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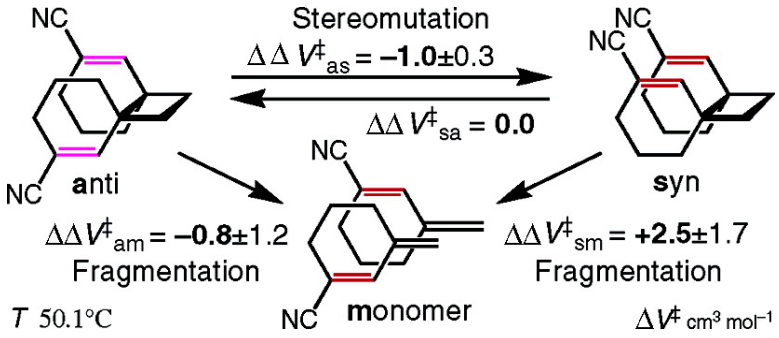

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Pressure Independence of Stereomutation and Fragmentation in the Bis-spirocyclobutanes, *anti*- and *syn*-2,9-Dicyanodispiro[5.0.5.2]tetradeca-1,8-dienes

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Abstract: Pressure dependent rate constants and volumes of activation for stereomutational interconversions of the cyclobutanes, *anti*- and *syn*-2,9-dicyanodispiro[5.0.5.2]tetradeca-1,8-dienes (*anti*-**6** and *syn*-**6**), and for their fragmentation to 1-cyano-3-methylenecyclohexene (**5**) have been determined. Although fragmentations might have been expected to have larger and thus more positive volumes of activation than stereomutation, both processes have essentially identical volumes of activation within experimental uncertainties at 50.1 °C over the pressure range, 1−3000 bar: $\Delta V^{\ddagger} = (+7.4 \text{ to } +9.9) \pm 2.0$ cm^3 mol^{-1}. While these positive values are consistent with the rate of entry into the hypothetical caldera being determined by breaking the weakest bond in the cyclobutanes, the insensitivity of the product-determining exit channels argues against the obligatory second bond-breaking being a significant factor in fragmentation.

Introduction

This work brings to a landing[1] our investigation of pressure dependence as a searchlight into the darkness of the caldera, arguably the link between educt and product in not-obviously concerted thermal reorganizations. Having passed through various stages, distinction between concerted and not-obviously concerted mechanisms on the basis of stereochemistry, energy of concert, response to pressure, and negation of vestigial influence of orbital symmetry on the fate of diradical intermediates, efforts continue to seek a measure of intellectual control over the events that follow initial generation of energy-credible diradicals and their passage from educt through caldera to products. Questions are addressed to the relative importance of the mode of entrance into the domain of diradicals (the caldera) and of internal rotations on the determination of products. Do diradicals continue on their way as diradicals-in-transit, or do they pause in the caldera as diradicals-as-intermediates long enough to establish, or approach, equilibria among product-related conformations prior to exit?

Cyclobutanes have played a key role in these explorations, not only because of a rich history in the field of thermal reorganizations rivaling that of the cyclopropanes[2,3] but also because of the great disparities in the thermochemistry of their various modes of reaction. These modes of reactions include the dimerization of olefins and dienes (olefin-olefin unions), its reverse, fragmentation of the related cyclobutanes (also dubbed cycloreversion or cleavage), which comprises a set of exit channels not available to cyclopropanes; stereomutation, the change from one stereoisomer to another; and ring enlargement, actualized in appropriate π-systems such as those containing proximate vinyl groups.

The effect of pressure is ideally studied in the distribution of products from cyclobutanes where fragmentation competes with stereomutation. If a larger increase in volume of reaction is expected to be associated with fragmentation, a substantially more positive volume of activation should be shown by fragmentation than by stereomutation.[4] Competition between racemization of optically active 1,3,4,6-tetraphenylhexa-1,5-diene ($\Delta V^{\ddagger} = -7.4$ cm^3 mol^{-1}) and the mutual interconversion of *rac*- and *meso*-1,3,4,6-tetraphenylhexa-1,5-diene ($\Delta V^{\ddagger} = +13.5$ and $+11.5$ cm^3 mol^{-1}, respectively) by way of the 1,3-diphenylallyl radical may serve as an example.[5]

Studies of the effect of pressure on the ethene−ethene union begin with the classical example of Stewart on the pressure dependence of the products of the thermal dimerization of chloroprene.[6] A deeper probing through deuterium-labeling follows in the work of Klärner, Krawczyk, Ruster, and Deiters.[7]

† Universität Duisburg-Essen.
‡ Harvard University.

(1) *Arch*., as at the end of a flight of stairs; *Ger*., *Treppenabsatz*.
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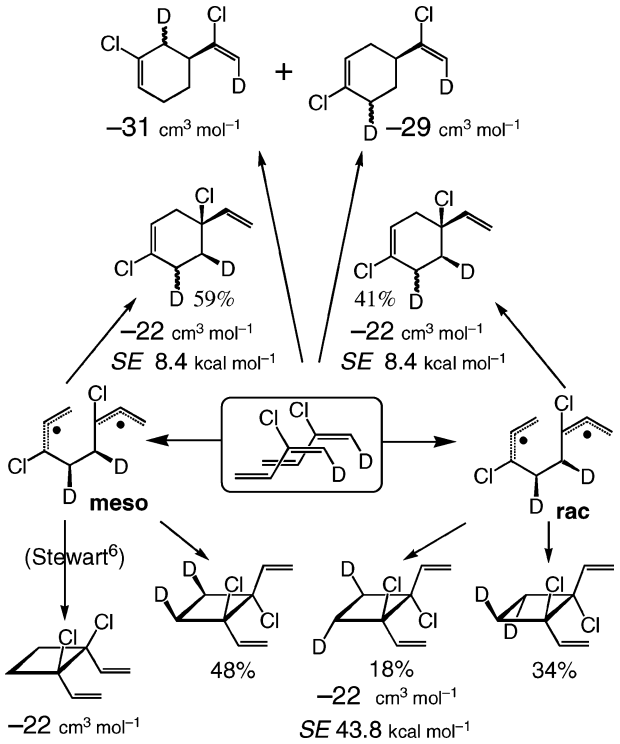

Figure 1. Products of the thermal dimerization of (*E*)-1-deuterio-2-chlorobutadiene at 50 °C are depicted with volumes of activation, $\Delta V^{\ddagger}$, and steric energies, SE, calculated by molecular mechanics (MM2).

Two of the products, 2- and 1-chloro-4-(1′-chlorovinyl)cyclohexene, are constitutionally of the [4 + 2] Diels−Alder type and have volumes of activation, $\Delta V^{\ddagger} = -31$ and -29 cm^3 mol^{-1}, respectively. A second set consisting of [2 + 2] *cis*- and *trans*-1,2-dichloro-1,2-divinylcyclobutanes and, surprisingly, a third product constitutionally of the Diels−Alder type, 1,4-dichloro-4-vinylcyclohexene, all have significantly less negative volumes of activation, $\Delta V^{\ddagger} = -22$ cm^3 mol^{-1} (Figure 1).[8] In a compelling analysis, Klärner concludes that the first set is concerted in mechanism while the second involves diradicals as intermediates, the former having a larger packing fraction than the latter. These works exemplify the power of pressure dependence to distinguish between a concerted set and a not-obviously concerted, diradical set in situations where the two are in competition with each other.

An example related to Stewart's is the thermal dimerization of cyclohexa-1,3-diene (Figure 2).[9] Here again, two products, an *endo*-bicycloöctene constitutionally of the Diels−Alder type and 5-(3′-cyclohexenyl)cyclohexa-1,3-diene, the result of a [6 + 4] hydrogen transfer, are associated with more negative volumes of activation, −28 and −32 cm^3 mol^{-1}, respectively, while the *exo*-bicycloöctene, and two [2 + 2] cyclobutane dimers have more positive volumes of activation, $\Delta V^{\ddagger} = -22$, −18, and −22 cm^3 mol^{-1}, respectively. The cyclobutanes serve as anchors for not-obviously concerted reactions, forbidden to

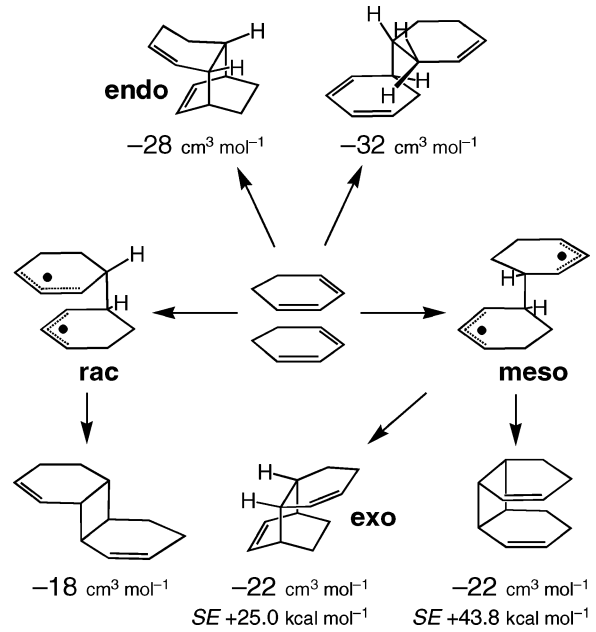

Figure 2. The products of the thermal dimerization of cyclohexa-1,3-diene at 70.5 °C are given with volumes of activation, $\Delta V^{\ddagger}$, and steric energies, SE, calculated by molecular mechanics (MM2).

be concerted by Woodward−Hoffmann rules,[10] and likely proceeding via a diradical intermediate. Particularly striking is the apparent difference in mechanism involved in the generation of the endo and exo Diels−Alder adducts.

A remarkable feature of both examples is the inability of pressure to distinguish among products derived plausibly from a *single* caldera. These include a pair of *trans*-1,2-cyclobutanes and a vinylcyclohexene from the racemic diradical derived by bond formation between the 1-positions of a pair of chloroprenes (Figure 1) and the exo Diels−Alder adduct and *meso*-cyclobutane plausibly derived from the meso diradical formed by the union of two cyclohexadienes at the 1-positions (Figure 2).

The present work completes a study of cyclobutanes designed to sharpen the focus on the effect of pressure on the ratio of products reached through two types of exit channels, stereomutation and fragmentation. The original choice of bis-spirocyclobutanes was driven by a desire to keep the system free of a third reaction mode of ring enlargement open to unrestrained vinylcyclobutanes and yet satisfy the need for the temperature of reaction to fall into a range experimentally convenient for the evaluation of volumes of activation.

The cyclobutane dimers of 3-methylenecyclohexene, *syn*- and *anti*-**2**, and of 1-phenyl-3-methylenecyclohexene, *syn*-**4** and *anti*-**4** (Figures 3 and 4, respectively), were the objects of the first study.[11] A modestly positive volume of activation ($\Delta V^{\ddagger} > 0$) was expected in the opening of the cyclobutane ring to a diradical as the first step.[12] Pressure might be expected to influence the subsequent reactions of the intermediate as well, fragmentation (to 3-methylenecyclohexene **1** or the 1-phenyl derivative **3**, respectively) and ring closure (detectable as stereomutation between *syn*-**2** and *anti*-**2** and *syn*-**4** and *anti*-**4**,

(8) As a first point, recall that the paradigm of the Diels−Alder reaction, the cycloaddition of ethylene to butadiene, is but weakly concerted (~7 kcal mol^{-1}). As a second, note that the two cyclohexenes of the first, highly likely concerted, constitutionally Diels−Alder set would have involved the less well stabilized diradicals had they been involved, whereas the not obviously concerted constitutionally Diels−Alder cyclohexene of the second set is derived, as are the two cyclobutanes, from the optimally stabilized racemic and meso diradicals.

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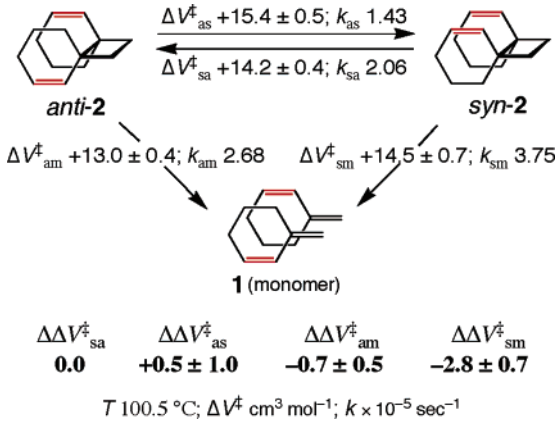

Figure 3. Thermal rearrangements of the [2 + 2] dimerization products of 3-methylenecyclohexene **1**, *anti*-**2** and *syn*-**2**, are shown, along with their volumes of activation, $\Delta V^{\ddagger}$, specific rate constants, and differences in volumes of activation, $\Delta\Delta V^{\ddagger}$, relative to the conversion of *syn*-**2** to *anti*-**2** taken as 0.0.

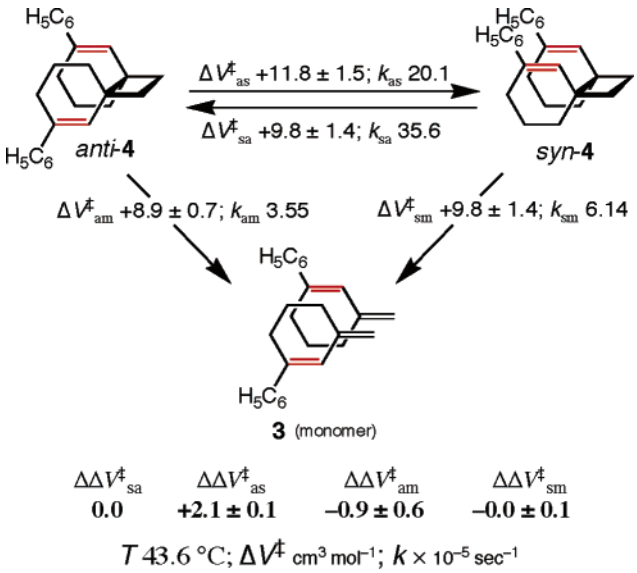

Figure 4. Thermal rearrangements of the [2 + 2] dimerization products of 1-phenyl-3-methylenecyclohexene **3**, *anti*-**4** and *syn*-**4**, are shown, along with their volumes of activation, $\Delta V^{\ddagger}$, specific rate constants, and differences in volumes of activation, $\Delta\Delta V^{\ddagger}$, relative to the conversion of *syn*-**4** to *anti*-**4** taken as 0.0.

respectively). Presumably, the volume of activation for fragmentation should be significantly more positive than that for reclosure to the cyclobutanes.[13]

In fact, the thermal reactions of *syn*-**2** and *anti*-**2** (Figure 3) and *syn*-**4** and *anti*-**4** (Figure 4) showed a pressure-induced deceleration of the overall reaction ($\Delta V^{\ddagger} > 0$) as expected. But neither showed any significant decrease in the ratio of the products of fragmentation and stereomutation. Perhaps, these examples had not been optimal for revealing small differences. A convenient temperature for the study of **1** and its dimers was on the high side, while that for the study of **3** and its dimers was too low both for kinetic studies of high precision and for

(13) In the case of the [2+2] cycloaddition of 1,1-difluoroallene, there is good evidence that the ratio of products derived from a diradical intermediate can indeed be pressure-dependent. At high pressure the product resulting from ring closure in the diradical intermediate is favored over that resulting from bond rotation followed by ring closure. Dolbier, W. R., Jr.; Weaver, S. L. *J. Org. Chem.* **1990**, *55*, 711−715.

Table 1. Pressure Dependence of the Rate Constants and Volumes of Activation for the Stereomutation, and Fragmentation to **5**, of *anti*-**6** and *syn*-**6** at 50.1 °C in *n*-Heptane/*tert*-Butylmethyl Ether (9:1)

p [bar]	*anti*-**6** → *syn*-**6** k_{as}[a]	*syn*-**6** → *anti*-**6** k_{sa}[a]	*anti*-**6** →**5** k_{am}[a]	*syn*-**6** →**5** k_{sm}[a]
1	11.1 ± 0.06	25.2 ± 1.2	3.78 ± 0.17	2.86 ± 0.33
500	8.94 ± 0.45	18.4 ± 0.8	2.38 ± 0.14	2.53 ± 0.25
1000	7.65 ± 0.46	16.4 ± 0.8	2.58 ± 0.14	1.84 ± 0.24
1500	7.37 ± 0.40	15.9 ± 0.8	2.30 ± 0.12	1.50 ± 0.20
2000	6.50 ± 0.22	13.0 ± 0.4	1.83 ± 0.11	1.34 ± 0.13
2500	4.20 ± 0.27	8.6 ± 0.4	1.60 ± 0.11	1.08 ± 0.16
3000	4.87 ± 0.25	9.5 ± 0.4	1.34 ± 0.10	0.76 ± 0.14
$\Delta V^{\ddagger}$[b]	$\Delta V^{\ddagger}_{as}$	$\Delta V^{\ddagger}_{sa}$	$\Delta V^{\ddagger}_{am}$	$\Delta V^{\ddagger}_{sm}$
$\Delta V^{\ddagger}_{l}$[c]	8.0 ± 3.0	9.0 ± 3.0	8.2 ± 3.2	11.5 ± 1.8
$\Delta V^{\ddagger}_{q}$[d]	9.1 ± 1.7	9.9 ± 1.7	7.4 ± 1.8	9.7 ± 0.9

[a] Rate constants in units of 10^{-5} s^{-1}. [b] Volumes of activation in cm^3 mol^{-1}. [c] Derived from kinetic data by the linear correlation, $\ln(k)\ p = a + bp$; $\Delta V_l^{\ddagger} = -bRT$. [d] Derived from the kinetic data by the nonlinear correlation, $\ln(k)\ p = a + bp + cp^2$; $\Delta V_q^{\ddagger} = -bRT$.

convenient separation and purification of *syn*-**4** and *anti*-**4** necessary for both to serve as educts.

The importance of placing this apparent lack of pressure dependence of products emerging from a *single* caldera on as firm a footing as possible prompted a search for a pair of cyclobutanes that would react at temperatures between the unsubstituted and the too reactive phenyl-substituted. The cyano group turned out to be a sufficiently less radical-stabilizing group than phenyl to be close to "just right"! The derived *anti*- and *syn*-2,9-dicyanodispiro[5.0.5.2]tetradeca-1,8-dienes, *anti*-**6** and *syn*-**6**, were stable enough to allow separation by high-pressure liquid chromatography, thus making possible a study of both isomers at the convenient temperature of 50.1 °C. Furthermore, we were interested in the question whether additional radical-stabilizing substituents such as the cyano group might lead to the formation of a more stable diradical that would show the reactive behavior expected of a conventional intermediate, namely a pressure-dependent product ratio.

The preparation of the precursor, 1-cyano-3-methylenecyclohexene (**5**), followed the procedure of Cronyn and Goodrich but required modification to become reliably reproducible.[14] Its photodimerization led to a mixture of *anti*-**6** and *syn*-**6** which could be separated by medium-pressure liquid chromatography (MPLC). The specific rate constants of the reversible stereomutation between *anti*-**6** and *syn*-**6** and fragmentation of *anti*-**6** to **5** and of *syn*-**6** to **5** were calculated by numerical integration from two sets of product ratios determined at 50.1 °C and different pressures starting from either enriched *anti*-**6** or *syn*-**6**. Further details of the kinetic analyses are given in the Experimental Section. Kinetic data are presented in the conventional way (Table 1) and also as ratios of rate constants for fragmentation relative to the rate of conversion of *syn*-dimer to *anti*-dimer (k_{sa} taken as 1.000) (Table 2). Estimates of relative rate constants at 1 bar and 50.1 °C were obtained by linear regression of the ratios in Table 2. The equilibrium constant, $K = k_{syn-6}/k_{anti-6} = 2.21$, translates to $\Delta\Delta G_{50^\circ} = -0.5$ kcal mol^{-1}. Steric energies calculated by MM2 for *syn*-**6** and *anti*-**6**, +41.6 and +40.0 kcal mol^{-1}, respectively, are in the same direction. There is nothing surprising about the thermochemistry of the system.

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Table 2. Pressure Dependence of the Rate Constants of *syn*-**6** and *anti*-**6** Relative to the Conversion, *syn*-**6** → *anti*-**6** (k_{sa} Set to 1.000), and the Differences in Volumes of Activation at 50.1 °C in *n*-Heptane/*tert*-Butylmethyl Ether

p [bar]	*syn*-**6** → *anti*-**6**	*anti*-**6** → *syn*-**6**	*anti*-**6** → **5**	*syn*-**6** → **5**
1	1.000	0.444	0.150	0.114
500	1.000	0.485	0.129	0.138
1000	1.000	0.466	0.157	0.112
1500	1.000	0.463	0.157	0.095
2000	1.000	0.501	0.141	0.103
2500	1.000	0.490	0.187	0.127
3000	1.000	0.511	0.141	0.079
	$\Delta\Delta V^{\ddagger}_{sa}$[a]	$\Delta\Delta V^{\ddagger}_{as}$[a]	$\Delta\Delta V^{\ddagger}_{am}$[a]	$\Delta\Delta V^{\ddagger}_{sm}$[a]
	0.0	**−1.0 ± 0.3**	**−0.8 ± 1.2**	**+2.5 ± 1.7**

[a] Differences in volumes of activation in $cm^3\ mol^{-1}$ derived from the ratios of rate constants by linear correlation, e.g., $\ln(k_{as}/k_{sa})\ p = a + bp$; $\Delta\Delta V^{\ddagger}_{as} = -bRT$. For stereomutation $\Delta\Delta V^{\ddagger}_{as} = \Delta V^{\ddagger}_{as} - \Delta V^{\ddagger}_{sa}$, and for fragmentations $\Delta\Delta V^{\ddagger}_{am} = \Delta V^{\ddagger}_{am} - \Delta V^{\ddagger}_{sa}$ and $\Delta\Delta V^{\ddagger}_{sm} = \Delta V^{\ddagger}_{sm} - \Delta V^{\ddagger}_{sa}$.

Discussion

Much as expected, the radical-stabilizing substituents, cyano and phenyl, decrease the Gibbs free energy activation barriers relative to the thermal reactions of the syn and anti dimers of the unsubstituted 3-methylenecyclohexene:

CN (50.1 °C): $\Delta\Delta G^{\ddagger}_{syn} = \Delta G^{\ddagger}_{syn-2} - \Delta G^{\ddagger}_{syn-6} =$
$29.32 - 24.19 = 5.13\ kcal\ mol^{-1}$

$\Delta\Delta G^{\ddagger}_{anti} = \Delta G^{\ddagger}_{anti-2} - \Delta G^{\ddagger}_{anti-6} =$
$29.62 - 24.64 = 4.98\ kcal\ mol^{-1}$

Ph (43.6 °C): $\Delta\Delta G^{\ddagger}_{syn} = \Delta G^{\ddagger}_{syn-2} - \Delta G^{\ddagger}_{syn-4} =$
$29.32 - 23.44 = 5.88\ kcal\ mol^{-1}$

$\Delta\Delta G^{\ddagger}_{anti} = \Delta G^{\ddagger}_{anti-2} - \Delta G^{\ddagger}_{anti-4} =$
$29.62 - 23.80 = 5.82\ kcal\ mol^{-1}$

Although the stabilizing effect of the cyano group is only slightly less than that of phenyl, the small difference has been just helpful enough to allow completion of an experimentally satisfying investigation of the effect of pressure.

Ratios of stereomutation to fragmentation in the unsubstituted parent system, *anti*-**2** and *syn*-**2**, at 72.1 °C are $k_{as}/k_{am} = 0.49/0.70 = 0.70$ and $k_{sa}/k_{sm} = 0.70/0.93 = 0.75$ at 72.1 °C, respectively, while the values from the phenyl analogues, *anti*-**4** and *syn*-**4**, at 43.6 °C are $k_{as}/k_{am} = 5.67$ and $k_{sa}/k_{sm} = 5.79$, respectively. Those from the cyano analogues, *anti*-**6** and *syn*-**6**, at 50.1 °C are $k_{as}/k_{am} = 2.94$, and $k_{sa}/k_{sm} = 8.81$, respectively. This enhancement of stereomutation over fragmentation (or this reduction of fragmentation relative to stereomutation!) by increasing stabilization of the diradical has already been noted when the activating substituents are basically butadienyl (stereomutation/fragmentation ~25 at 43.6 °C)[15] and hexatrienyl (stereomutation/fragmentation ~4000 at −25.1 °C).[16]

Quantitative comparisons of the relative ratios of stereomutation to fragmentation in the syn isomers are relatively unreliable because there is but a single observation starting from *syn*-**2** and none starting from *syn*-**4**. By contrast, the cyano system **6** could be investigated starting from both stereoisomers. The ratio of stereomutation to fragmentation in the rearrangement of *syn*-**6** is greater by a factor of 3.00 ($\Delta\Delta G^{\ddagger} = 0.70$ kcal mol^{-1}) than in the rearrangement of *anti*-**6**. On the assumption that *anti*-**6** has a lower enthalpy of formation than *syn*-**6**, it is tentatively proposed that a steric driving force for *anti*-**6** to undergo the necessary internal rotation prior to ring closure may be less than that for *syn*-**6**.

The most significant result of the present work is a more rigorous confirmation of the insensitivity of the ratio of stereomutation to fragmentation to increasing pressure. The anticipated repression of fragmentation vis-à-vis stereomutation by increasing pressure has not been observed. Presenting the available data as ratios emphasizes the *differences* in volumes of activation. The absence of any significant result favoring one way or the other seen in Figures 3, 4, and 5 emerges with striking clarity. The quite disparate geometry of the two exit channels has no effect.

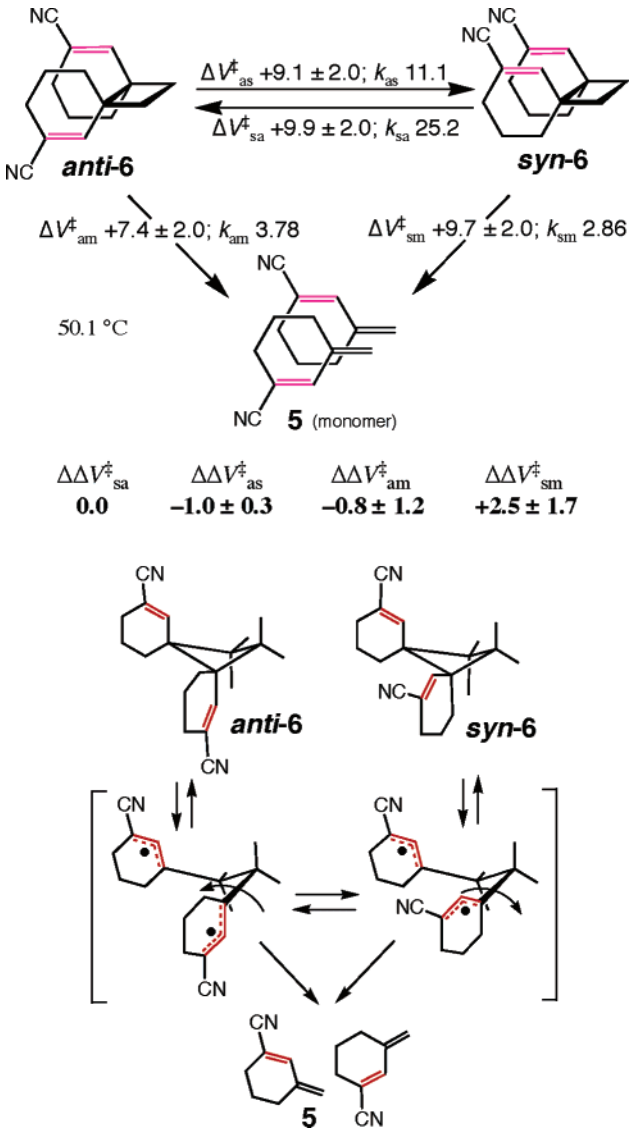

Figure 5. Thermal rearrangements of the [2 + 2] dimerization products of 1-cyano-3-methylenecyclohexene **5** (*anti*-**6** and *syn*-**6**) are shown, along with their volumes of activation, $\Delta V^{\ddagger}$, specific rate constants, and differences in volumes of activation, $\Delta\Delta V^{\ddagger}$, relative to the conversion of *syn*-**6** to *anti*-**6** taken as 0.0. A hypothetical diradical serving as an intermediate is also shown.

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(16) Doering, W. von E.; He, J.-n.; Shao, L.-m. *J. Am. Chem. Soc.* **2001**, *123*, 9153−9161.

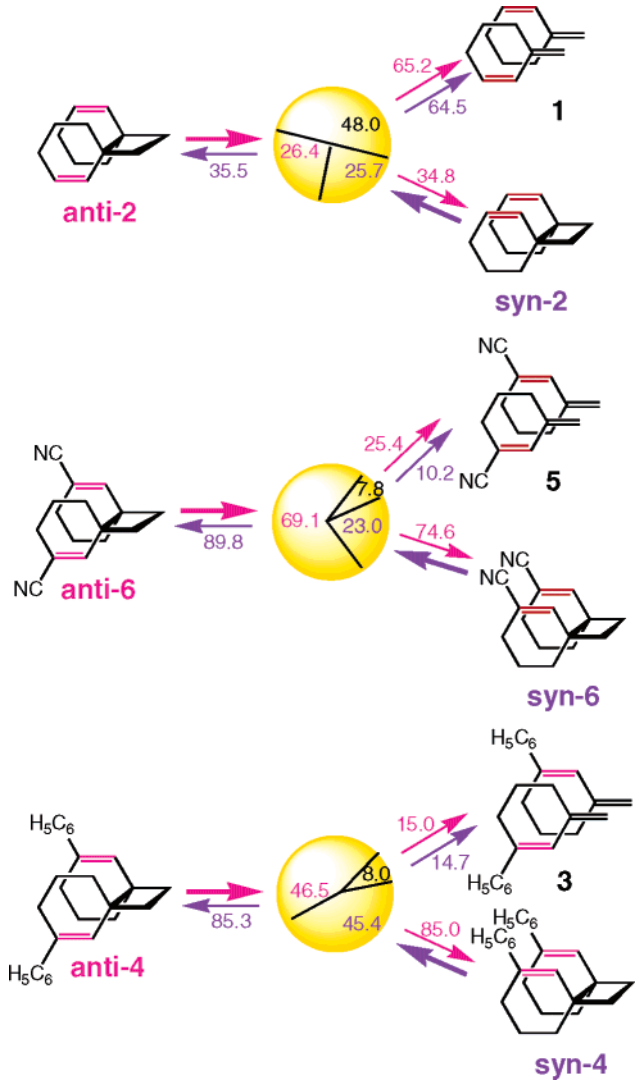

Figure 6. The fraction in % of each of the three components, anti (*a*), syn (*s*), and monomer (*m*), emanating from a purely hypothetical intermediate in common is calculated for the reactions in Figures 3, 5, and 4, from three equations: $a/m = k_{as}/k_{am}$; $s/m = k_{sa}/k_{sm}$, and $a + s + m = 1$.

Were the reactions under study here to consist of *two* competing exit channels proceeding from an intermediate in common, the behavior of the caldera could then (and always) be depicted in a graphical form (the pie representation in Figure 6), provided the *unobservable* return reactions were given the same relative values they had in the observable reactions. This virtual formulation is not applicable to systems comprising more than two exit channels. To give it visibility in this way does not imply support for a common intermediate as the full or even a partial description of the behavior within the caldera. What is seen is the remarkable decline in the proportion of fragmentation as the overall enthalpy of activation (stabilization in the diradical) decreases.[16]

In the examples of this and the preceding paper[11] as well all the other examples we have studied of not-obviously concerted rearrangements leading to multiple products but having essentially indistinguishable enthalpies of activation, none has been successfully accommodated by a *single* diradical intermediate in common that reaches equilibrium regardless of origin. "Reaches equilibrium" implies intramolecular vibrational relaxation being faster than sudden death by reclosure.

All the examples can be accommodated by a conceptual scheme of diradicals in transit. In this scheme each educt opens to a diradical consisting of an idiosyncratic distribution of conformations each individual among which is predestined to proceed to a unique product by its point of entry into the multidimensional potential energy surface representing the diradical (shades of a pin-ball machine!). An elegant, lucid account of the application is found in the analysis of vinylcyclopropane given by Doubleday, Li, and Hase.[17] The goal of trajectory analysis is the calculation of the trajectories followed to exit by a sufficiently large number of entry states to provide a statistically acceptable approximation of the experimental distribution of products apposite to the system. No simple (qualitative or pseudo-quantitative) ways of thinking about these pathways are expected to emerge, even though distributions among multiple products will have been predicted correctly.

Little has been revealed about the effect of temperature on the distribution among products emerging from multichanneled caldera. The only study in this series of cyclobutanes relates to the parent **2**. But these data are not of a precision sufficient to allow significant conclusions about the effect of temperature on product ratio to be drawn.[18] In the cyclopropane series, 1-cyano-2(*E*)-propenylcyclopropane at 207.1 and 387.4 °C reveals no significant effect of temperature on the ratios of *cis*- and *trans*-3-methyl-4-cyanocyclopentene, the products of ring enlargement.[19] Neither does any significant effect of temperature emerge in the studies by Baldwin and Keliher of bicyclo[3.1.0]-hexene.[20] Further kinetic studies of sufficiently high precision are desirable in this and other systems believed to involve multiple exit channels from the caldera. But there is of course a contradiction between any existing small differences in enthalpy of activation and the experimental complications involved in measuring temperature dependencies over necessarily very large ranges of temperature.

In these types of reaction, the overall energy of activation is consumed in the process of bond-breaking to the diradicals. The caldera may be generated essentially at thermal equilibrium with no significant excess of energy. If barriers to exit are of a magnitude comparable to $^3/_2RT$, no further activation by intermolecular collision is required and the Arrhenius equation is inapplicable.[21]

Among the conventional ways of thinking about product distribution, three are not helpful for explaining or predicting product ratios for conversions possibly involving diradical structures traversing a caldera: neither energies nor volumes of activation nor application of orbital symmetry theory are fruitful guides for anticipating or understanding product ratios. Perhaps the irrelevance of these three approaches may serve as a useful criterion that a reaction leading to two or more products may be proceeding by way of a caldera. Nonetheless, good

(17) Doubleday, C.; Li, G.-s.; Hase, W. L. *Phys. Chem. Chem. Phys.* **2002**, *4*, 304−312.
(18) From the temperature-dependent data in Table 1 of ref 11, including the data in Table 2 at 100.5 °C, the activation energies for the product ratios, k_{as}/k_{am} and k_{sa}/k_{sm}, are calculated to be 1.5 ± 0.8 and −3.1 ± 6.2 kcal mol^{-1}, respectively (standard errors!). Recalculation affords somewhat altered values for the energies of activation that emphasize the poorer quality of the data relating to *syn*-**2**: *anti*-**2** → *syn*-**2**, 31.4 ± 1.1; *syn*-**2** → *anti*-**2**, 34.2 ± 8.2; *anti*-**2** → **1** (methylenecyclohexene), 33.0 ± 1.9; *syn*-**2** → **1**, 30.3 ± 6.4 (95% confidence level).
(19) Doering, W. v. E.; Barsa, E. A. *J. Am. Chem. Soc.* **2004**, *126*, 12353−12362.
(20) Baldwin, J. E.; Keliher, E. J. *J. Am. Chem. Soc.* **2002**, *124*, 380−381.
(21) Menzinger, M.; Wolfgang, R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 438−444.

control of the effect of structural perturbations on the overall enthalpy of reaction remains.

Experimental Section

General. ^{1}H NMR spectra were taken on a Bruker DRX 500 mHz instrument. High-pressure equipment consisted of a Dieckers, Willich 4-kbar instrument. HPLC apparatus was by Jasco, Gross-Umstadt (column: Nucleosil 100-5 NO2 Vario Prep ET 250/10 column (Marcherey-Nagel), *n*-heptane/*tert*-butylmethyl ether (90−10); flow of 1.0 mL/min; UV-detector: 0−10 min at 254 nm, 10−30 min at 225 nm). MPLC: Kronlab, Sinsheim (column: YMC-Silica gel 120 Å, operated as above).

1-Cyano-3-methylenecyclohexene (5). A solution of 19.6 g (0.10 mol) of sodium metabisulfite in 32 mL of water was added dropwise at 25 °C over a 15-min period to 31.2 g (0.20 mol) of 1,4-dioxa-spiro-[4,5]decan-7-one in a 250-mL, round-bottomed flask accompanied by vigorous stirring. After being stirred for 2 h more, the homogeneous solution was added to 10.6 g of sodium cyanide (0.21 mol) in 22 mL of water. After being stirred for 20 h at 25 °C, the solution was diluted with 100 mL of ethyl acetate, stirred for 10 min, and filtered. The organic layer was separated from the water layer, which was extracted twice each with 20 mL of ethyl acetate. The combined organic layers were dried over $MgSO_4$ and concentrated in a vacuum to a residue which was treated with 30 mL of 3 N HCl. The resulting homogeneous solution was allowed to stand for 30 h, the initially homogeneous solution having separated into two layers. An extract of the aqueous layer with ethyl acetate (3 × 50 mL) was combined with the separated organic layer, washed with aqueous $NaHCO_3$ (2 × 75 mL), dried over $MgSO_4$, and concentrated to a yellow oil. Flash chromatography (petroleum ether/ethyl acetate: 3:1) afforded 17.6 g of 3-cyanocyclohex-2-enone: bp 83 °C at 2.2 mmHg (reported bp 105 °C at 3.8 mmHg); ^{1}H NMR (400 mHz, $CDCl_3$) 6.51 (s, 1H), 2.58−2.56 (m, 2H), 2.52−2.49 (m, 2H), 2.16−2.10 (m, 2H).

To a suspension of the Wittig reagent prepared from methyltriphenylphosphonium bromide (8.0 g) in 60 mL of dry THF and 10.5 mL of 2.0 M butyllithium, a solution of 2.46 g of the ketone above in 10 mL of THF at 0−5 °C was added dropwise over a period of 5 min. After being stirred for 1 h at room temperature, the solution was quenched with 0.5 mL of methanol. The resulting suspension was decanted slowly into 200 mL of pentane containing 15 g of Celite, stirred for 15 min, filtered, and concentrated by distillation through a 35-cm, helix-packed column. Passage through a short silica gel column (petroleum ether/ether: 6:1), concentration by fractional distillation, and crystallization overnight at −84 °C yielded a crystalline product (1.52 g), which could be separated from the supernatant liquid at low temperature. By 25 °C, the product had melted: ^{1}H NMR (400 mHz, $CDCl_3$) 6.83 (s, 1H), 5.13 (s, 2H), 2.40−2.32 (m, 2H), 2.32−2.28 (m, 2H), 1.80−1.72 (m, 2H); Exact mass (electron spray) calcd for C_8H_9N-(NH_4^+), 137.1079; found, 137.1079.

Photodimerization of 3-Cyano-1-methylenecyclohex-2-ene (5). A solution of 243 mg of 3-cyano-1-methylenecyclohex-2-ene and 30 mg of benzophenone in a mixture of 3 mL of *n*-heptane and 3 mL of acetone was partitioned among three ampules (5 mm × 150 mm). The ampules were freed of oxygen by three pump-freeze cycles, sealed under argon, and placed in a Pyrex irradiation apparatus that could be cooled by circulating ethanol at 0 °C. Irradiation with a high pressure mercury lamp (150 W) for 45 min generated only a small amount of insoluble polymer, which was removed by filtration through a short column of Al_2O_3. Analysis of the resulting mixture by HPLC on a Nucleosil 100-5 column with *n*-heptane/*tert*-butylmethyl ether at 254 nm showed only a single main product (t_R = 4.21 min) after 16.7 min of irradiation. Upon changing the UV−vis detector to 220 nm, a second photodimer became observable. In the routine procedure, 254 nm was used for the first 10 min of analysis, followed by a shift to 225 nm: *anti*-**6** (t_R = 15.38 min) and *syn*-**6** (t_R = 19.78 min). Samples could be separated by MPLC and stored in solution at −30 °C for use in the kinetic studies below. Attempts to remove solvent under reduced pressure at −20 °C for the purpose of obtaining NMR spectra on the pure dimers were unsuccessful owing to their still high reactivity. A spectrum of a mixture obtained by irradiation of **5** in toluene-d_8 follows: ^{1}H NMR (toluene-d_8) 6.27 (m, 5, 1H), 6.21 (m, *syn*-**6**, 1H), 6.14 (m, *anti*-**6**, 1H), 1.64−1.59 (m), 1.44−1.35 (m), 1.30−1.21 (m), 1.15−1.08 (m), 1.02−0.95 (m), 0.93−0.87 (m). UV−vis: *anti*-**6**, λ_{max} = 233 nm; *syn*-**6**, λ_{max} = 223 nm.

Table 3. Pressure Dependence of the Relative Concentrations of *anti*-**6**, *syn*-**6**, and **5** at 2000 bar and 50.1 °C in %

t (s)	*anti*-**6**	*syn*-**6**	**5**	Σ[a]	*t* (s)	*anti*-**6**	*syn*-**6**	**5**	Σ[a]
0	75.26	19.22	5.52	100.0	0	19.83	78.40	1.76	100.0
2460	67.50	23.28	9.22	92.8	2040	28.60	68.28	3.12	100.8
5580	61.29	25.45	13.26	94.2	4080	35.62	59.38	5.00	101.1
8160	57.05	26.05	16.90	94.0	6180	40.47	52.97	6.56	96.9
10440	53.87	25.79	20.34	93.7	8100	46.51	44.25	9.24	97.9
12840	50.76	25.39	23.85	94.1	10080	49.76	38.92	11.32	95.8
15360	48.72	24.33	26.95	93.3	12540	50.85	35.95	13.20	95.8
18060	46.38	23.79	29.82	94.3	14580	51.66	31.67	16.67	91.5
20340	44.12	22.54	33.34	91.9	16620	51.90	29.72	18.38	93.3
22740	42.03	22.29	35.68	91.4	18660	51.73	28.41	19.86	95.7
25500	41.41	20.86	37.72	93.5	20700	49.48	29.42	21.10	96.8
28500	38.98	19.63	41.39	92.4	22740	49.76	27.41	22.84	97.9
31500	37.05	18.81	44.14	93.9	24840	50.29	26.23	23.48	100.7
33660	35.31	18.32	46.36	93.4	26640	48.00	26.32	25.68	100.3
35880	33.39	17.28	49.33	90.9	28620	45.80	25.66	28.54	96.8

[a] Σ represents recovery vis-à-vis mesitylene and *p*-dicyanobenzene as internal standards.

High-Pressure Kinetics. To portions of the standard solutions of *anti*-**6** and *syn*-**6** prepared by irradiation and separation above by MPLC, mesitylene (**7**) and *p*-dicyanobenzene (**8**) as internal standards and catalytic amounts of bis-(3-*tert*-butyl-4-hydroxy-5-methylphenyl)-sulfide (BHMPS, Aldrich, No. 12,462-5) as radical scavenger were added. At each of the seven pressures indicated in Table 1, all at 50.1 °C, and at fifteen different time intervals, starting from each of two isomers, products are analyzed by HPLC with the Nucleosil column at a flow rate of 1 mL per min. Retention times in min are **7**, 2.74; **5**, 3.98; **8**, 12.66; *anti*-**6**, 14.67; and *syn*-**6**, 18.87. A single example at 2000 bar is given in Tables 3.

Specific rate constants are calculated from the two sets of product ratios by numerical integration using the program KINETIK of Dr. R. Fink which employs a Runge−Kutta procedure of fourth order and estimation of experimental uncertainties at the 95% confidence level by the method of Marquardt.[22] The program permits optimization of kinetic schemes with as many as seven components.

Concentrations of **5**, *anti*-**6**, and *syn*-**6** were calculated from the HPLC chromatograms using the following equations: $c(\textit{anti}\text{-}\mathbf{6})_t = [f_{\textit{anti}-\mathbf{6}} \times A_{\textit{anti}-\mathbf{6},t} \times c(\mathbf{8})_0]/A_{\mathbf{8},t}$, $c(\textit{syn}\text{-}\mathbf{6})_t = [f_{\textit{syn}-\mathbf{6}} \times A_{\textit{syn}-\mathbf{6},t} \times c(\mathbf{8})_0]/A_{\mathbf{8},t}$, and $c(\mathbf{5})_t = [f_{\mathbf{5}} \times F_{\mathbf{5},t} \times c(\mathbf{7})_0]/A_{\mathbf{7},t}$, where $f_{\textit{anti}-\mathbf{6}}$, $f_{\textit{syn}-\mathbf{6}}$, and $f_{\mathbf{5}}$ are HPLC UV factors for *anti*-**6**, *syn*-**6**, and **5**, respectively, and $A_{cpd,t}$ are HPLC peak areas of the various compounds. To determine the HPLC UV factors of *anti*-**6** and *syn*-**6**, a solution of 61.3 mg of **5** and 9.9 mg of **8** in 0.7 mL of acetone-d_8 was prepared, degassed, and irradiated for 1 h at 0 °C. After irradiation, the ratios among *anti*-**6**, *syn*-**6**, and **8** were determined by ^{1}H NMR and used in the HPLC analysis for the determination of the UV factors of *anti*-**6** and *syn*-**6**. For **5**, a solution of 19.95 mg of **5** and 117.5 mg of **7** in 100 mL of *n*-heptane/*tert*-butylmethyl ether (9:1) was prepared and analyzed three times by HPLC, the UV factors being evaluated by means of the following equations: $f_{\textit{anti}-\mathbf{6}} = (F_{\mathbf{8}}/F_{\textit{anti}-\mathbf{6}}) \times (I_{\textit{anti}-\mathbf{6}}/I_{\mathbf{8}}) = 0.2388$; $f_{\textit{syn}-\mathbf{6}} = (F_{\mathbf{8}}/F_{\textit{syn}-\mathbf{6}}) \times (I_{\textit{syn}-\mathbf{6}}/I_{\mathbf{8}}) = 0.2398$; and $f_{\mathbf{5}} = (F_{\mathbf{7}}/F_{\mathbf{5}}) \times (n_{\mathbf{1}}/n_{\mathbf{7}}) = 0.1302$, where I_{cpd} equals the integrated value of the NMR signal, and *n*, the molar amount of **5**.

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