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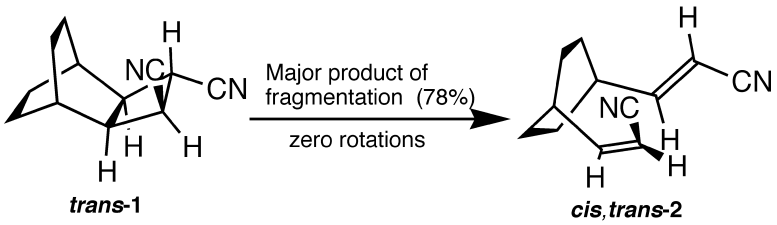

trans-1 *cis,trans*-2

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Conformational Restraint in Thermal Rearrangements of a Cyclobutane: 3,4-Dicyanotricyclo[4.2.2.0^{2,5}]decane

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Abstract: There being no study of a cyclobutane so fused to another cyclic system that an antiperiplanar conformation of the related diradical be precluded, the system in the title has been synthesized and studied for its thermal behavior. In comparison to the thermal behavior of unconstrained 1,2-dicyanocyclobutane in stereomutation and fragmentation to acrylonitrile, the constrained system shows a ~10-fold higher ratio of stereomutation to fragmentation to the three *cis*-1,4-bis-*β*-cyanovinylcyclohexanes. In these diolefins, a stereochemical correlation between the two olefinic fragmentation products is preserved. Revealed in the thermal rearrangement of isomer ***trans*-1** is a surprising excess (78%) of *cis*-1-*cis*-*β*-cyanovinyl-4-*trans*-*β*-cyanovinylcyclohexane, ***cis*,*trans*-2**, the result of zero internal rotations within the diradical-in-caldera prior to fragmentation (retention of configuration). Similarly, to a comparably striking extent, ***anti*,*cis*-1** gives ***trans*,*trans*-2** as its major product (71%), again by zero internal rotations.

Introduction

A new factor that may influence distribution among products from not-obviously concerted, purely thermal rearrangements of cyclobutanes is explored. A prior history can be reconstructed from references given in a recent contribution.[1] The possibility that fragmentation of a cyclobutane to two olefins might require, or at least be favored by, an antiperiplanar conformation in the intermediate diradical (the "caldera") has been suggested by Dewar et al.[2] and Halevi.[3] More recent theoretical work of Doubleday on cyclobutane has refuted this suggestion that an antiperiplanar conformation be required but still finds a small barrier to cleavage from synclinal conformations, in contrast to no barrier from the antiperiplanar.[4]

The specific system studied in this contribution is a cyclobutane so constructed as to preclude access to antiperiplanar conformations of the 1,4-diradical-like intermediates, yet flexible enough to allow access to synclinal conformations. The device selected involves fusion of a bicyclic system to the cyclobutane ring. Although a bicyclo[2.2.1]heptane system at first had seemed ideal [indeed ***trans*-5** (see Scheme 5 below) is known],[5] subsequent worries about the influence of the strain in that system (15 kcal mol^{-1}) on the identity of initial bond-cleavage (2,5- versus 3,4-) prompted the selection of a bicyclo[2.2.2]-octane system (8 kcal mol^{-1} of strain) as represented by ***anti*,*cis*-1** and ***trans*-1** in Figure 1.[6] Although this system is more flexible, and therefore less desirable, considerably less strain is placed on the 2,5-bond. While a dihedral angle of as much as 50° can be entertained in the related diradical resulting from cleavage of the 3,4-bond, a 180° twist to an antiperiplanar conformation is still precluded. The two cyano groups are introduced because their radical-stabilizing ability of ~8−11 kcal mol^{-1} each promises substantial control over the identity of the bond being broken. They also minimize steric repulsions and otherwise unwelcome competing reactions that often accompany the use of vinyl, for example, as a stabilizing group. A further important advantage is the existence for comparison of the thorough kinetic studies of *trans*- and *cis*-1,2-dicyanocyclobutane, the parent, reference compounds (***trans*-** and ***cis*-3**; Scheme 1).[7]

Results

Preparation of ***anti*,*cis*-1** and ***trans*-1** was uncomplicated but for our failure to find conditions for the transformation of the *cis*-diacid into the *cis*-diamide (Scheme 2). This inconvenience required two epimerizations instead of one in the final procedure, as shown. No significant amount of the third isomer, ***syn*,*cis*-1**, or its precursors appeared at any time, consistent with a higher MM2-calculated steric energy of 56.3 kcal mol^{-1} compared to that of ***trans*-1** (50.9 kcal mol^{-1}) and ***anti*,*cis*-1** (52.4 kcal mol^{-1}).

The three products of fragmentation (**2** in Figure 1) were obtained for purposes of assignment of structure by heating a sample of ***trans*-1** at 299 °C for ~16 h. Although ***trans*,*trans*-2**

(1) Doering, W. v. E.; Cheng, X−h.; Lee, Y−h.; Lin, T−z. *J. Am. Chem. Soc.* **2002**, *124*, 11642−11652.
(2) Dewar, M. J. S.; Krishna, S.; Calmer, H. W. *J. Am. Chem. Soc.* **1974**, *96*, 5240−5242; Dewar, M. J. S.; Kirschner, S.; Kollmar, H. W.; Wade, L. *J. Am. Chem. Soc.* **1974**, *96*, 5242−5244; Dewar, M. J. S.; Kirschner, S. *J. Am. Chem. Soc.* **1974**, *96*, 5246−5248.
(3) Halevi, E. A. *Helv. Chim. Acta* **1975**, *58*, 2136−2150.
(4) Doubleday, C. H., Jr. *J. Phys. Chem.* **1996**, *100*, 15083−15086.
(5) Tabushi, I.; Yamamura, K.; Yoshida, Z. *J. Am. Chem. Soc.* **1972**, *94*, 787−792.
(6) DeLuca, JoAnn Peters, Ph.D. Dissertation, Harvard University, 1986; *Diss. Abstr. Int. B* **1987**, *47*, 2434.
(7) Guyton, C. A., Ph.D. Dissertation, Harvard University, 1980; *Diss. Abstr. Int. B* **1980**, *41*, 1370; pp 153−185.

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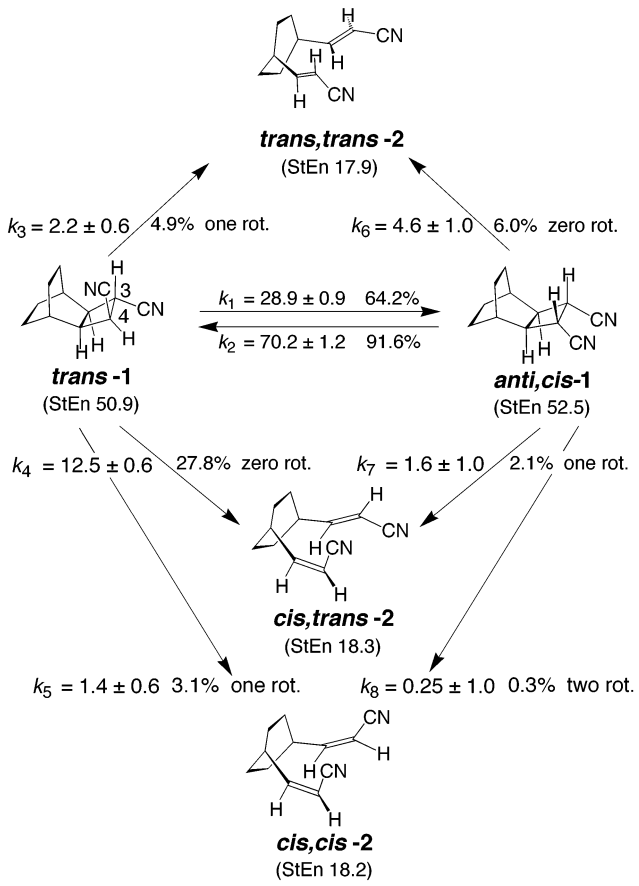
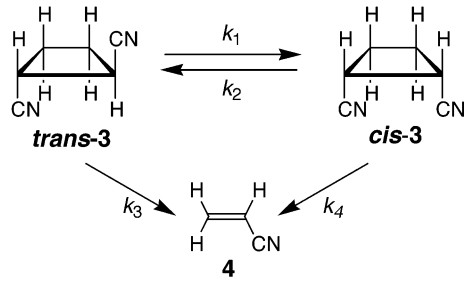


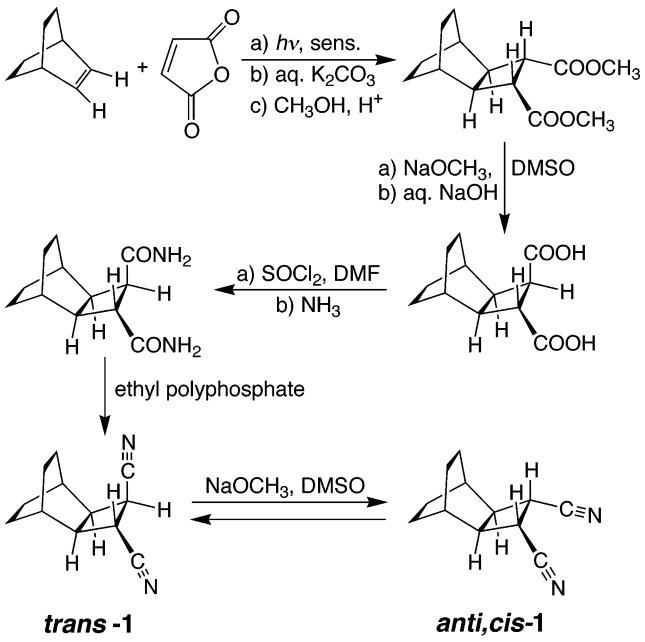
Figure 1. Thermal interconversion of ***anti*,*cis*-1** and ***trans*-1** and the three products of their fragmentation, ***trans*,*trans*-2**, ***cis*,*trans*-2**, and ***cis*,*cis*-2**, are shown along with their specific rate constants (all $k \times 10^{-6}$ s^{-1}) at 310.6 °C in *tert*-butylbenzene. Relative MM2 steric energies in twist-boat conformations are also indicated (StEn in kcal mol^{-1}). (Note the omission of ***syn*,*cis*-1**, consistent with its higher StEn of 56.3 kcal mol^{-1}). The minimum number of internal rotations (rot.) required by each path is also given.

Scheme 1

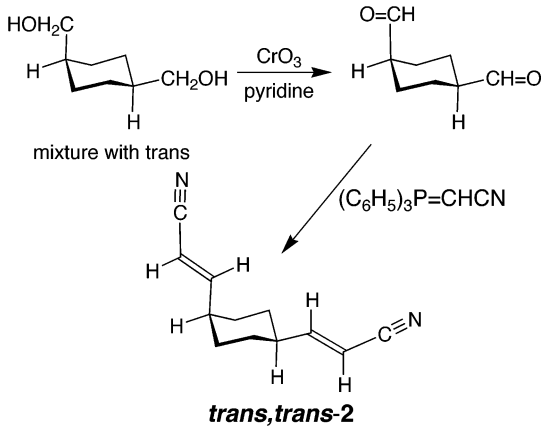


was cleanly separated by HPLC, the other two stereoisomers were obtained as a mixture in a ratio high enough (1:9) to permit confident identification of the olefinic-hydrogen portion of their NMR spectra. Geometrical assignments were made by analogy with the spectrum of acrylonitrile [5.64, (m, $J_{1,2}$ = 17.0 Hz, H-1); 6.23, (m, $J_{1,2}$ = 17.0 Hz, $J_{2,3}$ = 3.5 Hz, H-2 [trans to H-1]); 6.05, (m, $J_{1,3}$ = 11.5 Hz, H-3 [cis to H-1])]. Details are given in the Experimental Section and in the dissertation of DeLuca.[6] A compound identical to ***trans*,*trans*-2** was also obtained synthetically from a mixture of *cis*- and *trans*-1,4-bis-hydroxymethylcyclohexane via the mixture of dialdehydes, followed by reaction with cyanomethylenetriphenylphosphorane (Scheme 3).

Scheme 2



Scheme 3



Although the expected "irreversibility" of the product dienes was confirmed by the failure to detect any **1** upon heating a 9.9:1 mixture of ***cis*,*trans*-** and ***cis*,*cis*-2** at 299 °C, ***trans*,*trans*-2** appeared at a slow rate: 4.5% after 5.6 h ($k = \sim 2 \times 10^{-6}$ s^{-1}), by which time the ratio of ***cis*,*trans*-2** to ***cis*,*cis*-2** had decreased to 4.7:1. If the dimerization of unsubstituted acrylonitrile in the temperature range 150−170 °C be relevant, this slow interconversion among the dienes likely occurs by way of reentry into the caldera of diradicals as a first step in an otherwise thermodynamically thwarted cyclodimerization.

For the kinetic study, thermal rearrangements of ***trans*-1** and ***anti*,*cis*-1** are run to low conversion (15−20%) in *tert*-butylbenzene over the temperature range 256−311 °C. The data are given in Supporting Information, Table SI-1. Specific rate constants are evaluated by extrapolation to zero time and also by application of a multivariable program by courtesy of the late Professor Wolfgang R. Roth, the latter results being given in Table 1.

Discussion

The rates of thermal reorganizations of **1** and unsubstituted, 1,2-dicyanocyclobutane (**3**) are of the same order of magnitude

Table 1. Specific Rate Constants for the Stereomutation of ***trans*-1** (k_{tc}) and ***anti,cis*-1** (k_{ct}), and Their Fragmentation to the Mixture of Olefins **2** (k_{to} and k_{co}, Respectively)

T, °C	k_{tc}[a]	k_{ct}[a]	k_{to}[a]	k_{tc}[b]	k_{ct}[b]	k_{to}[b]	k_{co}[b]	K_{eq}
256.5	0.276 ± 0.011	0.74	0.103 ± 0.010	0.316 ± 0.007	0.849 ± 0.016	0.103 ± 0.067	0.001 ± 0.015	2.69
269.8	0.834 ± 0.040	2.20	0.256 ± 0.037					
281.1	2.204 ± 0.094	5.71	0.924 ± 0.087					
291.4	4.559 ± 0.187	11.63	1.968 ± 0.177					
300.4	10.77 ± 0.276	27.06	4.303 ± 0.260	12.33 ± 0.38	31.72 ± 0.62	4.30 ± 0.31	0.47 ± 0.56	2.57
310.4	21.75 ± 0.711	53.70	16.55 ± 0.649	28.95 ± 0.80	70.00 ± 1.10	16.17 ± 0.57	6.27 ± 0.90	2.42

Arrhenius Parameters

log k_{tc}	log k_{to}	log k_{tc}	log k_{ct}
$(14.00 \pm 0.33) - \frac{(50000 \pm 400)^c}{RT \ln 10}$	$(16.4 \pm 1.32) - \frac{(56900 \pm 3400)^d}{RT \ln 10}$	$14.55 - \frac{51000^e}{RT \ln 10}$	$14.56 - \frac{50000^e}{RT \ln 10}$

[a] Specific rate constants (in units of 10^{-6} s^{-1}) are calculated from the data in Table SI 1 starting from ***trans*-1** and using a simplified kinetic scheme of four rate constants: ***trans*-1** in reversible reactions with ***anti*,*cis*-1** (k_{tc} and k_{ct}) and the sum of all three dienes **2** (k_{to} and k_{-to}, the ratio k_{-to}/k_{to} being arbitrarily set to 1×10^{-5}; the equilibrium constants, k_{ct}/k_{tc}, at the various temperatures being set by the linear regression line obtained from the data in column 9). [b] Calculated from the data in Table SI 1 at 256.5, 300.4, and 310.4 °C starting from both of ***trans*-1** and ***anti*,*cis*-1**, and using a kinetic scheme of four rate constants involving the reversible stereomutation of ***trans*-1** and ***anti*,*cis*-1** (k_{tc} and k_{ct}) and their irreversible fragmentation to the sum of all three dienes **2** (k_{to} and k_{co}, respectively). [c] Calculated from the values in columns 1 and 2. [d] Calculated from the values in columns 1 and 4. [e] Calculated from the values in columns 1, 5, and 6, respectively.

Table 2. Specific Rate Constants[a] for the Stereomutation of *trans*- and *cis*-1,2-Dicyanocyclobutane (***trans*-3** and ***cis*-3**; k_1 and k_2, Respectively), and Fragmentation to Acrylonitrile (**4**, k_3 and k_4, Respectively; See Scheme 1)

T, °C[b]	k_1	k_2	k_3	k_4
225.0 ± 1.2	0.083 ± 0.007	0.216 ± 0.011	0.338 ± 0.051	0.654 ± 0.039
246.1 ± 0.2	0.667 ± 0.039	1.48 ± 0.11	3.07 ± 0.17	4.47 ± 0.41
257.0 ± 0.2	1.49 ± 0.10	3.69 ± 0.33	7.41 ± 0.82	10.5 ± 0.4
278.8 ± 0.1	9.10 ± 0.35	22.2 ± 0.8	43.4 ± 2.0	63.1 ± 1.9
289.0 ± 1.0	22.5 ± 1.3	53.1 ± 3.4	107 ± 8	165 ± 11.

Arrhenius Parameters

log k_1	log k_2	log k_3	log k_4
$(14.1 \pm 0.4) - \frac{(48200 \pm 900)}{RT \ln 10}$	$(14.2 \pm 0.2) - \frac{(47600 \pm 500)}{RT \ln 10}$	$(15.2 \pm 0.4) - \frac{(49400 \pm 1000)}{RT \ln 10}$	$(14.7 \pm 0.5) - \frac{(47600 \pm 1100)}{RT \ln 10}$

[a] Specific rate constants in units of 10^{-6} s^{-1}. [b] Mean $T = 257.0$ °C.

(see Tables 1 and 2, 257 °C). Apparently the fusion of the bicyclic system does not constitute a substantial perturbation on the basic reaction. Neither is there any significant difference in the activation parameters reported for stereomutation in Tables 1 and 2.

Discussion of fragmentation begins with a qualitative response to its surprisingly minor role [except at the highest temperature to be discussed below; see Table SI 1, 310.4 °C]. The quantitative aspects are compromised to some extent by the inability of our analysis by gas chromatography to determine with high quantitative accuracy the very small amounts of dienes **2** produced. This limitation is particularly marked in the behavior of ***anti*,*cis*-1**, where the extent of fragmentation is so small over the lower range of temperature (256.5−300.4 °C) that no useful information can be developed (see data in Table SI 1) but is conservatively estimated to be less than 2% of the total reaction.

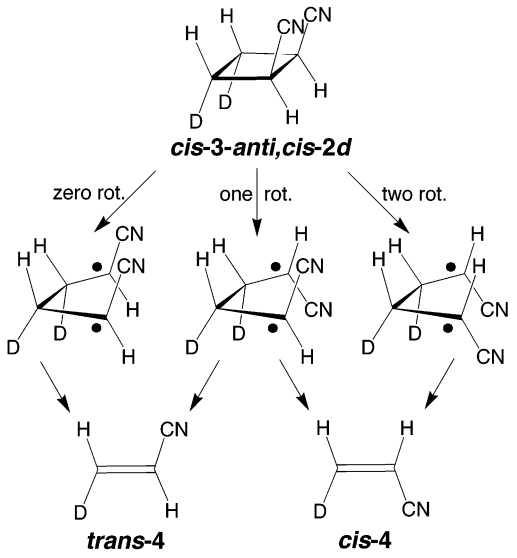
The reference compounds for comparison are the 1,2-dicyanocyclobutanes (**3**), which have *uninhibited* access to all conformational minima open to the intermediate diradicals prior to fragmentation. The results of a thorough examination made by Guyton in connection with her study of the stereochemistry of the dimerization of acrylonitrile (**4**) are recorded in Table 2.[8] Fragmentations (Fr) from ***trans*-3** and ***cis*-3** are favored over stereomutation (St) by factors (Fr/St) of 4.07 and 3.03, respectively. In the present example where access to antiperiplanar conformations is sterically prohibited, the reverse is true. The ratio Fr/St from ***trans*-1** has become ∼0.4 (Table 1, 256.5−300.4 °C). This striking reversal by a factor of ∼10 is consistent with the original stimulus for the present work. It confirms that an antiperiplanar conformation for diradicals from **3**, but not from **1**, may be ideal for processes leading to the two planar olefinic products, since fragmentations from the antiperiplanar geometry would require minimal geometrical adjustment beyond lengthening of the 3,4-bond. It is also consistent with the conclusion from Doubleday's calculations that the exit channel from the cyclobutane-derived caldera-defining fragmentation from the antiperiplanar conformation is downhill with no discernible barrier.[4]

Although increasing stability of the radical appears to be a significant factor influencing the ratio, Fr/St,[9] in this series, 1,2-cyanocyclobutane occupies a position intermediate between cyclobutane (Fr/St ≈ 3, $E_a = 61.8$ kcal/mol^{-1}) and a divinylcyclobutane (Fr/St ≈ 2, $E_a = 32.5$ kcal/mol^{-1}).[10] It is unlikely that an explanation for the factor ∼10 is to be found here.

Lack of accessibility to the antiperiplanar conformations not

(8) Doering, W. v. E.; Guyton, C. A. *J. Am. Chem. Soc.* **1978**, *100*, 3229−3230.
(9) Doering, W. v. E.; He, J.; Shao, L. *J. Am. Chem. Soc.* **2001**, *123*, 9153−9161.
(10) Doering, W. v. E.; Ekmanis, J. L.; Belfield, K. D.; Klärner, F.-G.; Krawzcyk, B. *J. Am. Chem. Soc.* **2001**, *123*, 5532−5541.

Scheme 4

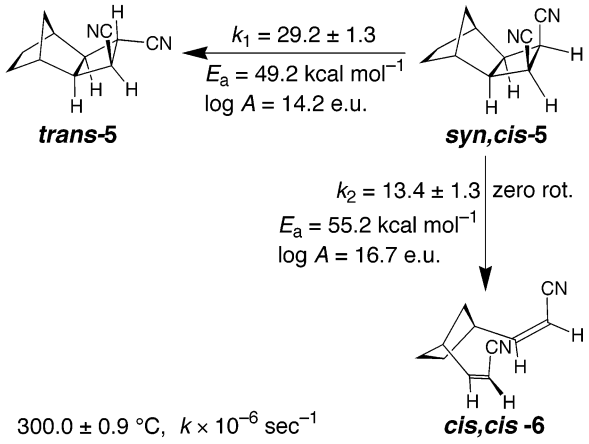


only removes any contribution to fragmentation from this mode, but it also removes a large segment of phase space from which reclosure (stereomutation) is normally barred. The expected overall effect is a decrease in the lifetime of the caldera, and a relative favoring of stereomutation. Whatever ultimately acceptable explanation may emerge, the barring of the antiperiplanar conformation to **1** has led to a significant decrease in fragmentation relative to stereomutation.

trans*-1** and ***anti*,*cis*-1**, among the many cyclobutanes in the literature that have been fragmented, are the first to retain stereochemical correlation between the pairs of olefins formed in the fragmentation. It has therefore become possible to deduce the *minimum* number of internal rotations needed to describe distribution among the three dienes of fragmentation. Cyclobutane, labeled as it has been by Guyton in her work on acrylonitrile (**4**) and its dimers **3**, serves to illustrate the limitations of the information available from simple cyclobutanes. Fragmentation of *cis*-1,2-dicyano-*anti*,*cis*-3,4-dideuteriocyclobutane (cis*-3-*anti*,*cis*-2*d*** of Scheme 4) generates the two acrylonitriles, ***trans*-4** and ***cis*-4**, by way of three intermediate diradicals formally resulting from zero, one, or two internal rotations about C2−C3 and C4−C1 bonds. Because each stereoisomer can result from *two* of these *three* diradicals, no conclusions about their relative contributions can be drawn (three variables, two observables!). The 61% retention of configuration (***trans*-4**) observed experimentally in the fragmentation of ***cis*-3-*anti*,*cis*-2*d*** does not, for example, allow any conclusion to be drawn about the relative amounts formed by zero and one internal rotation.

Nonetheless, the stereochemistry of fragmentation should be consistent with that observed in the reverse, more informative dimerization of *cis*-α,*β*-dideuterioacrylonitrile to six 1,2,3,4-tetradeuterio-1,2-dicyanocyclobutanes in which zero rotational processes can and have been unequivocally established (which see).[8] From the given data, the fraction of retained configuration, $(e_0 + t_1)/(e_0 + 2t_1 + e_2)$,[11] can be calculated to be 0.607 at 257 °C, 0.588 at 279 °C, and 0.580 at 289 °C, in good agreement with the 61% result from fragmentation.[7,8]

Scheme 5



In the present example, where correlation is strictly maintained by linkage of the two olefins of fragmentation, the major diene formed from ***trans*-1** over the temperature range, 256.5−300.4 °C is ***cis*,*trans*-2**, the product of "zero internal rotations" prior to fragmentation. [Strictly two internal rotations (one about each of carbon bonds 2,3 and 4,5—or any other comparable combination) also suffice]. At the highest temperature (310.4 °C), the ratio Fr/St increases: in ***trans*-1** to 0.77 from 0.39 ± 0.05 and in ***anti*,*cis*-1** to a value of 0.09 from undetectable (not necessarily zero). From the data in Figure 1, ***trans*-1** is seen to fragment to ***cis*,*trans*-2** (∼78%; $k_4/k_3 + k_4 + k_5$), the result of *zero* internal rotations prior to cleavage. The remaining dienes, ***trans*,*trans*-2** and ***cis*,*cis*-2**, 14% and 8%, respectively, are the product each of a single rotation. (The process of double rotation (two single rotations) is potentially observable as racemization of optically active ***trans*-1** but has not been explored in this investigation.) The major product of fragmentation of ***anti*,*cis*-1** is ***trans*,*trans*-2** (71%), again the result of *zero* rotations. Lesser products are ***cis*,*trans*-2**, the result of a single rotation (25%), and ***cis*,*cis*-2** (4%), the result of a double rotational process (two single internal rotations). In both instances the stereochemistry of the predominant diene has resulted from a zero rotational, Woodward−Hoffmann forbidden process.

The experimental outcome might be thought consistent with the incursion of a significant contribution from cleavage of the (wrong) 2,5 bond, for which a higher activation enthalpy has been estimated (see above). Were this process also to have contributed to fragmentation of ***trans*-1** in the lower temperature range, the actual value of Fr/St in cleavage of the 3,4-bond would become even smaller than that proclaimed above. In this connection, a cursory investigation of the more highly strained bicyclo[2.2.1] system, *syn*,*cis*-3,4-dicyanotricyclo[4.2.1.$0^{2,5}$]-nonane (***syn*,*cis*-5**), has revealed only ***cis*,*cis*-6**, the product of fragmentation by a zero-rotational process (Scheme 5). Suggestive of wrong-bond cleavage as the rationalization for the favoring of zero-rotation are the activation parameters extractable from the data in columns 1 and 4 of Tables 1 and SI-2. In both instances, the activation energy for fragmentation is ∼6−7 kcal mol^{-1} higher than that for stereomutation, while the frequency factors are higher by ∼log $A = 2.5$.[12] We have no

(11) From the three equations, $c + t + o = 1$, (where *c*, *t*, and *o* are the respective fractions of ***cis*-1**, ***trans*-1**, and the sum of the three dienes **2** emerging from the hypothetical caldera-in-common (example taken from Figure 1), $c/o = k_1/(k_3 + k_4 + k_5)$, and $t/o = k_2/(k_6 + k_7 + k_8)$, values for the three fractions can be obtained.

(12) These activation parameters are not the result of an extended, dedicated study and should be accepted with caution.

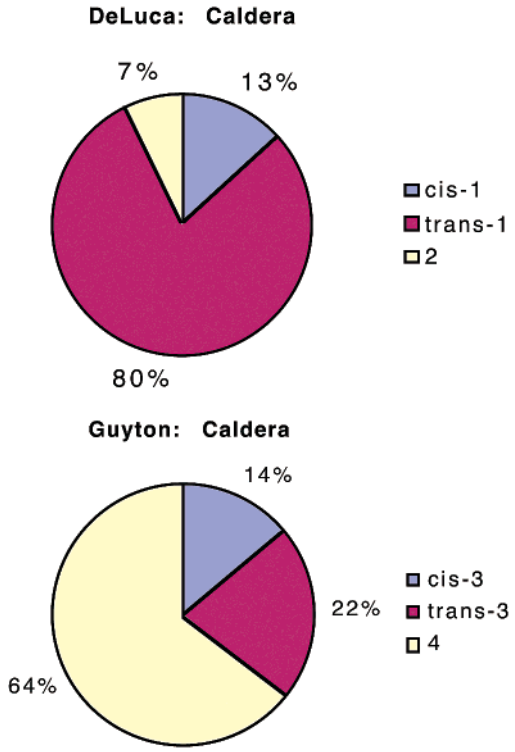


Figure 2. Diagram of the fractions in percent of *cis*- and *trans*-cyclobutanes and combined olefinic products of fragmentation (**2** and **4**, respectively) emerging from the hypothetical caldera of diradical intermediates in the thermal transformation of ***cis*-1** and ***trans*-1** (upper pie) and ***cis*-3** and ***trans*-3** (lower pie).

way of credibly estimating any difference in the relief of energy of strain in the bicyclooctane and bicycloheptane systems beyond noting that their respective energies of strain are 9.6 and 15.3 kcal mol^{-1}.

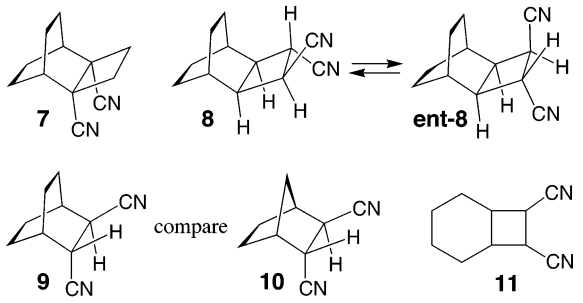
Although the favoring of zero rotation may not be associated with confidence with the behavior of the bis-cyanomethyl diradical prior to termination by fragmentation, the observation brings into view the possibility that otherwise nonobservable, zero rotational processes may be critical for a complete description of the exit channels from calderas of diradicals.

It seems worth exploring a *hypothetical* situation in which entry channels connect ***trans*-1** or ***anti*,*cis*-1** in a caldera-in-common. In earlier thinking, for example, refs 13 and 14 it was held that a common intermediate would require *identical* distributions among the products of the exit channels. On this basis, maximum values for participation of a caldera-in-common were deduced. In the present example, described in Figure 1, ***trans*-1** undergoes stereomutation to ***anti*,*cis*-1** (65%) and fragmentation to combined dienes **2** (35%). In sharp contrast, ***anti*,*cis*-1** undergoes stereomutation to ***trans*-1** (92%) and fragmentation to dienes **2** to the extent of only 8%. Without the inclusion of the identity reactions (e.g., ***trans*-1** returning to ***trans*-1**), this system would appear to be far from having a single caldera common to the two educts.

With its inclusion, a caldera-in-common becomes qualitatively tenable. Solution of the three equations transforming the experimental results may be expressed pie-graphically as the upper diagram in Figure 2.[11] Entry into the caldera from ***trans*-1**

(13) Doering, W. v. E.; Sachdev, K. *J. Am. Chem. Soc.* **1974**, *96*, 1168−1187.
(14) Doering, W. v. E.; Mastrocola, A. R. *Tetrahedron, Suppl. 1* **1981**, *17*, 329−344.

Chart 1



then leads to the two *observable* products in the ratio 13/7 (65%/35%), while entry from ***anti*,*cis*-1** produces its two *observable* products in the ratio 80/7 (92%/8%). In other words, the ratios of observable products are determined by differences in the *nonobservable*, identity reactions. (We reiterate that our inability adequately to define the ratios among the three dienes **2**, let alone to find that their ratios are *independent* of educt as required for full compatibility with a common intermediate, makes this discussion in its specific terms purely hypothetical.) If the same hypothetical analysis were to be applied to Guyton's experiments with the acyclic analogues, **3** and **4**, the lower diagram in Figure 2 results. Herein lies a proposition that may only be resolvable by theoretical calculation, for example à la Doubleday.[4]

The major surprise revealed by these geometrically constrained cyclobutanes, ***trans*-1** and ***anti*,*cis*-1**, in conjunction with earlier studies of the thermal chemistry of deuterium-labeled 1,2-dicyanocyclobutanes, is a substantial disfavoring of fragmentation relative to stereomutation. For ***trans*-1** (relative to ***trans*-3**), the Fr/St ratio is diminished by a factor of about 10, while for ***anti*,*cis*-1** (relative to ***cis*-3**), the Fr/St ratio is diminished by a factor of about 30. More questions are raised, perhaps, than are answered. Might a look at the severely geometrically restricted, isomeric 2,5-dicyanobicyclo[4.2.2.$0^{2,5}$]-octane, in which stereomutation is barred and fragmentation almost forced to be concerted, give useful information (Chart 1, **7**)? Would examination of the rate of racemization of ***trans*-1**, a two-rotational process overall, shed light on the extent to which a caldera-in-common is approached (Chart 1, **8**, **ent-8**)? If *trans*-1,2-dicyano-*cis*-3,4-dideuteriocyclobutane (***trans*-3-*cis*-2*d***) were to lead to a different composition of acrylonitriles (***trans*-** and ***cis*-4**) from that afforded by ***cis*-3-*anti*,*cis*-2*d***, could inferences be made about the degree to which a common steady-state caldera had been achieved? Might comparison of the activation parameters of the stereomutation of 2,3-dicyanobicyclo-[2.2.2]octane and 2,3-dicyanobicyclo[2.2.1]heptane (**9** and **10**) help resolve doubts about which bond is cleaved in the generation of dienes **2** from **1**? Could a look at the behavior of the various 7,8-dicyanobicyclo[4.2.0]octanes (**11**) add further insight?

Experimental Section

General Methods. NMR spectra were recorded on a JEOL-FX270 (270 MHz) or a Varian CFT20 (80 MHz) spectrometer in $CDCl_3$ unless otherwise stated, chemical shifts and coupling constants (*J*) being reported in ppm (δ) from tetramethylsilane, and hertz (Hz), respectively. Infrared spectra (IR) were recorded on a Perkin-Elmer model 598 spectrophotometer and reported in reciprocal centimeters (cm^{-1}). Quantitative gas chromatographic analysis (GC) was effected on a Perkin-Elmer model 990 instrument with flame ionization detector and

Hewlett-Packard 3380S integrator, using a 50-ft OV-225 capillary column. HPLC employed a Waters ALC/GPC 501 instrument fitted with a model 6000 solvent delivery system, a model UK6 injector, and a refractive index detector: column A, Waters μPorasil (25 cm); and column B, DuPont Zorbax Sil (25 cm). Melting points were determined without correction in a Hershberg apparatus.

Tricyclo[4.2.2.0^{2,5}]decane-*cis*-3,4-dicarboxylic Acid. Into an immersion-well photolysis apparatus fitted with a magnetic stirrer, a reflux condenser capped with a $CaSO_4$-filled drying tube, and a 450-W Hanovia mercury lamp contained in a Pyrex, water-cooled sleeve was placed a solution of 7.3 g of bicyclo[2.2.2]oct-2-ene [prepared in three steps from cyclohexa-1,3-diene and maleic anhydride following the procedure of Grob et al.[15] and Cimarusti and Wolinsky[16] (for details see ref 6)] in pentane (150 mL) and methylene chloride (250 mL) containing maleic anhydride (35 g) and acetophenone (21 g). The photolysis vessel, cooled in a bath refrigerated at 5 °C, was irradiated. The photolysis was interrupted twice during the first 24 h to allow filtration of the reaction mixture and cleaning of the sleeve. After a total of 43 h, the filtrate was concentrated under vacuum to a maroon liquid, which was extracted with boiling ether. The ethereal extract was filtered and concentrated to an oil, which was then boiled under reflux with 7.5% aqueous K_2CO_3 (200 mL) for 2.5 h. The resulting mixture was washed with ether, acidified, and extracted thrice with ether. The combined ethereal extracts were washed with water, dried over $MgSO_4$, and concentrated to an oil, which crystallized upon trituration with a mixture of benzene and acetone: 2.75 g; mp 188−190 °C dec; ^{1}H NMR (80 MHz) 3.5 (m, 2H), 2.7 (m, 2H), 1.6 (m, 10H); ^{13}C NMR (^{1}H decoupled) 128.40, 41.87, 37.53, 25.79, 25.04, 21.58; IR (mineral oil mull) 3300−2600, 1710, 1285, 1130, 880.

Tricyclo[4.2.2.0^{2,5}]decane-*trans*-3,4-dicarboxylic Acid. A solution of 0.75 g of the *cis*-diacid immediately above and 2 mL of concentrated H_2SO_4 in 20 mL of methanol was boiled under reflux for 3 h, poured into 50 mL of water, and extracted with ether. The ethereal extract was washed successively with water, saturated $NaHCO_3$, and water, then dried over $MgSO_4$, and finally concentrated to crystalline dimethyl tricyclo[4.2.2.0^{2,5}]decane-*cis*-3,4-dicarboxylate: 0.71 g; mp 66−68 °C; ^{1}H NMR (80 MHz) 3.7 (s, 6H), 3.5 (m, 2H), 1.9−1.4 (m, 10H); IR (mineral oil mull) 1720, 1275, 1180, 1040, 990.

Freshly prepared 3 N sodium methoxide (3 mL) was added to a solution of 2.71 g of the diester above in 10 mL of dimethyl sulfoxide (DMSO). After 30 min of stirring, the solution was poured into ice water, acidified with 6 N HCl, and extracted three times with ether. After being washed with water, dried ($MgSO_4$), and concentrated, the ether solutions afforded a residual yellow oil (2.76 g), which was refluxed for 2 h with 50 mL of 5% aqueous NaOH. Workup in the usual fashion gave a residue, from which 1.33 g of tricyclo[4.2.2.0^{2,5}]-decane-*trans*-3,4-dicarboxylic acid was obtained after crystallization from $CHCl_3$ (filtrate contains mainly the cis starting material): mp 208−215 °C (dec); ^{1}H NMR (80 MHz, acetone-d_6) 3.65 (m, 1H), 3.55 (m, 1H), 2.60 (m, 1H), 2.50 (m, 1H), 1.8−1.6 (m, 10 H); ^{13}C NMR (^{1}H decoupled, acetone-d_6) 175.56, 174.78, 41.63, 40.63, 39.44, 37.83, 26.17, 26.06, 25.98, 25.79, 22.66, 21.96; IR (mineral oil mull) 2720, 2640, 1690, 1310, 1255, 1245, 950, 730.

***trans*-3,4-Dicyanotricyclo[4.2.2.0^{2,5}]decane (*trans*-1)**. A mixture of 0.50 g of the diacid prepared immediately above, 1.0 mL of dry THF, and 2 mL of thionyl chloride in 20 mL of anhydrous benzene was refluxed for 1.5 h, concentrated in a vacuum to a partly crystalline solid, which was extracted with several small portions of anhydrous benzene. The combined benzene extracts were introduced by filtration through glass-wool into a round-bottomed flask fitted with a septum and a condenser capped with a $CaSO_4$ drying tube. After the stirred mixture was briefly cooled in an ice bath, anhydrous ammonia was bubbled through it for 15 min. The now viscous mixture rested overnight before having a precipitate removed by filtration. The diamide was washed with benzene, methylene chloride, and water: 75−90% of theoretical yield, dec >220 °C, varied from 75 to 95% of theoretical: IR (mineral oil mull) 3340, 3180, 1665, 1400, 1205, 1105, 720.

Ethyl polyphosphate[17] (4.6 g) and 0.46 g of crude diamide above were boiled under reflux in 20 mL of $CHCl_3$ for 24 h. Filtered through glass wool, and stirred with 50 mL of 25% aqueous K_2CO_4 for 1 h, the chloroform solution was successively washed with water, dried over $MgSO_4$, and concentrated to an oil, which partially crystallized when triturated with hexane. Recrystallization from methanol/water gave 0.24 g (62%) of ***trans*-1**: mp 105.5−107.0 °C; ^{1}H NMR (270 MHz) 3.7 (m, 1H), 2.9 (m, 1H), 2.7 (m, 1H), 2.3 (m, 1H), 1.9−1.3 (m, 10H); ^{13}C NMR (^{1}H decoupled) 41.06, 37.50, 27.30, 24.82, 24.66, 24.44, 24.25, 21.42, 20.61 (quaternary C atoms not seen above baseline); IR (CH_2Cl_2) 2950, 2895, 2890, 2250, 1485, 1465.

***anti,cis*-3,4-Dicyanotricyclo[4.2.2.0^{2,5}]decane (*anti,cis*-1)**. A solution of 0.18 g of ***trans*-1** in 3 mL of dried DMSO, to which 0.3 mL of freshly prepared 1.5 N sodium methoxide had been added, was stirred for 5 min, poured into a separatory funnel containing 50 mL of ice water, and extracted twice with 15 mL each of benzene. The benzene extracts, washed with water and dried over $MgSO_4$, were concentrated to an oil (0.18 g), which was separated into two fractions by chromatography on silicagel with hexane/ethyl acetate. That of shorter retention time is ***trans*-1**, while that of longer is ***anti*,*cis*-1**: mp 121−122 °C; ^{1}H NMR (270 MHz) 3.55 (m, 2H), 2.97 (m, 2H), 1.6 (m, 10H); ^{13}C NMR (^{1}H decoupled) 40.31, 26.68, 25.06, 23.98, 20.61 (quaternary C atoms not seen above baseline); IR (CH_2Cl_2) 2950, 2890, 2250, 1485, 1465.

The Three *cis*-Bis-1,4-(2′-cyanoethenyl)cyclohexanes. A solution of 25 mg of ***trans*-1** and 5 mg of diphenylamine in 2.0 mL of *tert*-butylbenzene was divided into four equal quantities; each was placed into ammonia-treated, silanized Pyrex tubes, which were degassed and sealed in vacuo. The ampules were heated for 945 min in the fluidized bath at 299 °C. Analysis of the recombined solutions by capillary GC (190 ° C, 12 psi He) revealed five compounds: ***cis*,*cis*-2** (retention time, 11 min), ***trans*-1** (rt, 13 min), ***cis*,*trans*-2** (rt, 18 min), ***trans*,*trans*-2** (rt, 38 min), and ***anti*,*cis*-1** (rt, 48 min). Separation by HPLC (column B, 4% ethyl acetate in hexane, 1.0 mL/min) afforded four fractions: ***trans*-1** (rt, 10 min), a 1:9 mixture of ***cis*,*cis*-2** and ***cis*,*trans*-2** (rt, 15 min), ***trans*,*trans*-2** (rt, 24 min), and ***anti*,*cis*-1** (rt, 33 min): ^{1}H NMR (270 MHz) ***cis*,*cis*-2** 6.55 (dd, J = 10.9, J = 9.9), 5.32 (dd, J = 10.8, J = 0.5), 2.85 (m), 1.6 (m); ***cis*,*trans*-2** 6.77 (dd, J = 16.5, J = 6.3), 6.49 (dd, J = 10.9, J = 9.9), 5.35 (dd, J = 16.5, J = 1.6), 5.31 (dd, J = 10.9, J = 0.7), 2.85 (m), 2.49 (m), 1.6 (m); ***trans*,*trans*-2** 6.73 (dd, J = 16.5, J = 6.3, 2H), 5.33 (dd, J = 16.5, J = 1.6, 2H), 2.41 (m, 2H), 1.7−1.6 (m, 8H); IR ($CHCl_3$) 2940, 2870, 2230, 1730, 1630, 1450, 970.

Reaction of Cyclohexane-1,4-dicarboxaldehyde with Cyanomethylenetriphenylphosphorane. The dialdehyde was prepared by the addition of a solution of 1.2 g of *cis*- and *trans*-bis-1,4-(hydroxymethyl)-cyclohexane in 3 mL of acetone to a reagent prepared from 10.2 g of chromium trioxide and 16.4 mL of anhydrous pyridine.[18] After 15 min of being stirred, the supernatant solution was decanted from the tarry solid, which was extracted twice with ether. The combined ether solutions were washed with 5% aqueous NaOH, water, 0.5 N HCl, water and brine and finally dried and concentrated to give 0.5 g of crude dialdehyde. Solid cyanomethylenetriphenylphosphorane was prepared by boiling 12 g of triphenylphosphine and 3.5 g of chloroacetonitrile in 50 mL of benzene for 8 h and treating the resulting crystalline phosphonium salt in 50 mL of water with NaOH to precipitate 3.7 g of the phosphorane.

A benzene solution (25 mL) of dialdehyde (0.5 g) and phosphorane (2.7 g) was boiled under reflux for 4 h, concentrated to a brown oil,

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(17) Pollman, W.; Schramm, G. *Biochim. Biophys. Acta* **1964**, *80*, 1−7.
(18) Ratcliffe, R.; Rodehorst, R. *J. Org. Chem.* **1970**, *35*, 4000−4002.

which was extracted thrice with ether. The ether extracts were filtered, and again concentrated to an oil. This process, intended to remove triphenylphosphine oxide, was repeated. The major product, isolated by chromatography on silica gel (hexane/ethyl acetate) and purified by crystallization from methanol/water, was a *trans*-bis-1,4-(*trans*-2′-cyanoethenyl)cyclohexane: ^{1}H NMR (80 MHz) 6.54 (dd, $J = 16.5$, $J = 6.5$, 2H), 5.27 (dd, $J = 16.4$, $J = 1.4$, 2H), 2.3−1.0 (m, 8H); IR ($CHCl_3$) 2985, 2940, 2860, 2235, 1635, 1115. A minor product was shown to be identical to ***trans*,*trans*-2** by co-injection on capillary GC column, and by co-injection on HPLC column B: ^{1}H NMR (80 MHz, C_6D_6) 6.05 (dd, $J = 16.8$, $J = 6.4$, 2H), 4.63 (dd, $J = 16.8$, $J = 1.6$, 2H), 1.5 (br m), 0.9 (m).

Kinetics of the Rearrangement of *trans*-1 and *anti*,*cis*-1. In a typical experiment, a stock solution of ***trans*-1** (0.25%), hexacosane (0.13%), and diphenylamine (0.05%) in *tert*-butylbenzene was prepared. Aliquots (200 μL) were degassed and sealed in vacuo in Pyrex ampules (100 × 4 mm i.d.) prepared by first soaking in aqueous ammonia (20%) overnight, rinsing with water and acetone, and drying and then treating with dichlorodimethylsilane (20% in benzene), rinsing with benzene, acetone, and drying. The sealed tubes were heated in a Tecam FB-07 fluidized alumina bath, the temperature being monitored by an iron−constantan thermocouple and Leeds and Northrop 8686 millivolt potentiometer. For the 256 °C temperature, heating was by insertion into the vapors of boiling biphenyl.

Analysis of the contents of the ampules was by GC, column A (190°, 12 psi He). The analyses reported in Table SI-1 were the averages of three separate GC analyses.

Thermal Rearrangement Among Dienes 2. A solution of ∼5 mg of a 9.9:1 mixture of ***cis*,*trans*-2** and ***cis*,*cis*-2** in 1.5 mL of *tert*-butylbenzene containing 2.8 mg of diphenylamine was divided into aliquots (∼200 μL) and placed in Pyrex tubes as noted above. After being heated in the fluidized alumina bath at 199 °C for various periods, the tubes were removed and their contents analyzed by capillary GC, each three times. Results are given in the Table 3. No trace of ***trans*-1** or ***anti*,*cis*-1** was seen.

Table 3. Thermal Rearrangement of a Mixture of ***cis*,*trans*-2** and ***cis*,*cis*-2** at 199 °C

time, h	***cis*,*trans*-2**	***cis*,*cis*-2**	***trans*,*trans*-2**	ratio[a]
0	90	10	0	9.0:1
3.03	85	12	2.6	7.1:1
5.61	78	17	4.5	4.6:1

[a] The ratio of ***cis*,*trans*-2** to ***cis*,*cis*-2**.

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Supporting Information Available: Unrefined kinetic data from the thermal transformations of ***trans*-** and ***cis*-1** are contained in Table SI-1, while those from ***syn*,*cis*-5** are found in Table SI-2 (PDF). This material is available free of charge at the Internet at http://pubs.acs.org.

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