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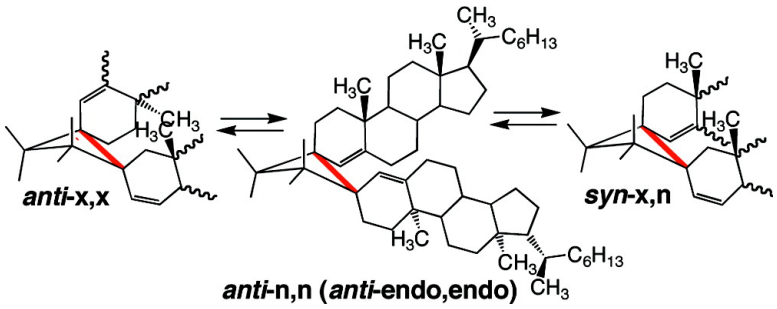

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An Effect of Bulk on the Ratio of Fragmentation to Stereomutation in Three Cyclobutane Dimers of 3-Methylenecholest-4-ene

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Abstract: The effect of a large increase in mass and extension of substituents on the thermal rearrangement of a 1,2-divinylcyclobutane system has been investigated by the introduction of two 3-cholest-4-ene units. The ratio of two types of exit channel, fragmentation and stereomutation (Fr/St), from a widely accepted diradical intermediary (caldera) has increased significantly relative to the ratio in a simpler system. We believe this to be the first example of the influence of a ponderal effect on the ratio of two competing processes in a thermal rearrangement. The internal torsional rotations necessary prior to reclosure for the realization of stereomutation have been markedly depressed. One of the three stereoisomeric cyclobutanes reacts substantially more slowly than the other two. In its structure, determined by X-ray diffraction, the two cholestenyl wings are folded closely together within van der Waals radii. The slower reaction may reasonably be ascribed to a relative lowering of heat of formation in this ground-state conformation.

Introduction

The responses of cyclopropanes and cyclobutanes to heat have in common stereomutation and ring enlargement, when aptly substituted by olefinic groups and the like. Cyclobutanes can undergo a further reaction, that is, fragmentation to a pair of olefins by a two-step, diradical mechanism now generally believed to be not concerted and consequently not subject to Woodward−Hoffmann considerations, while appropriate cyclopropanes uniquely can be transformed to propenes by an intramolecular shift of a hydrogen atom.

For some time we and others have focused on the influence of constitutional perturbations on the reactions of cyclobutanes to heat. In one such study, stabilization of the intermediary diradicals has emerged as a major factor in determining the ratio of fragmentation to stereomutation (Fr/St). While deuterium-labeled cyclobutane reveals a ratio of Fr/St = ∼3 at 380 °C and 1.5 at 1048 °C,[1,2] and the 1,2-dicyanocyclobutanes give comparable values, trans-, Fr/St = 4, and cis-, Fr/St = 3 (225 °C),[3,4] as the intermediary diradicals are increasingly stabilized—by a double bond (**2**), a 1,3-diene (**3**), and a 1,3,5-triene (**4**)—these ratios decrease, being ∼1.9 (100 °C),[5] ∼0.04 (44 °C),[6] and ∼0.00025 (−22.7 °C), respectively (Scheme 1).[7] In a related series, *cis*-1-cyano-2-vinyl- and *trans*-1-cyano-2-vinyl-cyclobutane show ratios at 191.7 °C of 0.50 and 0.66, respectively,[8] while 1-cyano-2-(*Z*)- and 1-cyano-2-(*E*)-propenyl show overall ratios at 198 °C of 0.54 (cis) and 0.88 (trans), and 0.71 (cis) and 0.87 (trans), respectively.[9]

In the course of revealing the absence of an effect of pressure on the ratio,[10] it was also observed that the values of Fr/St for the anti and syn dimers of 3-phenyl-methylenecyclohex-2-ene at 43.6 °C were 0.18 and 0.17, respectively, and those for 3-cyano-methylenecyclohex-2-ene at 50.1 °C were 0.34 and 0.11, respectively.

In another study, whether fragmentation might be diminished relative to stereomutation by blocking the accessibility of a transoid (antiperiplanar) conformation in the intermediary 1,4-diradical has been examined by DeLuca in a more constricted tricyclic 1,2-dicyanocyclobutane system.[4] Although the value of Fr/St at 257 °C (0.56) is lower by a factor of ∼10 than that of the corresponding unrestricted 1,2-dicyanocyclobutane (Fr/St = 5), fragmentation from a gauche conformation still occurs but at a significantly reduced level.

In the present work, the possible effect on Fr/St of bulk, mass, weight, extension ("ponderal" effect),[11] as one will, is explored.

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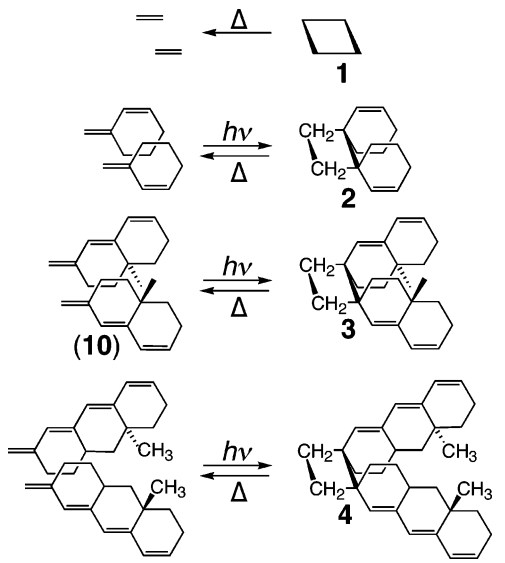
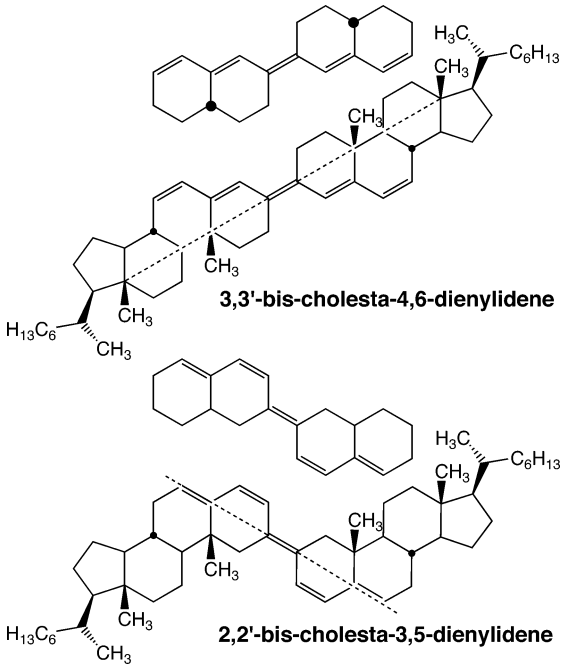
Scheme 1

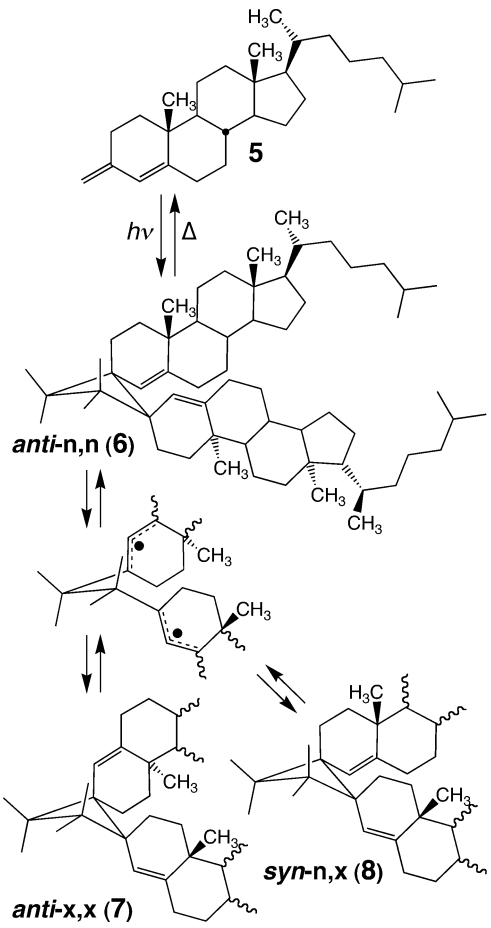


Scheme 2



The approach is similar to the comparison of simpler pentadienes in cis−trans isomerization about a carbon−carbon double bond with the paddle-like 2,2′- and the cylinder-like 3,3′-bis-cholesta-4,6-dienylidene (Scheme 2).[12,13] Although no definitive conclusion could be drawn from that work, the detailed mechanism differs profoundly from that obtained in the cyclobutane reactions. The latter involve initial homolytic cleavage of an sp3−sp3 carbon−carbon bond to a 1,4-diradical, while the former involves converting the sp2−sp2 component of a carbon−carbon double bond by a 90° torsion into a 1,2-diradical. The compounds selected for the present exploration are the three

Scheme 3



cylinder-like cyclobutanes obtainable photochemically from 3-methylenecholest-4-ene (**5**) (Scheme 3). Compound **5**, being optically pure, felicitously may form but three cyclobutane dimers, not the six derivable from racemic **5**.

Results

The dimerization of **5**, photosensitized by acetophenone, gives a mixture from which compound **6** crystallizes easily. Its structure is determined by X-ray diffraction to be that of the endo,endo dimer, *anti*-n,n (**6**) (Scheme 3, Figure 1). A second isomer **7** can also be isolated by crystallization. Its structure, likewise determined by X-ray crystallography, is that of the exo,-exo dimer, *anti*-x,x (**7**) (Figure 2). The third isomer is not obtained pure but can be enriched to the extent of 64%. The conformations of **6** and **7** determined by X-ray (Figures 1 and 2) agree so well with those calculated by molecular mechanics (MM2) that the third possible isomer, *syn*-n,x (**8**), may be confidently assigned the conformation calculated by molecular mechanics (Figure 1).

The response of *anti*-n,n (**6**), *anti*-x,x (**7**), and *syn*-n,x (**8**) to being heated at 98.4 °C in benzene-d_6 for various lengths of time is presented in Table 1 (relative concentrations normalized). Similar tables of data acquired at 110.7 °C and 117.8 °C are given in Supporting Information, Tables S-1 and S-2. The reactions are clean, but lead in the end exclusively to monomer **5** by fragmentation. Accordingly, regardless of starting material, concentrations of **6**, **7**, and **8** go through maxima and ultimately to zero.

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(13) (a) Doering, W. v. E.; Birladeanu, L.; Cheng, X.-h.; Kitagawa, T.; Sarma, K. *J. Am. Chem. Soc.* **1991**, *113*, 4558−4563. (b) Doering, W. v. E.; Shi, Y.-q.; Zhao, D.-c. *J. Am. Chem. Soc.* **1992**, *114*, 10763−10766. (c) Doering, W. v. E.; Birladeanu, L.; Sarma, K.; Shao, L.-m. *J. Am. Chem. Soc.* **1996**, *118*, 6660−6665.

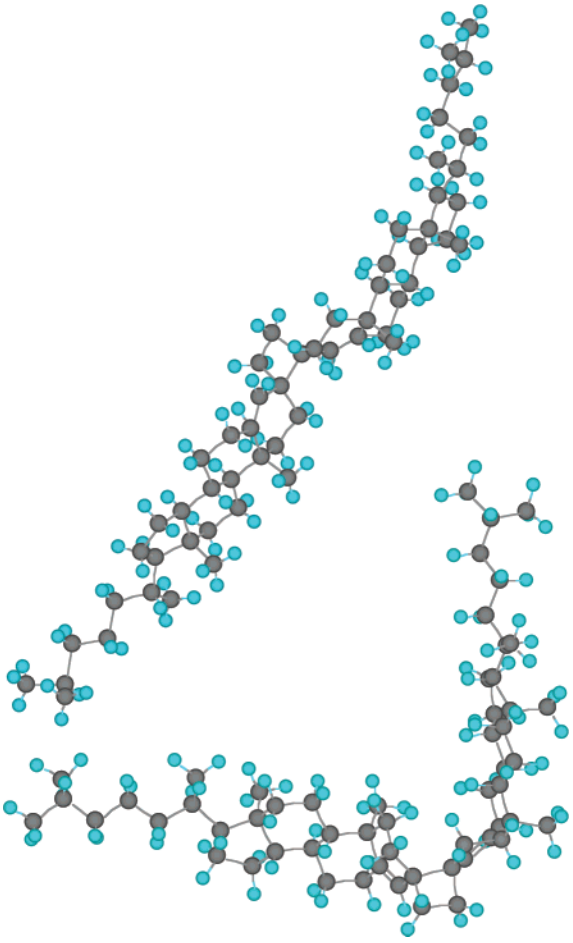


Figure 1. The upper depiction shows the X-ray crystallographic structure of *anti*-n,n (**6**); the lower the structure of *syn*-n,x (**8**) as calculated by molecular mechanics (MM2).

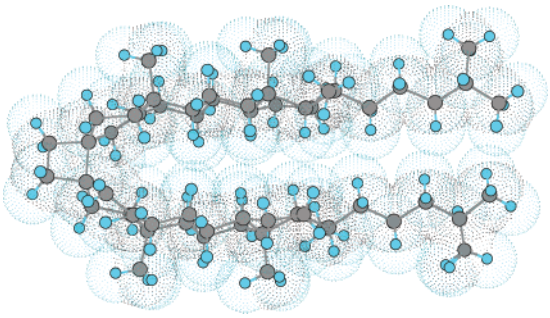


Figure 2. The X-ray crystallographic structure of *anti*-x,x (**7**) is shown with van der Waals radii included (CS Chem3D Pro).

Specific rate constants are calculated from the data in Tables 1, S-1, and S-2 by the program KINETIC of Dr. R. Fink, which handles kinetic schemes containing up to seven components, and incorporates a program of Marquardt that generates error limits in rate constants at the 95% confidence level.[14] The four-component kinetic model of nine parameters (Figure 3) understandably omits the three nonobservable, essentially irreversible thermal dimerizations of **5** to **6**, **7**, and **8**. In principle the nine-parameter model can be handled easily, but in practice some of the data pertaining to the much slower stereomutations are of too low a precision and too small a magnitude to allow the generation of quantitatively significant specific rate constants

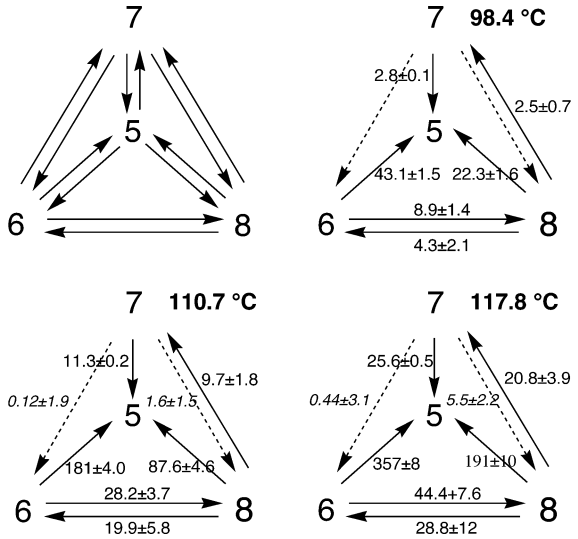


Figure 3. Shown at the upper left is the twelve-parameter kinetic model starting from the dimers, *anti*-n,n (**6**), *anti*-x,x (**7**), and *syn*-n,x (**8**). The other models are simplified by the omission of the nonobservable dimerizations of **5** to **6**, **7**, and **8**, and the transformations of **6** to **7** and **7** to **6** and **8**. From the resulting six-parameter model, rate constants (units of 10^{-6} sec^{-1}, 95% confidence level) are obtained at 98.4, 110.7, and 117.8 °C.

or their inclusion in the calculations. Using the full nine-parameter model, the program produces some negative rate constants in its efforts to minimize the sum of the squares of the differences between calculated and observed concentrations. Exclusion of the transformation of **6** to **7** from the model is warranted on the basis of being essentially non-observable (cf. columns 3 of Table 1, S-1, and S-2). The resulting eight-parameter equation works with the data at 110.7 and 117.8 °C, but still not with all the data at 98.4 °C. Further simplification to a six-parameter model by the exclusion of the transformations of **7** to **6** and **7** to **8** (cf. columns 6 and 8 of Table 1 and Figure 3) leads to sensible results. These are not the only ways of handling the data, all of which are available to the motivated reader in Tables 1, S-1, and S-2.

The disparity in precision of the rate constants for fragmentation, the major pathway, and stereomutation, the minor pathways, originates in the method of analysis by ^{1}H NMR. A more or less constant error of 2% translates into a rapidly increasing error in the determination of components of decreasing concentrations. Such difficulties are inherent in systems having widely disparate rate constants, no matter how calculated. In particular the method of analysis cannot deal with the slower pathways. Nothing is to be done in a system that is operationally irreversible, short of employing an analytical method of much greater sensitivity, such as one like the combination of gas chromatography and radioactivity introduced by Wolfgang and MacKay.[15] In the present work, high precision in the rate constants of the minor reactions would be essential were the conclusions to be based on differences in Arrhenius parameters. But the obtained precision suffices to establish that stereomutations are significantly slower than fragmentation. The data at the three temperatures (Tables 1, S-1, and S-2) reveal the disappearance of **6** → **5** as the fastest (columns 2 and 5) and **8** → **5** as comparable (columns 12 and 13), while that of **7** → **5**

(14) Marquardt, D. W. *J. Soc. Ind. Appl. Math.* **1963**, *11*, 431−441.

(15) Wolfgang, R.; MacKay, C. F. *Nucleonics* **1958**, *16*, 69−73; MacKay, C.; Wolfgang, R. *Science* **1965**, *148*, 899−907.

Table 1. Fragmentation and Stereomutation on Heating the Three Dimers, **6**, **7**, and **8**, of 3-Methylenecholest-4-ene (**5**) at 98.4 °C

T, sec	6[a]	7	8	5	6	7	8	5	6	7	8	5
0	0.977	0.023	0.000	0.000	0.039	0.940	0.000	0.021	0.218	0.127	0.640	0.015
1800	0.863	0.027	0.028	0.082	0.039	0.924	0.000	0.037	0.194	0.121	0.622	0.063
3600									0.180	0.127	0.591	0.102
5400	0.736	0.021	0.037	0.206								
7200									0.157	0.135	0.527	0.181
10800	0.549	0.030	0.062	0.359	0.026	0.909	0.000	0.064				
14400									0.126	0.135	0.429	0.309
21600	0.324	0.029	0.066	0.582	0.021	0.879	0.000	0.100				
28800									0.080	0.141	0.291	0.488
43200	0.129	0.030	0.063	0.778	0.010	0.830	0.000	0.159				
57600									0.039	0.140	0.143	0.678
90000	0.024	0.034	0.032	0.909	0.000	0.736	0.000	0.263				
115200									0.019	0.131	0.047	0.803
172800					0.000	0.598	0.000	0.402				
262800	0.000	0.022	0.000	0.979								
345600					0.000	0.380	0.000	0.620				
666000					0.000	0.163	0.000	0.838				

[a] Analysis by ^{1}H NMR (600 MHz; ppm δ): **6**, 5.80; **7**, 5.43; **8**, 5.73, 5.77; **5**, 4.79, 4.88, 5.96.

Table 2. Specific Rate Constants[a] for the Reactions of **6**, **7**, and **8** at Three Temperatures

reaction	98.4 °C	110.7 °C	117.8 °C	$k_{117.8}/k_{98.4}$	E_a[b]	log *A*
6 → **5**	43.1 ± 1.5[c]	181 ± 4.0[c]	357 ± 8[c]	8.28 ± 0.5[c]	31.5 ± 0.8[c]	14.1 ± 0.5[c]
		181 ± 3.8[d]	357 ± 7[d]			
7 → **5**	2.8 ± 0.1[c]	11.3 ± 0.2[c]	25.6 ± 0.5[c]	9.14 ± 0.5[c]	32.9 ± 0.8[c]	13.8 ± 0.5[c]
		9.8 ± 1.5[d]	20.7 ± 2.4[d]			
8 → **5**	22.3 ± 1.6[c]	87.6 ± 4.6[c]	191 ± 10[c]	8.57 ± 1.1[c]	32.0 ± 1.8[c]	14.1 ± 1.1[c]
		88.3 ± 4.4[d]	193 ± 8[d]			
6 → **7**						
6 → **8**	8.9 ± 1.4[c]	28.2 ± 3.7[c]	44.4 ± 7.6[c]	4.99 ± 1.2[c]		
		28.1 ± 3.5[d]	44.2 ± 6.2[d]			
7 → **6**		0.12 ± 1.9[d]	0.44 ± 3.1[d]			
7 → **8**		1.6 ± 1.3[d]	5.5 ± 2.2[d]			
8 → **6**	4.3 ± 2.1[c]	19.9 ± 5.8[c]	28.8 ± 12[c]	6.70 ± 3.5[c]		
		19.9 ± 5.6[d]	28.8 ± 10[d]			
8 → **7**	2.5 ± 0.7[c]	9.7 ± 1.8[c]	20.8 ± 3.9[c]	8.32 ± 2.9[c]		
		9.8 ± 1.7[d]	21.3 ± 3.1[d]			

[a] In units of 10^{-6} sec^{-1}; uncertainties at the 95% confidence level. [b] In kcal/mol. [c] Calculated on the basis of the six-parameter model (see text). [d] Calculated on the basis of the eight-parameter model (see text).

is noticeably slower (columns 7 and 9). From the specific rate constants in Table 2, Arrhenius parameters are estimated for the three fragmentations using the rate constants at the highest and lowest temperatures. A measure of the uncertainties results from using a procedure described recently.[16] The values for **6** → **5** are $E_a = 31.5 + 0.8$ kcal mol^{-1}, $\log A = 14.1 \pm 0.5$, for **7** → **5** are $E_a = 32.9 \pm 0.8$ kcal mol^{-1}, $\log A = 13.8 \pm 0.5$, and for **8** → **5** are $E_a = 32.0 \pm 1.8$ kcal mol^{-1}, $\log A = 14.1 \pm 1.1$. Reliable Arrhenius parameters for the stereomutations are not obtainable.

Discussion

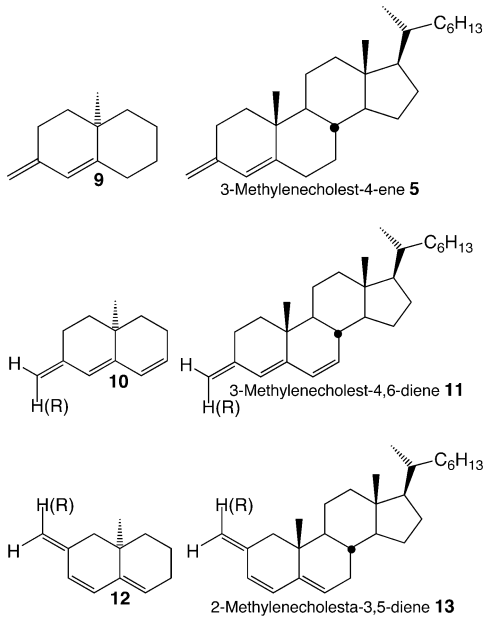
The close similarity in rates of fragmentation of the simple parent examined by Ekmanis[5] and the present example substituted by two large steroids is impressive. Thus, *anti*-**2** undergoes fragmentation to 3-methylenecyclohexene (Scheme 1) at 100.5 °C with a specific rate constant of 26.8×10^{-6} sec^{-1}. The comparable rate constants for fragmentation of **6** and **8** are 43.1×10^{-6} sec^{-1} and 22.3×10^{-6} sec^{-1} at 98.4 °C (Table 2), respectively. The difference in the bulk of the substituents seems to have had little effect on the rate-determining cleavage of the 1,4-bond to a singlet diradical (Scheme 3).

The rates of fragmentation of **7** → **5** are slower at 98.4, 110.7, and 117.8 °C than those of fragmentations **6** → **5** by factors of 15, 16, and 14, respectively, and slower than those of **8** → **5** by factors of 8, 8, and 7, respectively, An explanation may lie in the conformation of **7**. From the structure determined by X-ray crystallography, rings C and D and the side chain of the cholestene substituents are seen to lie in close contact *in the crystal* (see Figure 2). In contrast to **6** and **8**, the two cholestene systems in **7** lie not only parallel to each other but at distances commensurate with those of van der Waals minima (see Figures 1 and 2). Consistently, MM2 calculations (gas phase) point to a much higher value of the "non-1,4 van der Waals" interaction: −27.1 kcal mol^{-1} for **7** compared to −13.2 and −14.6 kcal mol^{-1} for **6** and **8**, respectively (total steric energies: 115.2, 126.2, and 128.4 kcal mol^{-1}, respectively). It may be relevant that a molecule of *m*-xylene of crystallization occupies space *between* molecules of the steroid and is not intercalated between the two wings of **7**. We suggest that **7** starts from a significantly lower heat of formation than either **6** or **8**. Some fraction of this attractive force may have to be lost in passing to the transition region of the 1,4-diradical and lead to on overall slowing of the generation of the diradical.

Stereomutations are slower than fragmentations in the responses of all three stereoisomers. It is particularly true of the thermal rearrangement of **6** → **7**, which is relatively much too

(16) Doering, W. v. E.; Keliher, E. J. *J. Am. Chem. Soc.* **2007**, *129*, 2488−2495.

Scheme 4



slow for its rate constant to be estimated even approximately. This reaction requires *two* internal rotations in the diradical prior to reclosure, whereas a *single* rotation of the bulky substituent suffices in the stereomutations of **6** → **8** and **8** → **7**. A statistical factor of 2 favoring the single rotation in **6** → **8** is suggested in the ratios to **8** → **6** within the limitations of the large uncertainties.

The only other observation bearing on the ratio of double to single rotation of which we are aware is found in the system of dimers **3** derived from **10** (Scheme 1), in which the ratio of double to single rotation is 1.4 at the much lower temperature of −22.7 °C.[6] Better comparisons might have been of the cyclobutane dimers of 3-methylenecholesta-4,6-diene (**11**) with **10**, or of the dimers of **5** with those of **9** (Scheme 4).

The ratios of fragmentation to stereomutation, Fr/St, in **2** and in the present series are significantly different. The ratio is 1.90 in *anti*-**2** at 100.5 °C, and 1.75 in *syn*-**2**,[5] while the ratios at 98.4, 110.7, and 117.8 °C for (**6** → **5**)/(**6** → **8**) are 4.8 ± 0.8, 6.4 ± 0.8, and 8.0 ± 1.4, respectively, and those for (**8** → **5**)/(**8** → **7**) are 8.9 ± 1.1, 9.0 ± 1.7, and 9.2 ± 1.4, respectively. The large, bulky steroid substituents are associated with a small favoring of fragmentation over stereomutation.

The contrast with the lack of a definitive effect on cis−trans isomerization about the carbon−carbon double bond is clear. This reorganization, depicted in Scheme 2, was thought ideal for revealing the effect of increasing bulk in a simple reaction that involved a purely internal rotation (torsion) culminating in a 90° twisted, noninteractive diradical as transition region. In the event, no significant effect could be established.[13b]

In the rotationally closely related thermal enantiomerization of bridged 1,1′-binaphthyls, Green and Morawetz created an elegant series with increasingly large substituents in the 6 and 6′ positions.[17a] With each increase (e.g., from phenyl to *p*-diphenyl to *p*-dihexylpentaphenyl), the rate in decalin solution at 150 °C decreases; the slowing from the parent binaphthyl to the pentaphenyl being by a factor of 0.44.

(17) (a) Park, J.-w.; Green, M. M.; Morawetz, H. *Macromolecules* **2001**, *34*, 5719−5722. (b) Yi, R.; Hoz, S. *J. Phys. Org. Chem.* **2002**, *15*, 782−786.

In the fragmentation and stereomutation of the cyclobutanes of Scheme 3, the ponderal effect appears to be significant if not overwhelming in magnitude. We speculate that an explanation may lie in the fundamental difference in the paths to the transition states. In the enantiomerizations of binaphthyls,[11] a succession of small rotations may lead to a transition state of zero degrees without having to occur in a single step requiring maximum readjustment in the solvent to the internal rotation. The ultimate activation energy may then be limited to overcoming the steric energy in the zero-degree geometry of the transition state.

A similar situation may prevail in cis−trans isomerizations about the carbon−carbon double bond. If this 90° rotation were to occur in one massive disruption to the order of the solvent, the larger were the mass and extension into the solvent, the greater would be the slowing of rate. Were it to have occurred as a succession of small steps finally reaching the 90° transition region in which the 2p−2p interaction has been overcome, the order in the solvent would not have been disrupted in a single massive movement by the large group. While the overall process had involved a large displacement, it would have been achieved by a succession of many displacements, each of small magnitude.

By contrast, in the reactions of the cyclobutane the primary rate-determining step is generally accepted to involve the generation of a caldera of noninteractive 1,4-diradicals by *cleavage of a carbon−carbon single bond* (Scheme 3). In this step, an indeterminate amount of internal rotation may be required to achieve a noninteractive geometry. Further internal rotations are now required before regeneration of cyclobutanes with stereomutation can be achieved. Within the very short-lived caldera, the time available for achievement of these conformations may be limited.

On the basis of a hypothetical explanation of this type, it may be predicted that *fragmentation* to **5** will not have been accompanied by significant internal rotation. This prediction could be tested experimentally by incorporating a single substituent in the exocyclic methylene groups of **12** and **13** and thereby introducing an additional stereocomponent, *E* and *Z*. This approach has been explicated if not experimentally elaborated in a related paper.[5]

Further insight into the origin of the ratio of fragmentation to stereomutation might be gained by comparing the difference between the cyclobutane dimers of **10** and the cylinder-like **11** with the difference between the cyclobutane dimers of **12** and the paddle-like **13**. Such a comparison might reveal the importance of extension compared to that simply of mass on the ratio (Scheme 4).

Conclusion

The major contribution from the present work is the uncovering in the three cyclobutane dimers of 3-methylenecholest-4-ene of significantly higher ratios of fragmentation to stereomutation. This observation may find a tentative explanation in terms of a relatively stronger resistance of the large steroid component to the internal rotations required in the caldera prior to exit by reclosure to cyclobutanes with stereomutation. Before such factors as weight and extensivity can be more than entertained as elements determining product-distribution, much further work is indicated.

Experimental

General. ^{1}H NMR spectra (600 MHz) and ^{13}C spectra (125 MHz) were measured in benzene-d_6 with a Varian INOVA 600 instrument and are reported in ppm (δ). The designations p, s, t, q stand for primary, secondary, tertiary, and quaternary carbon atoms, respectively, as determined by distortionless enhancement by polarization transfer (DEPT). Spin relaxation times (T_1) were determined by the inversion−recovery method in benzene-d_6.

3-Methylenecholest-4-ene (5). A solution of (+)-cholest-4-en-3-one (3.3 g, 8.4 mmol, Aldrich Chemical) in 15 mL of THF was added to an ice-cooled suspension of methylenetriphenylphosphorane (from 9.3 g of methyltriphenylphosphonium bromide and 16 mL of a 1.6 M ethereal solution of methyllithium) in 90 mL of anhydrous THF. The mixture was stirred for 24 h at room temperature. The resulting yellow solution was treated with 5 mL of water and 60 mL of ether, washed with water (2 × 100 mL), dried over $MgSO_4$, filtered, and concentrated to a solid (4.57 g), which was crystallized from ether/methanol (12 mL/4 mL) at 4 °C to give 1.83 g of colorless needles. A second crop (0.59 g) brought the yield to 78% of theory. ^{1}H NMR: 0.67 (s, 3H), 0.74 (dt, J = 2.93, 12.01 Hz, 1H), 0.85−0.93 (m, 2H), 0.95 (dd, J = 1.47, 6.59 Hz, 6H), 0.96 (s, 3H), 1.00 (d, J = 6.44 Hz, 3H), 1.06 (m, 4H), 1.18−1.47 (m, 11 H), 1.55 (m, 2H), 1.68 (m, 2H), 1.83 (m, 1H), 1.96 (dt, J = 3.22, 12.89 Hz, 1H), 2.07 (m, 1H), 2.21 (dt, J = 4.98, 13.18 Hz, 1H), 2.28 (dt, J = 3.22, 14.64 Hz, 1H), 2.38 (t, J = 16.69 Hz, 1H), 4.79 (s, 1H), 4.88 (s, 1H), 5.96 (s, 1H). ^{13}C NMR: 12.22 (p), 18.47 (p), 18.96 (p), 21.77 (s), 22.77 (p), 23.03 (p), 24.38 (s), 24.56 (s), 27.69 (s), 28.40 (t), 28.64 (s), 32.77 (s), 33.13 (s), 36.15 (t), 36.22 (t), 36.64 (s), 37.59 (s), 37.64 (q), 39.92 (s), 40.24 (s), 42.71 (q), 54.44 (t), 56.37 (t), 56.56 (t), 108.39 (s), 123.54 (t), 144.07 (q), 148.60 (q). For the vinyl H signals at 4.79, 4.88, and 5.96 ppm, values of T_1 are 1.25, 1.24, and 2.12 s^{-1}, respectively.

The stability of 3-methylenecholest-4-ene **5** is demonstrated by heating a sample (10.5 mg) and 18-crown ether as internal standard (5 μL of a 0.4 M solution in benzene-d_6) in a NaOH-washed Pyrex NMR tube for 72 h at 98 °C. Analysis by ^{1}H NMR showed no change.

Photodimerizaton of 3-Methylenecholest-4-ene 5. 3-Methylenecholest-4-ene (3.2 g, 8.4 mmol) in a Pyrex flask containing freshly distilled benzene (110 mL) was stirred and deoxygenated with a stream of argon for 20 min. After the addition of acetophenone (0.56 g), irradiation was conducted for 72 h at room temperature with a Hanovia 450-watt medium-pressure mercury arc lamp. Evaporation of the benzene left a residue, which was crystallized from diethyl ether (58 mL)/methanol (10 mL) at room temperature to give 436 mg of colorless needles **6** (*anti*-n,n). Recrystallization from toluene at room temperature afforded a crystal suitable for X-ray analysis. ^{1}H NMR: 0.69 (s, 6H), 0.82 (dt, J = 4.10, 12.37 Hz, 2H), 0.89−1.04 (m, 4H), 0.93 (dd, J = 1.68, 6.59 Hz, 12H), 0.98 (s, 6H), 1.02 (d, J = 6.52 Hz, 6H), 1.04−1.14 (m, 8H), 1.15−1.39 (m, 12 H), 1.40−1.48 (m. 8H), 1.49−1.61 (m, 6H), 1.62−1.67 (m, 2H), 1.70−1.75 (m, 2H), 1.76−1.90 (m, 8H), 1.95−2.04 (m, 4H), 2.16 (dt, J = 3.22, 12.89 Hz, 2H), 2.29 (dt, J = 3.51, 13.84 Hz, 2H), 5.80 (s, 2H). ^{13}C NMR: 12.27 (p), 18.98 (p), 19.35 (p), 21.88 (s), 22.76, (p), 23.00 (p), 24.39 (s), 24.56 (s), 28.38 (t), 28.64 (s), 30.96 (s), 33.35 (s), 33.83 (s), 34.77 (s), 36.23 (t), 36.29 (t), 36.63 (s), 37.60 (s), 39.90 (s), 40.37 (s), 42.84 (q), 45.19 (q), 54.47 (t), 56.50 (t), 56.66 (t), 125.22 (t), 144.60 (q). Although 27 ^{13}C NMR signals are observed, that at 28.61 ppm is twice as broad as the others. The spin-relaxation time for the signal at 5.80 ppm is 0.68 s.

The mother liquors from the ether/methanol crystallizations above were concentrated to dryness, dissolved in ether (50 mL), and cooled at −78 °C for 48 h to yield 215 mg of a second isomer as a colorless solid. Recrystallization from *m*-xylene at 4 °C afforded a crystal suitable for X-ray analysis. This isomer, **7** (*anti*-x,x), shows a single signal at 5.43 ppm. ^{1}H NMR: 0.73 (s, 6H), 0.97−1.00 (m, 2H), 0.98 (dd, J = 4.25, 6.59 Hz, 12H), 1.01 (s, 6H), 1.09 (d, J = 6.37 Hz, 6H), 1.10−1.17 (m, 4H), 1.19−1.33 (m, 12H), 1.33−1.50 (m, 12H), 1.51−1.64 (m, 12 H), 1.67−1.84 (m, 6H), 2.01−2.13 (m, 8H), 2.20−2.28 (m, 4H), 5.43 (s, 2H). ^{13}C NMR 12.36 (p), 19.19 (p) (this signal is double the intensity of the other signals), 21.84 (s), 22.84, (p), 23.08 (p), 24.57 (s), 25.97 (s), 28.66 (t), 28.97 (s), 29.40 (s), 31.90 (s), 33.40 (s), 33.64 (s), 35.67 (s), 36.62 (t), 36.96 (t), 37.15 (s), 37.36 (q), 39.95 (s), 40.61 (s), 43.21 (q),45.34 (q), 55.64 (t), 56.89 (t), 57.60 (t), 127.35 (t), 145.03 (q). Relaxation time of the signal at 5.43 ppm is 0.71 ± 0.01 s.

The remaining material in the ethereal mother liquors was chromatographed (neutral alumina, 2 cm i.d. × 24 cm, 10:1 hexanes/ethyl acetate) to yield 324 mg of a mixture, which was dissolved in benzene (0.4 mL), cooled at 4 °C for 24 h to afford 166 mg of solid. Analysis by ^{1}H NMR revealed the three isomers (5.80, 5.77, 5.73, and 5.43 ppm) and a small amount of **5** (5.96, 4.87, and 4.78 ppm): **8** (*syn*-n,x), 64%; **6** (*anti*-n,n), 21%; **7** (*anti*-x,x), 13%; **5**, 2%. The two unique features of the ^{1}H NMR spectrum associated with this enriched sample of **8** (*syn*-n,x) were signals for olefinic protons at 5.73 (s, 1H) and 5.77 (s, 1H) ppm.

Heating the Three Dimers of 3-Methylenecholest-4-ene 5: 6 (*anti*-n,n), 7 (*anti*-x,x), and 8 (*anti*-n,x). Pyrex NMR tubes were prepared by treating with 30% NaOH for 8 days, washing 20 times with water, washing 10 times with acetone, and drying in vacuo. The samples—9−12 mg of **6** (*anti*-n,n) and **7** (*anti*-x,x); 24−27 mg of enriched **8** (*anti*-n,x)—and 5 μL of a 0.4 M solution of 18-crown ether as internal standard in benzene-d_6 were placed in the NMR tubes, made up to 0.7 mL of benzene-d_6, degassed through three freeze−pump−thaw cycles, and sealed in vacuo. Heating was in the vapors of heptane (bp 98.4 ± 0.2 °C), toluene (bp 110.7 ± 0.2 °C), and *n*-butyl alcohol (bp 117.8 ± 0.1 °C) boiling under reflux. Quantitative analysis was effected by ^{1}H NMR using the signals for the olefinic hydrogen atoms given above. The results are given in Tables 1, S-1, and S-2.

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Supporting Information Available: Two tables of kinetic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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