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The Cyclohexadienyl Radical in the Thermal Syn−Anti Isomerization of Two Crossed Pentaenes of the Type of Bis-Homofulvalene

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Abstract: To augment the elucidation of the dependence of enthalpy of stabilization on configuration among the pentadienyl radicals, a designer pentaene of the (*Z,Z*) type, (*R,R*)-5,5′,6,6′,7,7′,8,8′-octahydro-4a,4a′-dimethyl-2,2′-bi-4a(*H*)-naphthylidene, has been prepared and subjected to a kinetic study of cis, trans isomerization about its central double bond. The resulting activation parameters and those of a more complicated example, 3,3′-bicholesta-1,4-dienylidene, are essentially identical, their mean values being $\Delta H^{\ddagger} = 36.8$ kcal/mol and $\Delta S^{\ddagger} = +1.8$ eu. This enthalpy of activation is significantly higher than those of pentaenes of the (*E,E*) and (*E,Z*) configuration. Conjugative interaction in coplanar cross-conjugated systems of the bis-homofulvalene type not having been experimentally evaluated or estimated by theoretical calculation, an enthalpy of stabilization for the cyclohexadienyl radical is not definitively to be extracted at the present time. If conjugative interactions are to be equated to four Kistiakowsky butadiene units and the difference in steric energies between educt and 90°-twisted state are to be estimated by the MMEVBH program, an enthalpy of stabilization of the cyclohexadienyl radical of ∼20 kcal/mol results.

The (*Z,Z*) is one of three configurations of the pentadienyl radical. Although it has remained undetected experimentally in its paradigmatic, *alicyclic* form, it has been thoroughly scrutinized theoretically by Fort, Hrovat, and Borden.[1] By contrast, a *cyclic* relative, the cyclohexadienyl radical, which is the accepted intermediate in the addition of radicals to benzene and derivatives, has attracted extensive experimental attention. Efforts to bring its enthalpy of stabilization to ground include examination of the kinetics of the reaction of cyclohexa-1,3-diene with nitric oxide by Benson and co-workers;[2] determination of the heat of reaction of cyclohexa-1,4-diene with *tert*-butyloxyl (photoacoustic calorimetry) by Griller and co-workers;[3] several investigations of the reaction of benzene and hydrogen atoms, most recently given a unified interpretation by Tsang;[4] and loss of methyl radical from 3,3,6,6-tetramethylcyclohexa-1,4-diene.[5,6] Perhaps surprisingly, the thermochemistry of the cyclohexadienyl radical seems not to have been assessed theoretically at the highest, currently affordable level.

Geometrical, thermal, first-order, cis−trans isomerization about a double bond passes through a 90° conformation, which is economically formulated as a singlet diradical. This reaction has been used to gain information about the thermochemistry of the (*E,E*) and (*E,Z*) configurations of the pentadienyl radical.[7] In the present work, two crossed pentadienes corresponding to the (*Z,Z*) configuration of the pentadienyl radical, shown in Scheme 1, have been prepared: one in the steroid series parenthetical to a vain search for an effect of “solvent friction” on rate of isomerization;[7b,d] another, less highly substituted, consonant with the previously studied, (*E,E*) and (*E,Z*) pentaenes.

The first, 3,3′-bicholesta-1,4-dienylidene (**1**), is prepared as a mixture of stereoisomers, *anti*-**1** and *syn*-**1** (*anti*: defined with rings D and D′, trans and 10 and 10′ methyl groups, cis; *syn*, analogously), by Mukaiyama-Tyrlik-McMurry reductive coupling[8] of cholesta-1,4-dien-3-one;[9] the second, *anti*-**2** and *syn*-**2**, similarly, from (*R*)-(+)-5,6,7,8-tetrahydro-4a-methyl-2(3***H***)-naphthalenone (**5**), as depicted in Scheme 1. Although each stereoisomer is obtained in essentially equal amounts, in both instances a single pure stereoisomer can be separated by crystallization. These are held to be *syn*-**1** and *anti*-**2**, respectively, on the basis of nuclear Overhauser enhancements (see Experimental Section) and, in the case of *syn*-**1**, of an X-ray crystallographic analysis.[10] Auspiciously for study of the kinetics of thermal interconversion of syn and anti isomers, the vinyl hydrogen atoms of both isomers of **1** and **2** are quantitatively distinguishable in the ^{1}H NMR spectra, as can be inferred from the affiliated chemical shifts included in Scheme 1 and discussed in detail in the Experimental Section.

Rearrangement of the bicholesta-1,4-dienylidenes (**1**) is clean in that spectra taken at the longer times of reaction, at which the (pseudo)equilibrium constant seems to be reassuringly close

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[⊗] Abstract published in *Advance ACS Abstracts,* July 1, 1996.

(1) Fort, R. C., Jr.; Hrovat, D. A.; Borden, W. T. *J. Org. Chem.* **1993**, *58*, 211−216.

(2) Shaw, R.; Cruikshank, F. R.; Benson, S. W. *J. Phys. Chem.* **1967**, *71*, 4538−4543.

(3) (a) Hawari, J. A.; Engel, P. S.; Griller, D. *Int. J. Chem. Kinet.* **1985**, *17*, 1215−1219. (b) Griller, D.; Wayner, D. D. M. *Rev. Chem. Intermed.* **1986**, *7*, 31−44. (c) Burkey, T. J.; Majewski, M.; Griller, D. *J. Am. Chem. Soc.* **1986**, *108*, 2218−2221.

(4) (a) Tsang, W. *J. Phys. Chem.* **1986**, *90*, 1152−1155. (b) Nicovich, J. M.; Ravishankara, A. R. *J. Phys. Chem.* **1984**, *88*, 2534−2541 (q. v. for other relevant references). (c) Sauer, M. C., Jr.; Mani, I. *J. Phys. Chem.* **1970**, *74*, 59−63. (d) James, D. G. L.; Suart, R. D. *Trans. Faraday Soc.* **1968**, *64*, 2752−2769. (e) Sauer, M. C., Jr.; Ward, B. *J. Phys. Chem.* **1967**, *71*, 3971−3983. (f) Yang, K. *J. Am. Chem. Soc.* **1962**, *84*, 3795−3799.

(5) Wüstefeld, M., reported in ref 6, Tables 25, 37, 38, and 45.

(6) Roth, W. R.; Staemmler, V.; Neumann, M.; Schmuck, C. *Liebigs Ann.* **1995**, 1061−1118.

(7) (a) Doering, W. von E.; Kitagawa, T. *J. Am. Chem. Soc.* **1991**, *113*, 4288−4297. (b) Doering, W. von E.; Birladeanu, L.; Cheng, X-h.; Kitagawa, T.; Sarma, K. *J. Am. Chem. Soc.* **1991**, *113*, 4558−4563. (c) Doering, W. von E.; Sarma, K. *J. Am. Chem. Soc.* **1992**, *114*, 6037−6043. (d) Doering, W. von E.; Shi, Y.-q.; Zhao, D.-c. *J. Am. Chem. Soc.* **1992**, *114*, 10763−10766.

(8) McMurry, J. E. *Chem. Rev.* **1989**, *89*, 1513−1524, and references cited therein.

(9) (a) Pinder, A. R.; Robinson, R. *J. Chem. Soc.* **1952**, 1224−1231. (b) Wilds, A.; Djerassi, C. *J. Am. Chem. Soc.* **1946**, *68*, 1712−1715.

(10) This structure, determined by Mr. Mihai Azimioara, will be published elsewhere.

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Scheme 1

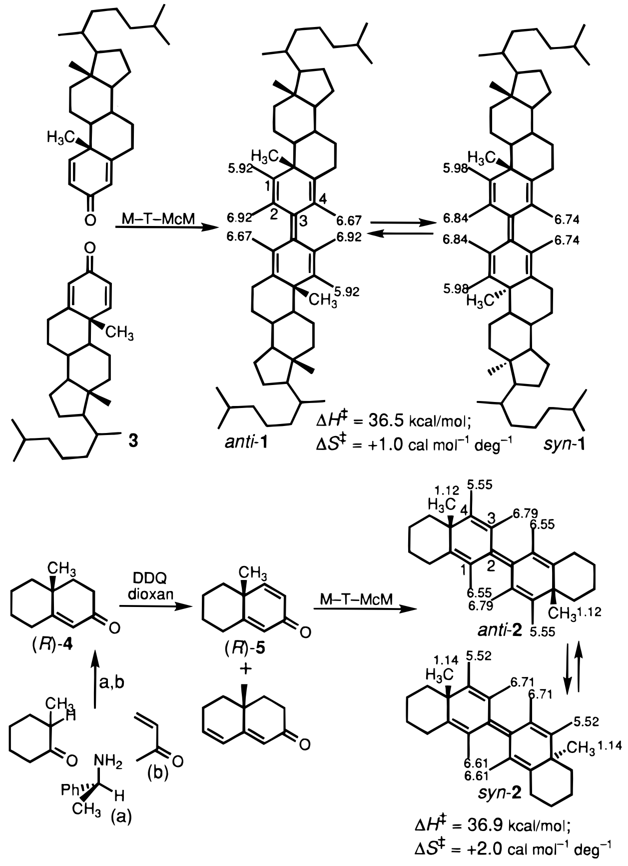

Table 1. Kinetics of Thermal Interconversion of *Syn*- and *Anti*-3,3′-Bicholesta-1,4-dienylidene (**1**) in Benzene-d_6: Specific Rate Constants and Activation Parameters

T, °C	k_1[a]	K[b]
154.0 ± 0.1	3.10 ± 0.02[c]	0.94
169.4 ± 0.1	13.75 ± 0.2	0.98
186.1 ± 0.1	63.38 ± 0.5	0.97
196.6 ± 0.1	170.8 ± 2.2	1.00

Arrhenius Parameters[d]
$E_a = 37.4 \pm 0.5$ kcal/mol
$\log A = 13.6 \pm 0.3$

Eyring Parameters[e]
$\Delta H^{\ddagger} = 36.5 \pm 0.5$ kcal/mol
$\Delta S^{\ddagger} = 1.0 \pm 1.2$ eu

Thermodynamics[f]
$\Delta\Delta H^{\circ} = 0.4 \pm 0.2$ kcal/mol
$\Delta\Delta S^{\circ} = 0.9 \pm 0.5$ eu

[a] Starting isomer, mp 232 °C, is *syn*-**1**. Specific rate constants are calculated by linear regression of the usual expression for reversible first-order reactions: $(k_1 + k_{-1}) = (1/t)\ln[(X_{eq} - X_0)(X_{eq} - X)]$; values of k in units of 10^{-6} s^{-1}. [b] Values of $K[k_1\,(\text{syn} \rightarrow \text{anti})/k_{-1}]$ are obtained from values of X_{eq} that lead to the best fit of the data. [c] Double standard errors for 90% confidence limits. [d] By linear regression of the Arrhenius expression. [e] Calculated at 175.3 °C. [f] Calculated by linear regression of the usual expression, $\ln K = T\Delta S - \Delta H$.

Table 2. Thermal Isomerization of *anti*-**2** to *syn*-**2** in Benzene-d_6: Specific Rate and Equilibrium Constants and Activation Parameters

T, °C	k_1[a]	K
144.5 ± 0.2	1.08 ± 0.01[b]	1.07
144.5 ± 0.2	1.09 ± 0.01	1.07
152.2 ± 0.2	2.54 ± 0.01	1.06
152.2 ± 0.2	2.49 ± 0.01	1.07
160.9 ± 0.1	6.10 ± 0.03	1.06
169.3 ± 0.1	13.86 ± 0.17	1.08
169.3 ± 0.1	13.92 ± 0.12	1.05
177.2 ± 0.1	29.80 ± 0.21	1.07
177.2 ± 0.1	30.45 ± 0.21	1.05
177.4 ± 0.1	29.75 ± 0.64	1.07

Arrhenius Parameters[b]
$E_a = 37.80 \pm 0.11$ kcal/mol
$\log A = 13.82 \pm 0.06$

Eyring Parameters[b,c]
$\Delta H^{\ddagger} = 36.9 \pm 0.12$ kcal/mol
$\Delta S^{\ddagger} = 2.0 \pm 0.3$ eu

[a] Calculated by linear regression of the usual expression for reversible first-order reactions: $(k_1 + k_{-1}) = (1/t)\ln[(X_{eq} - X_0)(X_{eq} - X)]$; K = 1.05 − 1.08; $k \times 10^{-6}$ s^{-1}. [b] Double all standard errors for 90% confidence limits. [c] Calculated at 161.0 °C.

to one, are uncontaminated, even by hydrogen atoms of the aromatic type. However, recoveries, as measured against an internal standard, fall off at the longer times of reaction. Attempts to suppress this hap have come to little (details in Experimental Section). However, beyond decreasing the precision of measured relative concentrations slightly, this complication is of little consequence provided both stereoisomers disappear at the same rate, a condition that seems quite likely satisfied.

Although recoveries are no better at the longest times in the simpler pentaenes, *anti*-**2** and *syn*-**2**, the kinetics in the two systems are essentially identical, as can be seen in Tables 1 and 2 (basic data given in Tables 1S and 2S, respectively, as supporting information). The weighted mean of the two sets of activation parameters affords an enthalpy of activation, $\Delta H^{\ddagger}$ = 36.8 kcal/mol, and an entropy of activation, $\Delta S^{\ddagger}$ = +1.8 eu. Although the precision of these values seems satisfactory, their accuracy is open to some question owing to the entropy of activation being more positive in value than those previously encountered in isomerizations of this type ($\Delta S^{\ddagger}$ −3 to −5 eu). If the explanation lies in a more negative entropy of formation in the starting pentadienes, there is little cause for concern. Such an interpretation is consistent with a crystallographic study of *syn*-**1**,[10] which points to a near planar, quite rigid structure for the cyclohexadienylidencyclohexadiene (4,4′-dihydrodiphenyl, bis-homofulvalene) system.[11]

The experimental enthalpy of activation is 3.3 kcal/mol lower than that of closely related *triene* **6**[7d] (see Scheme 2) and indicates a small empirical stabilization; it is 1.1 kcal/mol higher than that of (*E*,*Z*) pentaene **8**,[7d] 0.7 kcal/mol above that of 2,2′-bicholesta-3,5-dienylidene;[7b] and 4.4 kcal/mol above that of the isomeric (*E*,*E*) pentaene **7**.[7d,12] On these bases, the (*Z*,*Z*) is the least stabilizing of the three configurations of the pentadienyl radicals, having an empirical stabilizing effect 2.2 kcal/mol less than that of the (*E*,*E*)-pentadienyl radical. This observation is qualitatively in agreement with the theoretical calculations of Fort, Hrovat, and Borden of the unsubstituted (*E*,*E*) and (*Z*,*Z*) pentadienyl radicals,[1] the latter having been found to be less well stabilized by 5.6 kcal/mol. Note, however, that (*Z*,*Z*)-penta-1,4-dien-3-yl is sterically a far cry from the cyclohexa-1,4-dien-3-yl radical.

Behind the wide, long-standing interest in the perturbing effect of substituents on the enthalpy of the carbon free radical lies

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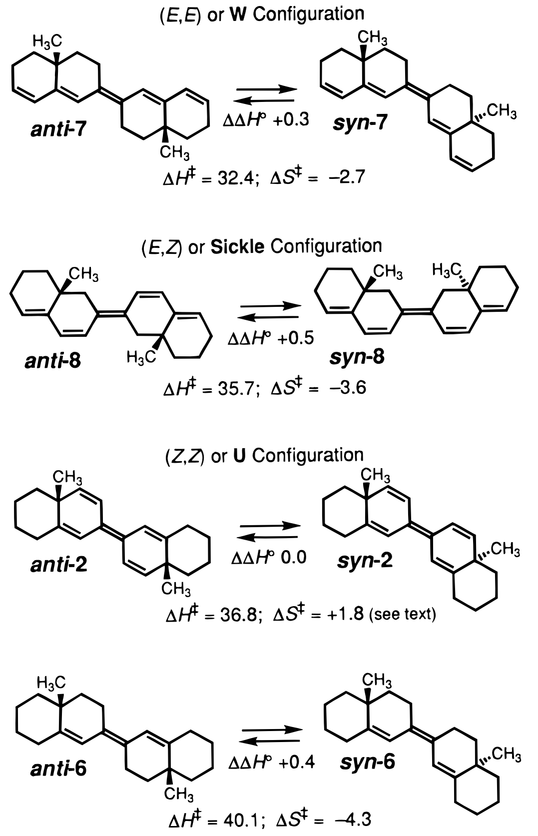
(11) (a) Traetteberg, M.; Bakken, P.; Almenningen, A.; Lüttke, W.; Janssen, J. *J. Mol. Struct.* **1982**, *81*, 87−103. Lütke, *J. Mol. Struct.* **1982**, *81*, 87−00. (b) Noltemeyer, M.; Janssen, J.; Lüttke, W. *J. Mol. Struct.* **1982**, *81*, 105−112. This structure has been redetermined by Professor Roland Boese, Institut für Anorganische Chemie, Universität Essen. and will be published elsewhere.

(12) Two other (*E*,*E*) pentaenes[7b] (data on all previously studied trienes and pentaenes in the series of semirigid polyenes are collected in Table 4 of ref 7d) are essentially indistinguishable.

Scheme 2



the hope of establishing values for "enthalpies of stabilization", which might be useful in the prediction of the enthalpic part of the rate constant in a variety of reactions mechanistically thought to involve the free radical as an approximation to the rate-determining transition state. Of paramount importance in this exercise is the oft repeated, recognition that enthalpy of stabilization does not exist independent of its definition; that there is no *absolute* enthalpy of stabilization[13] in the sense of an enthalpy of formation; and that definitions may be created *ad libitum* but survive only through their usefulness (cf. "aromaticity"!).

Primary interest in this and past works has been confined to evaluation of the magnitude of the effect of perturbations by olefinic substituents on the paradigmatic thermal interconversion of *cis*- and *trans*-ethene.[7] These perturbations may result in an empirical lowering or raising of the enthalpy of activation (stabilizing or destabilizing effect, respectively). They are considered to operate on the educt through steric and electronic interactions and on the transition state (approximated by a 90° twisted geometry) likewise through steric and electronic interactions; that is, each of four strands of a thread need explicitly to be considered in the construction of differences between starting state and transition state. In the paradigm, the four factors are set to zero by definition. In perturbations of the paradigm, the so-called (electronic) enthalpy of stabilization defines the electronic interaction of the perturbing substituent(s) and the transient free radicals assumed to describe the transition state. In this conceptual scheme, experimental enthalpy of activation is composed of two electronic interactions of the substituent with the paradigm—enthalpy of conjugation in the educt and enthalpy of stabilization in the transition state, both hoped to be constants—and two steric factors, which are expected to vary from one example to another. Disentwinement of these factors is the object of much theoretical and experimental effort.

In the series of all-trans trienes, pentaenes, heptaenes, and nonaenes,[7a,c] transannular interactions in the ground state were assumed to dominate steric interactions and, within the pairs of anti and syn isomers and to an acceptable approximation, to be unchanging within the series of polyenes. They could safely be neglected as significant contributors to observed differences in enthalpies of activation.[14] Transannular steric factors at the 90°-twisted conformation were assumed to be negligible owing to the large increase in distance of separation between "ortho" hydrogen atoms of the two conjoined ring systems. A further factor may have been the influence on steric energy of bond angles as they changed from those in the starting olefins to those in the model free radicals, but no datum exists to our knowledge on which to base a parametrization of force field programs, for example, that might have been looked to as a means of addressing the question.

In the comparison between pentaenes of the (*E*,*E*) and (*E*,*Z*) type (cf. **7** and **8** in Scheme 2), these assumptions appear still to be acceptable. But in the present comparison of (*Z*,*Z*)-**2** with (*E*,*E*)-**7** and (*E*)-**6**, attenuation of transannular interactions must differ significantly in its contribution to observed enthalpies of activation.

Molecular mechanical or force field programs seem to offer a straightforward way to disentwine the strands of steric interactions in the educts from the four-stranded thread.[15] Three programs have been applied: the MM2 of Allinger;[16] the MM2ERW, presently the most extensively parametrized program for hydrocarbons;[17] and the MMEVBH, a program combining the MM2ERW force field program with the valence bond Hamiltonian of the Heisenberg type introduced by Maynau and collaborators[18] and further extended by Roth et al.[6] The resulting steric energies, tabulated in Table 3S (supplementary information), are encouraging at the level of accuracy required for significance.[19] Among the three, MMEVBH affords the best agreement with experimental differences in heats of formation between pairs of anti and syn isomers. In particular, it predicts the greater stability of the anti isomers, which the other two programs do not.

The MMEVBH program,[6] painstakingly constructed to handle steric factors in hydrocarbons, conjugated and unconjugated olefins, radicals and diradicals, appears to be the best available for estimation of the steric corrections needed in both the educt and the 90°-twisted conformation. Applied to triene **6**, the calculated decrease in "steric energy" driving the rearrangement is calculated to be 7.0 kcal/mol. When coupled with the intrinsic rotational barrier of ethene (65.9)[20] and conventional correction for conjugative interaction by two Kistiakowsky units, the experimental enthalpy of activation leads to an enthalpy of stabilization (RSE) for the allyl radical of 13.2 kcal/mol.[21,22] When applied to pentaene **2**, a smaller steric correction of 4.2

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[13] See, for example: Clark, K. B.; Wayner, D. D. M.; Demirdji, S. H.; Koch, T. H. *J. Am. Chem. Soc.* **1993**, *115*, 2447−2453.

[14] In all cases, the observation of values of $\Delta\Delta_fH^\circ$ (favoring the anti isomer) varying narrowly between 0.3 and 1.0 kcal/mol was considered reassuring.

[15] But see Lipkowitz, K. B. *J. Chem. Educ.* **1995**, *72*, 1070−1075.

[16] As made available in the CSC Chem3D Plus program by Cambridge Scientific Computing, Inc.

[17] Roth, W. R.; Adamczak, O.; Breuckmann, R.; Lennartz, H.-W.; Boese, R. *Chem. Ber.* **1991**, *124*, 2499−2521.

[18] See ref 6 for references.

[19] We are much indebted to Dr. Johannes Benkoff for these calculations.

[20] Doering, W. v. E.; Roth, W. R.; Bauer, F.; Breuckmann, R.; Ebbrecht, T.; Herbold, M.; Schmidt, R.; Lennartz, H.-W.; Lenoir, D.; Boese, R. *Chem. Ber.* **1989**, *122*, 1263−1275.

[21] $[(65.9) - (40.1 + 7.0) + (2 \times 3.75)]/2 = 13.2$ kcal/mol.

[22] Doering, W. v. E.; Roth, W. R.; Bauer, F.; Boenke, M.; Breuckmann, R.; Ruhkamp, J.; Wortmann. O. *Chem. Ber.* **1991**, *124*, 1461−1470.

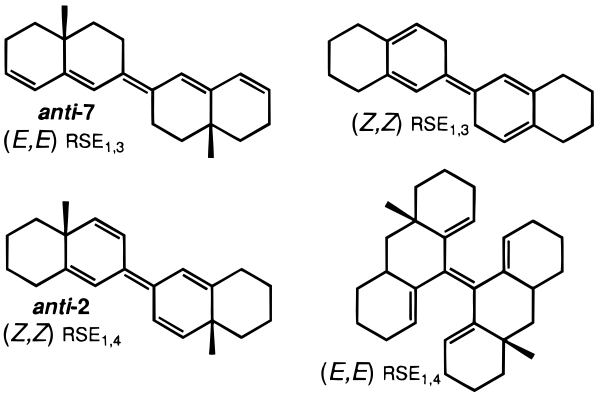
kcal/mol emerges and leads, in combination with a total of four Kistiakowsky units of conjugative interaction for the crossed system, to an enthalpy of stabilization for the cyclohexadienyl radical of 20.0 kcal/mol.[23−25]

Electronic effects in the starting conjugated polyenes are represented by conjugative interactions between the paradigm and the perturber. In the polyene series, this factor is held to enter only once and to have the value of a Kistiakowsky unit (3.75 kcal/mol) invariant with the order of the perturbing polyene.[7c,26−28] This procedure would be incorrect if, as now indicated by Roth's MMEVBH calculations, the unit were to increase (or decrease) with the number of double bonds in the conjugated polyene.[27a] With this reservation, handling conjugative interaction in pentaene *anti*-**7** and higher polyenes presents no major difficulty.

That is not true of the twice crossed pentaene *anti*-**2**, for which there is neither any experimentally based enthalpy of conjugation available nor any immediate prospect of having the heats of combustion and sublimation determined for 1-(4′-4′-dimethylcyclohexa-2,5-dienylidene)-4,4-dimethylcyclohexa-2,5-diene, the simplest stable and available model for the bis-homofulvalene system present in **1** and **2**. Catalytic hydrogenation, an alternative possibility, is suspect in polyenes containing tetra-substituted double bonds.[29]

Indeed, not even the heat of formation of the simplest planar crossed triene, methylenecyclohexa-1,4-diene (*p*-isotoluene), is known with sufficient accuracy. From a study of its gas-phase ion chemistry, Bartmess[30] has deduced a heat of formation of 36 ± 3 kcal/mol, 24 ± 3 kcal/mol above that of toluene (12.1 kcal/mol). This value is 10.7 kcal/mol below that of the heat of formation, 46.7 kcal/mol, of a strain-free model calculated by means of Benson group equivalent values[31] uncorrected for conjugative interaction. Application of Bartmess' proposed uncertainty in the least favorable direction decreases the discrepancy to 7.7 kcal/mol, a value that would be fully accommodated by two Kistiakowsky units. Also bearing on the problem is a preliminary result from Professor Rogers on the heat of hydrogenation of 3-methylene-6,6-dimethylcyclohexa-1,4-diene (ΔH_{H2} −76.8 kcal/mol)[32] to 1,1,4-trimethylcyclohexane (estimated heat of formation, −50.8 kcal/mol).[33] The resulting heat of formation of the triene (+26.0 kcal/mol) is 2.7 kcal/mol lower than that calculated by MMEVBH, 28.7 kcal/mol. Not withstanding, to accept the operation of a total of four Kistakowsky units in the starting, crossed pentaene **2** is a simple, if possibly ingenuous, expedient, which leads to the stabilization energy of 20.0 kcal/mol noted above.

Scheme 3



Direct comparison of "enthalpies of stabilization" derived for *anti*-**7** (16.9 kcal/mol)[7a] and *anti*-**2** (20.0 kcal/mol) is not warranted because their stabilization enthalpies are defined in different ways. The need for explicit recognition of this point has been most clearly explicated by Roth in terms of the shorthand notations, RSE$_{1,3}$ and RSE$_{1,4}$.[34] In Scheme 3 are shown what would have been proper comparisons from this point of view (not from some others!): *anti*-**7** of type (*E*,*E*)-RSE$_{1,3}$ might have been compared with (*Z*,*Z*)-RSE$_{1,3}$ or *anti*-**2** (*Z*,*Z*)-RSE$_{1,4}$ with (*E*,*E*)-RSE$_{1,4}$. In the reality of this paper, *anti*-**2** affords a stabilization energy defined in terms of a type of RSE$_{1,4}$, *anti*-**7** in terms of a type of RSE$_{1,3}$. Correction of this dissimilarity is simply, if dubitatively, achieved by adding one Kistiakowsky unit to the RSE$_{1,3}$ value, 16.9 kcal/mol, derived for the (*E*,*E*)-pentadienyl radical *anti*-**7**,[7a] whence, all other factors remaining equal, the hypothetical value RSE$_{1,4}$ for pentadienyl radical, (*E*,*E*)-RSE$_{1,4}$, would become 20.7 kcal/mol. Thus, little difference in stabilization energies is discernible when both are similarly defined as stabilization energies of the RSE$_{1,4}$ type. By an identical correction, the stabilization enthalpy of *anti*-**2** could have been translated into an RSE$_{1,3}$ value of 16.3 kcal/mol.

In comparison to the several other values already in the literature (RSE$_{1,4}$) for the enthalpy of stabilization of the cyclohexadienyl radical, 24.6;[2] 25.4;[3] 22.9;[4] and 26.7 kcal/mol,[5,6] the value, 20.0 kcal/mol, from this work is low. Within reasonable uncertainties, it is in fair agreement with the value, 21.4 kcal/mol, recommended by Roth.[6]

Another sighting on the *W* and *U* configurations of the pentadienyl radicals is obtained by examination of the cycloreversion of cyclobutane **9** and comparison with **10**.[35] As shown in Scheme 4, the cyclobutane **9** can be produced by sensitized irradiation at −75 °C of 4,4-dimethylmethylenecyclohexa-2,5-diene. Although no distinction can be made between head-to-head or head-to-tail structure on the basis of the NMR spectrum, the rapid rate of disappearance of **9** and reappearance of the monomeric triene at −31.6 °C is better reconciled by the head-

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(23) We express many thanks to Professor Wolfgang R. Roth, Ruhr Universität, Bochum, for suggesting and making these calculations.

(24) $[(65.9) - (36.8 + 4.2) + (4 \times 3.75)]/2 = 20.0$ kcal/mol.

(25) Because the derivation includes correction for steric factors by the MMEVBH program, the resulting value for the enthalpy of stabilization can be applied to other systems for the purpose of predicting enthalpies of activation involving the cyclohexadienyl radical *only* if this same program is used to estimate any steric corrections.

(26) Pedley, J. B.; Naylor, R. D.; Kirby, S. P. *Thermochemical Data of Organic Compounds*, 2nd ed.; Chapman and Hall: London, 1986.

(27) (a) As indicated in Table 17 of ref 6. The final effect would be an increase in the stabilization energies of the polyenyl radicals as summarized.[7c] Beyond this theoretical indication, there is no experimental evidence bearing on the question. (b) With reference to the espousal of 5 kcal/mol for a Kistiakowsky unit,[1] the reader is referred to the following exercises upon heats of formation:[26] (*i*) butadiene, butene-1, *n*-butane; (*ii*) (*E*)- and (*Z*)-pentadiene-1,3, (*E*)- and (*Z*)-pentene-2, pentene-1, *n*-pentane; (*iii*) 2-methylbuta-1,3-diene, 2- and 3-methylbutene-1,2-methylbutane; (*iv*) hexa-1,3,5-triene,[28] hexa-1,5-diene, (*Z*)-hexene-3, *n*-hexane; (*v*) 2,3-dimethylbutadiene, 2,3-dimethylbutene-1,2,3-dimethylbutane.

(28) (a) Fang, W.; Rogers, D. W. *J. Org. Chem.* **1992**, *57*, 2294−2297. (b) Turner, R. B.; Mallon, B. J.; Tichy, M.; Doering, W. v. E.; Roth, W. R.; Schröder, G. *J. Am. Chem. Soc.* **1973**, *95*, 8605−8610.

(29) Turner, R. B.; Meador, W. R.; Doering, W. v. E.; Knox, L. H.; Mayer, J. R.; Wiley, D. W. *J. Am. Chem. Soc.* **1957**, *79*, 4127−4133.

(30) (a) Bartmess, J. E. *J. Am. Chem. Soc.* **1982**, *104*, 335−337; (b) Bartmess, J. E.; Griffith, S. S. *J. Am. Chem. Soc.* **1990**, *112*, 2931−2936.

(31) Benson, S. W. *Thermochemical Kinetics*, 2nd ed.; Wiley: New York, 1976.

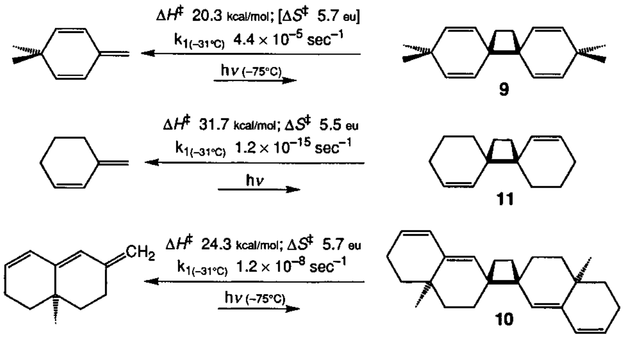
(32) We are grateful to Professor D. W. Rogers, Long Island University, for the communication of this preliminary result.

(33) Derived from experimental heats of formation of cyclohexane (−29.5 kcal/mol), 1-methylcyclohexane (−37.0 kcal/mol), and 1.1-dimethylcyclohexane (−43.3 kcal/mol);[26] in good agreement with MMEVBH calculated value of −51.0 kcal/mol[17] and Benson uncorrected value of −51.7 kcal/mol.[31]

(34) See Scheme 6, page 1075 of ref 6.

(35) Doering, W. von E.; Belfield, K. D.; He, J.-n. *J. Am. Chem. Soc.* **1993**, *115*, 5414−5421.

Scheme 4



to-head structure.[36,37] On being warmed to 0 °C, **9** reverts rapidly and completely to the monomer. By monitoring the disappearance of **9** at −31.6 °C, an approximate specific rate constant, $k = 4.4 \times 10^{-5}$ s^{-1}, can be estimated (Scheme 4). From this quantity and the assumption of a log A factor (14.47) identical to that determined for cyclobutane **10**, an estimated activation energy of ∼21 kcal/mol can be calcualted. An informative comparison of **9** with the Ekmanis dimer **11** reveals a decrease of ∼11 kcal/mol in enthalpy of activation resulting from the formal change from two allyl radicals to the two cyclohexadienyl radicals assumed to approximate the transition state.[38] A similar comparison of **10** with **11** reveals a lowering of ∼7 kcal/mol.

Conclusions

The experimental values of the activation parameters for the thermal cis−trans isomerizations of **1** and **2** agree very closely with each other. Translation into an estimation of the enthalpy of stabilization of the cyclohexadienyl radical is presently hampered by the absence of apposite thermochemical information about crossed trienes and the bis-homofulvalene type of pentaene. Nonetheless, their mean—$\Delta H^{\ddagger} = 36.8$ kcal/mol, $\Delta S^{\ddagger} = +1.8$ eu—may be compared with the parameters for the triene **7**—$\Delta H^{\ddagger} = 40.1$ kcal/mol, $\Delta S^{\ddagger} = -4.3$ eu—by, first, correcting the former for extra enthalpy of conjugation in the educt—taken arbitrarily to be −7.5 kcal/mol (two Kistiakowsky units)—and, second, correcting for a difference between the two in the contribution made by relief of steric energy −2.8 kcal/mol. The resulting corrected difference in enthalpies of activation is 12.8 kcal/mol, corresponding to an enthalpy of stabilization of the RSE$_{1,4}$ type of 20.0 kcal/mol for the cyclohexadienyl radical. The discrepancy between this value and many of those in the literature would be ameliorated by an augmentation of conjugative interaction in crossed trienes. At the moment, two pieces of evidence, but no high level quantum mechanical calculations, point suggestively in that direction.[39]

Experimental Section

General Methods. Unless explicitly noted, ^{1}H and ^{13}C NMR spectra are measured in C_6D_6 solution by a Bruker AM-500 spectrometer. Spin−lattice relaxation times (T_1) are determined by the inversion-recovery method with use of vacuum-sealed solutions in C_6D_6. Chemical shifts are reported in parts per million from TMS (δ). Infrared spectra are recorded on a Nicolet Impact 400D FT IR instrument and reported in cm^{-1}. Liquid samples are observed as thin films on a NaCl plate; solid samples are measured as thin layers prepared by evaporating $CHCl_3$ solutions on a NaCl plate. UV−visible electronic spectra are determined with a Varian Cary 1E UV−visible spectrophotometer and are reported as λ_{max} in nm and coefficients of extinction (ϵ). Optical rotations are measured on a Perkin-Elmer Polarimeter 241; enantiomeric excess (ee) is determined with a Hewlett Packard 5890 Series II gas Chromatograph using a Chiral-dex G-TA column (20 m × 0.25 mm ID; Advanced Separation Technology, Inc.). High resolution mass spectra are measured on a Jeol AX 505 spectrometer equipped with a data recovery system.

(*R*)-(−)-4,4a,5,6,7,8-Hexahydro-4a-methyl-2(3*H*)-naphthalenone (4). This compound is synthesized by the method of Revial and Pfau[40] from 2-methylcyclohexanone (23.0 g, 0.205 mol), methyl vinyl ketone (15.1 g, 0.216 mol), and (*S*)-(−)-α-methylbenzylamine (25.0 g, 0.206 mol) in >99% of purity and 55% of theoretical yield: 18.5 g; $[\alpha]^{20}_{D} = -228°$ ($c = 1.20$, ethanol); ee >99%; ^{1}H NMR ($CDCl_3$) 5.72 (s, 1 H), 2.50−1.34 (m, 12 H), 1.23 (s, 3H); IR 2927, 2859, 1677, 1627, 1448, 1431, 1326, 1261, 1225, 1186, 858.

(*R*)-(+)-5,6,7,8-Tetrahydro-4a-methyl-2(3*H*)-naphthalenone (5). A solution of 3.00 g (18.3 mmol) of ketone (*R*)-**4** and 5.00 g (22.9 mmol) of dichlorodicyanoquinone (DDQ) in 200 mL of anhydrous dioxane is boiled under nitrogen and reflux for 24 h. After filtration and removal of dioxane *in vacuo*, the residual oil is diluted with 200 mL of ethyl ether, washed with 5% aqueous NaOH (2 × 30 mL), saturated $NaHCO_3$ (2 × 30 mL), water, and dried over Na_2SO_4. Solvent is removed *in vacuo* leaving a yellow oil (3.00 g), which GLC shows to be a mixture of the desired ketone **5**[41] and 3,4,5,6-tetrahydro-4a-methyl-2(3*H*)-naphthalenone[7d] in a ratio of 4:1. Chromatography on silica gel on elution with mixtures of hexane−ethyl acetate in ratios varying from 20:1 to 5:1 affords 1.66 g (56% of theoretical yield) of (*R*)-**5** as a colorless oil of 98% purity: $[\alpha]^{20}_{D} = +61.9°$ ($c = 1.25$, ethanol); ee > 99% (determined by GLC); ^{1}H NMR ($CDCl_3$) 6.75 (d, 1 H, $J = 9.9$ Hz, H-4), 6.18 (dd, 1 H, $J = 9.9$ Hz, $J' = 1.7$ Hz, H-3), 6.07 (s, 1 H, H-1), 2.46−2.40 (m, 1H), 2.01−1.98 (m, 1 H), 1.83−1.68 (m, 3 H), 1.35−1.28 (m, 2 H); IR 2936, 2860, 1663, 1627, 1605, 1444, 1395, 1397, 1268, 942, 880, 815.

Cholesta-1,4-dien-3-one (3). This ketone is prepared from 2,4-dibromocholestan-3-one by a procedure slightly modified from that of Pinder and Robinson[9a] in turn modified from that of Wilds and Djerassi[9b] [7.2 g, mp 189.5−190 °C (lit.[9a] mp 193 °C)] by boiling in freshly distilled collidine (31 mL) for 80 min. The cooled solution is filtered from collidine hydrobromide (4.9 g, 91.8% theoretical yield), which is washed with 5 20-mL portions of ether. The filtrate is concentrated *in vacuo* to a dark residue, which is boiled in methanol for 15 min. The cooled solution is filtered and concentrated *in vacuo* to a residue (2.7 g, brown oil), which is chromatographed on silicagel (elution with 5% ether-hexane) to give colorless, crystalline ketone **3**: 2.5 g (49% of theoretical yield): mp 110−110.5 °C [lit. mp 111−111.5 °C[9a]; 110−112 °C[9b]]; ^{1}H NMR (400 MHz) 6.47 (d, 1 H, $J = 10.2$ Hz), 6.32 (dd, 1 H, $J = 10.2$ Hz, $J' = 1.7$ Hz), 6.19 (s, 1 H), 1.89−1.70 (m, 4 H), 1.60−1.40 (m, 5 H), 1.41−1.10 (m, 9 H), 1.0−0.9 (m, 5 H), 0.77−0.60 (m, 4 H), 0.94 (d, 3 H, $J = 1.2$ Hz), 0.92 (d, 3 H, $J = 1.2$ Hz), 0.77 (s, 3 H), 0.58 (s, 3 H); IR 2938, 2868, 2853, 1666, 1627, 1603, 1466, 1441, 1402, 1240, 929, 886.

Reductive Coupling. Dienones **3** and **5** are converted to the corresponding ylidenes **1** and **2**, respectively, by the Mukaiyama-Tyrlik-McMurry reaction[8] following published procedure.[42] Activated zinc dust and dry pyridine are added slowly to a solution of $TiCl_4$ in THF,

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(36) The behavior of this methylenecyclohexadiene is quite normal on sensitized irradiation and only under conditions of rapid thermal cycloreversion of its corresponding cyclobutane is the vinylog of the di-π-methane rearrangement realized in an uncharacteristically low quantum yield (0.003)![37]

(37) Zimmermann, H. E.; Hackett, P.; Juers, D. F.; McCall, J. M.; Schröder, B. *J. Am. Chem. Soc.* **1971**, *93*, 3653−3662; Zimmermann, H. E.; Juers, D. F.; McCall, J. M.; Schröder, B. *J. Am. Chem. Soc.* **1971**, *93*, 3662−3674.

(38) Ekmanis, J. L., Ph.D. Dissertation, Harvard University, Cambridge, MA, 1976. *Diss. Abstr. Int. B* **1976**, *37*, 224B (Order No. 76-14,401).

(39) Suggestions for further clarification include application of the calorimetric method of Bartmess and Griffith[30b] to methylenecyclohexadiene (*p*-isotoluene); determination of heats of hydrogenation of further model compounds such as the mono- and di-olefins related to 3-methylene-6,6-dimethylcyclohexa-1,4-diene; establishment of the temperature dependence of the equilibrium constants among the several isomers of a triene such as 4,4-dimethylcyclohexa-1,4-dienylidene-4′,4′-dimethylcyclohexane.

(40) Revial, G.; Pfau, M. *Organic Synthesis* **1992**, *70*, 35−45.

(41) (a) Naya, K.; Okayama, T.; Fujiwara, M.; Nakata, M.; Ohtsuka, T.; Kurio, S. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 2239−2245. (b) Alunni, S.; Minuti, L.; Taticchi, A. *J. Org. Chem.* **1991**, *56*, 5353−5356.

(42) Lenoir, D. *Synthesis* **1977**, 553−554.

freshly distilled from $LiAlH_4$, under nitrogen at 0 °C with stirring. This titanium reagent is then treated with the solution of the dienone in THF and stirred at 0 °C for 30 min, after which starting material is shown by TLC (silica gel, eluted with hexane) to be completely reacted. Quenching with $NaHCO_3$, extracting with CH_2Cl_2, drying over $MgSO_4$, filtering through a short silica gel column, and removing solvent *in vacuo* affords the product as a mixture of syn and anti isomers.

Assignments of structure are based on nuclear Overhauser enhancements determined by the gated decoupling method by using degassed solutions in C_6D_6 and a relaxation delay and a saturation period between pulses five times the longest T_1's of the relevant protons.

(*R*,*R*)-5,5′,6,6′,7,7′,8,8′-Octahydro-4a,4a′-dimethyl-2,2′-bi-(3*H*)-naphthylidene (2). Application of the Mukaiyama-Tyrlik-McMurry reaction to (*R*)-(+)-5,6,7,8-tetrahydro-4a-methyl-2(3*H*)-naphthalenone [(*R*)-**5**] (0.63 g, 4 mmol in 10 mL of THF), $TiCl_4$ (6.0 mL, 55 mmol), zinc (7.02 g, 110 mmol), and pyridine (3.6 mL) in 150 mL of THF affords, after flash chromatography on silica gel (hexane), 0.53 g (91% theoretical yield) of **2** as a 50:50 mixture of syn and anti isomers. Four recrystallizations from pentane afford (*R*)-*anti*-**2** (*vide infra*), 98% of purity: mp 142 °C; $[\alpha]^{20}_D = -148°$ ($c = 0.11$, hexane); ^{1}H NMR 6.79 (dd, 2 H, $J = 10$ Hz, $J' = 1.9$ Hz, H-3, H-3′), 6.55 (s, 2 H, H-1, H-1′), 5.55 (d, 2 H, $J = 10$ Hz, H-4, H-4′), 2.32−2.25 (m, 2 H), 2.04−2.01 (m, 2 H), 1.69−1.64 (m, 2 H), 1.50−1.41 (m, 8 H), 1.28−1.23 (m, 2 H), 1.12 (s, 6 H); IR 3040, 2970, 2923, 2849, 1657, 1549, 1464, 1439, 1175, 974, 858, 767; UV−vis: 330 (5.26×10^4), 346.5 (5.14×10^4); *m*/*z* calcd for $C_{22}H_{28}$, 292.2191; found, 292.2193.

Partial assignment of NMR frequences to the three hydrogen atoms in the vinyl region of the other isomer (*syn*-**2**, *vide infra*) can easily be made by subtraction: ^{1}H NMR 6.71 (dd, 2 H, $J = 10.2$ Hz, $J' = 1.4$ Hz, H-3, H-3′), 6.61 (s, 2 H, H-1, H-1′), 5.52 (d, 2 H, $J = 10.2$ Hz, H-4, H-4′), 1.14 (s, 6 H).

Distinction between the stereoisomeric structures relies on nuclear Overhauser enhancement: irradiation at 6.55 ppm shows an enhancement at 6.79 ppm of 30%, while irradiation at 6.61 ppm shows no enhancement at 6.71 ppm. Because symmetry in the syn isomer places two *identical* vinyl hydrogen atoms in proximity, no enhancement between hydrogen atoms H-1 and H-3′ (and *vice versa*) can be seen. Consequently, the doublet at 6.71 ppm and the singlet at 6.61 ppm are assigned to *syn*-**2**, while the doublet, 6.79 ppm, and the singlet, 6.55 ppm, are assigned to *anti*-**2**.

For quantitative analysis, the H-1 singlets at 6.55 ppm (*anti*-**2**) and 6.61 (*syn*-**2**) are used. Recovery is determined from the ratio of the sum of the H-4 doublets at 5.55 ppm (*anti*-**2**) and 5.52 (*syn*-**2**) to that of the internal standard (18-crown-6; 3.52 ppm).

3,3′-Bicholesta-1,4-dienylidene (1). This compound is obtained by the procedure above from cholesta-1,4-dien-3-one (**3**) [0.310 g (0.8 mmol) in 5 mL of THF] and titanium reagent prepared from 1.2 mL of $TiCl_4$ (11 mmol), 1.4 g of Zn (22 mmol) and 1 mL of pyridine in 30 mL THF at 0 °C: 0.250 g (92% theoretical yield) of light yellow crystals consisting of a 50:50 mixture of syn and anti isomers. Three recrystallizations from pentane afford the less soluble isomer (*syn*-**1**, *vide infra*) in >99% of purity: mp 231−232 °C: ^{1}H NMR 6.84 (dd, 2 H, $J = 10.2$ Hz, $J' = 1.4$ Hz, H-2, H-2′), 6.74 (s, 2 H, H-4, H-4′), 5.98 (d, 2 H, $J = 10.2$ Hz, H-1, H-1′), 2.41 (dt, 2 H, $J = 13.2$ Hz, $J' = 3.9$ Hz), 2.14, (d, 2 H, $J = 12.8$ Hz), 2.01 (d, 2 H, $J = 8$ Hz), 1.88−1.77 (m, 2 H), 1.73 (d, 2 H, $J = 11.3$ Hz), 1.63 (dd, 2 H, $J = 13.1$ Hz, $J' = 2.6$ Hz), 1.59−1.49 (m, 4 H), 1.49−1.33 (m, 10 H), 1.32−1.15 (m, 10 H), 1.14 (s, 6 H, H-19, H-19′), 1.13−0.99 (m, 10 H), 1.00 (d, 6 H, $J = 6.3$ Hz, H-21, H-21′), 0.96−0.90 (m, 14 H), 0.71 (s, 6 H, H-18, H-18′); UV−vis 352 (4.18×10^4), 335 (3.83×10^4).

Although the more soluble isomer (*anti*-**1**, *vide infra*) has not been enriched beyond 60:40, a partial assignment of NMR frequences can be made cleanly for three hydrogen atoms in the vinyl region (but for none in the allylic and aliphatic region): ^{1}H NMR 6.92 (dd, 2 H, $J = 10.2$ Hz, $J' = 1.3$ Hz, H-2, H-2′), 6.67 (s, 2 H, H-4, H-4′), 5.92 (d, 2 H, $J = 10.2$ Hz, H-1, H-1′).

Syn and anti isomers are distinguished by nuclear Overhauser enhancement of vinylic proton resonances at 322 K (400 Mz). Irradiation at 6.63 ppm shows an enhancement at 6.88 ppm of +16%, while irradiation at 6.69 ppm shows no enhancement at 6.82 ppm. Protons resonating at 6.84 and 6.74 ppm (300 K; 500 Mz) are consequently assigned to *syn*-**1**, while those resonating at 6.92 and 6.67 ppm are assigned to *anti*-**1**. The correctness of this assignment is supported by the striking similarity of the spectra of **1** and **2** in the vinyl regions.

For quantitative analysis, the H-1 singlets at 6.67 ppm (*anti*-**1**) and 6.74 (*syn*-**1**) are used. Recovery is determined from the ratio of the sum of these two signals to that of the internal standard (18-crown-6; 3.52 ppm).

Kinetic Measurements. Kinetics are determined essentially as described before.[7] Samples in sealed NMR tubes are heated in the vapors of solvents of appropriate boiling point. Analysis is by ^{1}H NMR employing in both instances the singlet olefinic hydrogen atoms, as noted above. In both instances, recovery remains satisfactory until the longest reaction times, as may be seen in greater detail in Tables 1S and 2S, which contain the experimental data for all runs of both **1** and **2**, and are available as supporting information.

By the time equilibrium is reached, recovery in the case of **1** has dropped as low as 34%. In probing for possible means of suppressing the factors responsible for the low recovery, several experiments were carried out with variations on a standard set of conditions: *T*, 196 °C; time, 3.0 h; internal standard: ∼0.05% 18-crown-6; solvent: C_6D_6; reactant: ∼0.1% syn isomer. The following recoveries were obtained: no additive, 77%; 9,10-dihydroanthracene (∼90 mol%), 91%; 4,4′-thio-bis-(6-*tert*-butyl-3-methylphenol) (∼30 mol%), 84%; triphenylmethane (∼40 mol%), 80%; benzoylperoxide (∼135 mol%), 0%. No solution to the problem was found.

In the case of **2**, recovery was not as bad but still not good, varying from 76−88% by the time equilibrium had been reached. In calculating specific rate constants and Arrhenius parameters, it made no significant difference, however, whether all data were used or the last couple of points were omitted.

Photodimerization of 1-Methylene-4,4-dimethylcyclohexa-2,5-diene. The starting triene is prepared following a published procedure:[37] ^{1}H NMR (toluene-d_8, 500MHz) 6.13 (d, 2 H, $J = 9.9$ Hz), 5.49 (d, 2 H, $J = 9.9$ Hz), 4.83 (s, 2 H), 0.95 (s, 6 H). Irradiations are carried out in toluene-d_8 at −75 °C in Pyrex NMR tubes that had been degassed and sealed. Analysis was directly by NMR spectroscopy as noted above. After irradiation for 2 h, no change was observed. In the presence of benzophenone as triplet sensitizer [10 mol% (2 h) and 30 mol% (8 h)], ∼5% and ∼37%, respectively, of peaks corresponding to a new compound **9** are seen. When either tube is warmed to room temperature for 5 min, peaks only of the monomer remain. Assignment of a symmetrical cyclobutane structure is based on NMR spectrum: ^{1}H NMR (toluene-d_8, 500MHz) 5.70 (d, 4 H, $J = 10.1$ Hz), 5.55 (d, 4 H, $J = 10.1$ Hz), 1.95 (s, 4 H), 1.06 (s, 6 H), 1.01 (s, 6 H). Kinetics are followed at −31.6 °C by NMR at that temperature with the results shown in Table 4S.

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Supporting Information Available: Tables 1S and 2S contain the unprocessed experimental data from which Tables 1 and 2 are derived, respectively, Table 3S contains a comparison of heats of formation and steric energies calculated for compounds **2**, **6**, **7**, and **8** by MM2, MMERW, and MMEVBH methods, and Table 4S contains the data for the kinetics of the thermal cycloreversion of compound **9** in toluene-d_8 at −31.6 °C to 1-methylene-4,4-dimethylcyclohexa-2,5-diene (11 pages). See any current masthead page for ordering and internet access instructions.

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