25 °C) is also 0.74.⁴¹ It appears that EIE, which involves full conversion of two sp² C–H bonds into two sp³ bonds, is independent of the system studied.

Turning now to the bond-breaking centers, the KIE at 3,3' positions is significantly larger in divinylcyclobutane than in divinylcyclopropane (1.230 vs 1.163). The corresponding EIEs were computed to be 1.264 and 1.208 at the same temperature (25 °C). We may conclude that the bond-breaking centers of both systems are “product-like”, with the divinylcyclobutane system being somewhat more like the product in this respect. This observation is consistent with the calculated TS geometries where the breaking bond is 1.988 Å in **5cc** whereas it is 2.139 Å in **2cc**. It is tempting to simply mention that the more bond breakage with divinylcyclobutane accounts for the relatively higher activation energy for its rearrangement.

As mentioned previously, the experimental KIEs are available only for bond-making centers.¹⁵ The calculated d_4 KIE at the vinyl termini of divinylcyclopropane **4** is in good agreement with the corresponding experimental value (0.80 vs 0.78 ± 0.09). However, the calculated KIE⁴²

(32) Zavitsas, A. A. *J. Phys. Chem. A* **2003**, *107*, 897.

(33) Møller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618.

(34) Krishnan, R.; Binkly, J. S.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650.

(35) Optimizations with the spin-unrestricted DFT and MP2 methods were carried out with use of the “guess=(mix,always)” option of Gaussian98. The vertical singlet–triplet separation at the UB3LYP/6-31G(d) level was 48.6 kcal/mol, indicating that the presence of a nearby diradical structure is unlikely. Note also that no stable triplet state nearby the **6tt** structure could be located at the UB3LYP/6-31G(d) level.

(36) The RMP2(full)/6-31G(d) optimization yielded 1.714 Å for this bond length.

(37) It should be noted that the definition of KIE in terms of free energies is exactly equivalent to the Bigeleisen–Mayer formulation (Bigeleisen, J.; Wolfsberg, M. *Adv. Chem. Phys.* **1958**, *1*, 15), which was sometimes employed in previous work (see ref 11c). Use of a few free energy values instead of a multitude of (3*N* – 6) frequencies is obviously more convenient.

(38) Please note that there is a misprint in eq 2 of ref 11c (Bigeleisen–Mayer formulation of KIE); in the ratios u_H/u_D and u_H^2/u_D^2 , the subscripts H and D should be reversed.

(39) (a) Houk, K. N.; Gustafson, S. M.; Black, K. A. *J. Am. Chem. Soc.* **1992**, *114*, 8565. (b) Wiest, O.; Houk, K. N.; Black, K. A.; Thomas, B. *J. Am. Chem. Soc.* **1995**, *117*, 8594.

(40) (a) Ishida, T.; Spindel, W. In *Isotope Effects in Chemical Processes*; Advances in Chemistry Series; American Chemical Society: Washington, DC, 1969; Vol. 89, pp 192–247. (b) Bigeleisen, J.; Lee, M. W.; Mandel, F. *Annu. Rev. Phys. Chem.* **1973**, *24*, 407. (c) Bigeleisen, J.; Ishida, T. *J. Chem. Phys.* **1975**, *62*, 80.

(41) There is a sign misprint in Conrad's empirical equation in ref 15. The correct expression is as follows: $-\log K^{H/K^2} = 291.6/2.3RT - 0.0818$.

for divinylcyclobutane **1** falls outside of the error margins compared to its experimental value (0.87 vs 0.96 ± 0.02). Furthermore, the difference is too large to be accountable by scale factors. Agreement with Gajewski's value required a nonsensical scale factor of 0.50.⁴³ Tunneling corrections with use of the one-dimensional Bell model were negligible.⁴⁴ Since the two molecules **1** and **4** are quite similar, it is surprising that the same method predicts one system well, but not the other. Concerned with the relatively small size of the 6-31G(d) basis set, we repeated the B3LYP calculations for **1** employing the valence triple-split 6-311+G(d,p) basis set including diffuse functions on heavy atoms and polarization functions on the hydrogens. The resulting optimized geometry of **2cc** was within 0.06 Å (the breaking and forming bond lengths were 2.188 and 2.441 Å, respectively) of that with 6-31G(d).⁴⁵ The predicted activation energy, 24.2 kcal/mol, is closer to the experimental value, 24.0 kcal/mol.^{7a,b} The calculated bond-making d_4 KIE in **1** improved somewhat to 0.892 (at 77.7 °C), but still fell significantly short of the experimental value.

Theoretical calculation of KIEs appears to be reliable since there are many successful applications in the literature.^{11c,39,46} This is so despite the well-known deficiencies of the theoretical methods in the prediction of individual vibrational frequencies. The force constant matrix is the same for both the protonated and the deuterated species; however, the quality of the force constants depends on the quality of the wave function. On the other hand, KIEs calculated at different levels of theory (e.g. Hartree–Fock vs DFT) are quite similar. Apparently, errors due to the force constants are averaged out to insignificant amounts when KIEs are computed. The discrepancy between our predictions and Gajewski's measurements for divinylcyclobutane might then be due to an alternative reaction path involving a lower energy TS than the aromatic TS we have found. We have searched for nonconcerted alternatives for both rearrangements, involving the intermediacy of tight (1,4-diyl) and loose (bis-allyl) diradicals, but our attempts to locate stationary points for these species were all unsuccessful. Failure to locate diradicals might have been anticipated, perhaps, since such diradicaloid structures in the unsubstituted parent 1,5-hexadiene turned out to be spurious after a long-lasting debate.^{11e} Furthermore, Doering and co-workers have found strong experimental

(42) Allowing for equilibria between **1tt**, **1ct**, and **1cc** raises the calculated d_4 KIE value by a factor of 1.005. This is clearly negligible.

(43) Note also that employing a scale factor of 0.5 is equivalent to using a temperature $T = 350.85/0.5 = 701.7$ K, at a scale factor of unity.

(44) Bell, R. P. *The Tunnel Effect in Chemistry*; Chapman & Hall: London, UK, 1980; pp 60–63.

(45) The B3LYP/6-311+G(d,p) optimized geometries and energies of **1tt** and **2cc** are available in the Supporting Information.

(46) (a) Storer, J. W.; Raimondi, L.; Houk, K. N. *J. Am. Chem. Soc.* **1994**, *116*, 9675. (b) Yoo, H. Y.; Houk, K. N. *J. Am. Chem. Soc.* **1994**, *116*, 12047. (c) Olson, L. P.; Li, Y.; Houk, K. N.; Kresge, A. J.; Schaad, L. J. *J. Am. Chem. Soc.* **1995**, *117*, 2992. (d) Zipse, H.; Apaydin, G.; Houk, K. N. *J. Am. Chem. Soc.* **1995**, *117*, 8608. (e) Olson, L. P.; Niwayama, S.; Yoo, H. Y.; Houk, K. N.; Harris, N. J.; Gajewski, J. J. *J. Am. Chem. Soc.* **1996**, *118*, 886. (f) Beno, B. R.; Houk, K. N.; Singleton, D. A. *J. Am. Chem. Soc.* **1996**, *118*, 9984. (g) DelMonte, A. J.; Haller, J.; Houk, K. N.; Sharpless, K. B.; Singleton, D. A.; Strassner, T.; Thomas, A. A. *J. Am. Chem. Soc.* **1997**, *119*, 9907. (h) Houk, K. N.; Strassner, T. *J. Org. Chem.* **1999**, *64*, 800. (i) Keating, A. E.; Merrigan, S. R.; Singleton, D. A.; Houk, K. N. *J. Am. Chem. Soc.* **1999**, *121*, 3933. (j) Meyer, M. P.; DelMonte, A. J.; Singleton, D. A. *J. Am. Chem. Soc.* **1999**, *121*, 10865.

support in favor of the concerted mechanism for the rearrangement of **1** into **3**.⁴⁷ If the actual TS is near the one employed in this work, then we have no plausible explanation for why the predicted KIEs in divinylcyclobutane are so much off from Gajewski's measurements.⁴⁸

Conclusions

We have investigated the Cope rearrangements of *cis*-1,2-divinylcyclobutane and *cis*-1,2-divinylcyclopropane at the (U)B3LYP/6-31G* level, and explored the difference in the activation energies of these rearrangements in the light of secondary KIEs. For the rearrangement of *cis*-1,2-divinylcyclobutane, we located three TSs, i.e. endo-boatlike, chairlike, and exo-boatlike TSs, with barriers of 25.0, 26.9, and 31.4 kcal/mol, respectively, to afford *cis,cis*-, *cis,trans*- and *trans,trans*-1,5-cyclooctadiene with reaction enthalpies -17.3 , -3.2 , and 12.2 kcal/mol. Similarly, for the rearrangement of *cis*-1,2-divinylcyclopropane, we located endo-boatlike, chairlike, and exo-boatlike TSs with barriers of 19.7, 32.4, and 44.1 kcal/mol, respectively, to form *cis,cis*-, *cis,trans*-, and *trans,trans*-1,4-cycloheptadiene with reaction enthalpies -20.1 , 8.9, and 43.9 kcal/mol. The lowest activation barriers predicted for these reactions are in good agreement with the experimental values. The reaction paths of both rearrangements are intervened by enantiomerization saddle points of the products. These points lie at approximately the same height, 6.5–6.6 kcal/mol, above the minima of corresponding products, indicating that cyclooctadiene (**3cc**) and cycloheptadiene (**6cc**) have similar ring strain.

Chemists traditionally visualize the minimum energy path (MEP) of a concerted reaction as a simple path in which the minima corresponding to the reactant and product are directly connected by the TS. In other words, a single saddle point is thought to intervene the two minima. The possibility of two or more consecutive saddle points along the MEP is normally considered unlikely. As illustrated in Figure 2, this view of MEP may have to be modified for molecules with more than a few degrees of freedom.²⁹ Thus the MEP in the rearrangement path of **1cc** has three consecutive saddle points (and the associated ridges) whereas that of **4cc** has two. Generally, such behavior of MEP may be expected if the reaction under consideration has the following properties: (i) the reactant and/or the product have lower symmetry than the TS and (ii) the vibrational mode with imaginary frequency is totally symmetric.

The secondary KIEs calculated at various positions are as expected in magnitude although one of them falls outside of the experimental value. Comparison of d_4 KIEs with the limiting EIEs indicates that there is a small bond making of similar magnitude⁴⁹ in the TSs of both **1** and **4** (d_4 KIE: 0.832 (vs EIE = 0.535) and 0.816 (vs EIE

(47) Doering, W. v. E.; Birladeanu, L.; Sarma, K.; Teles, J. H.; Klarner, F. G.; Gehrke, J. S. *J. Am. Chem. Soc.* **1994**, *116*, 4289.

(48) In a study by Singleton and co-workers (ref 46j) on KIE in aliphatic and aromatic Claisen rearrangement, the tendency of theoretical methods to generally underpredict the secondary deuterium KIEs was noted. Of the three positions they investigated, the largest error involved the α -d substitution (see Table 3 in ref 46j). In contrast, their calculated KIE at the terminal position (γ -d), which should be compared with the present work, agreed satisfactorily with their new experimental results.

= 0.549) for **1** and **4**, respectively). There is a somewhat more pronounced difference between the two molecules regarding their bond-breaking centers. The calculated d_2 KIEs (and EIEs) are 1.230 (1.264) and 1.163 (1.208) for **1** and **4**, respectively. The larger bond cleavage with *cis*-1,2-divinylcyclobutane is attributed to the relatively higher activation energy for its rearrangement.

(49) As a measure of the magnitude of bond formation (or bond breakage) in TS we used the exponent i in the linear free energy relation (see, for example, ref 15); i.e., $\ln \text{KIE} = i \ln \text{EIE}$. Values of i are 29% and 34% for the d_1 substitution at 298 K in **1** and **4**, respectively. Similarly, $i = 88\%$ and 80% for d_2 KIEs in the two molecules.

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Supporting Information Available: Optimized Cartesian coordinates and energies for all stationary points, and two figures depicting the structures of all species considered in this work. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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