decrease in amplification, as the length of the hydrophobic segment is increased, also remains to be clarified. We presently suspect, however, that self-aggregation of the surfactant polymers in solution and/or at the liposomal surface may be an important factor in this regard. Despite these questions which remain to be answered, all of the results that are presented herein, clearly demonstrate that *a very substantial amplification of the membrane-disrupting activity of a bolaphile is possible through polymerization, and that the magnitude of this amplification is a sensitive function of the structure and composition of the hydrophobic segment.* Operationally, one of the supramolecular surfactants (**IIc**) has been found to exhibit a membrane-disrupting activity which was more than 300 times greater than that observed for Triton X-100.

From a practical standpoint, supramolecular surfactants extend nonionic detergents into a new and uncharted domain in membrane-disrupting activity, which should be exploited. It is particularly significant to note that in preliminary in vitro studies, one polyester, having a structure which is very similar to that of Ie, exhibited substantial protection for human CD4+ lymphocytes against HIV-1; i.e., a 100% level of protection was observed when a polymer concentration of 53 μg/mL is used.[4,8] While the precise mechanism of anti-HIV action and the ultimate therapeutic utility of this and related polymers remain to be established, these results, nonetheless, lend strong support to our belief that a careful and systematic examination of supramolecular surfactants (and their corresponding bolaphiles) as antimicrobial agents is warranted.

Studies that are now in progress are aimed at (i) developing a more complete "library" of membrane-disrupting agents, (ii) defining the interactions between such agents and phospholipid membranes, and (iii) searching for correlations that may exist between membrane-disrupting activity and antimicrobial action.

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(8) In preliminary in vivo studies, Ic, Id, Ie, and If, when injected intraperitoneally into outbred white mice (up to 50 mg/kg), do not show any signs of toxicity: Jayasuriya, N.; Juliano, R. L.; Regen, S. L. Unpublished results.

Kinetics of the Thermolysis of [*n*.2.2]Propellanes and Related Compounds. Mechanism of the Thermolysis of Bicyclo[2.2.0]hexanes

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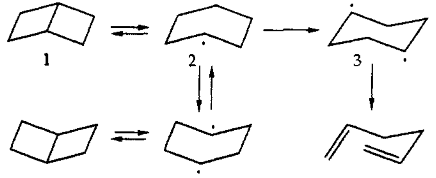
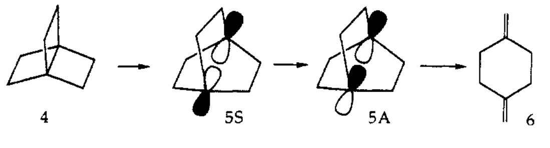
Abstract: The thermolyses of a series of 1,4-bridged bicyclo[2.2.0]hexanes have been studied. With bridges having three or more carbons, the compounds have higher activation energies than for bicyclo[2.2.0]hexane, indicating that the bridge prevents the formation of a chair cyclohexane-1,4-diyl, forcing the reaction to proceed via an orbital symmetry disallowed process. It appears likely that [2.2.2]propellane and its derivatives react via the same mechanism, and the driving force from strain relief appears to be the major factor in reducing its activation energy. The thermolysis of the relatively unstrained [3.3.2]propellane occurs at a significantly higher temperature and leads to a mixture of products which also were found in the thermolysis of 1,5-dimethylenecyclooctane. The thermolysis of the latter at 420 °C formed the propellane. The strain relief in the cleavage of the central bond in this group of propellanes were estimated via a combination of ab initio and molecular mechanics calculations and was found to be correlated with the changes in activation energy. The thermolyses of [3.2.1]- and [4.2.1]propellanes also are reported and were found to be less reactive than expected on the basis of strain energy relief.

The thermolysis of small ring hydrocarbons containing cyclobutane rings has received considerable attention.[1] Bicyclo[2.2.0]hexane (**1**) has been studied both with regard to its kinetics and stereochemistry of ring opening, and a multistep process appears well established.[2-4] The observation of ring inversion proceeding more rapidly than ring opening,[3] along with the stereochemical observations[4] are well accounted for by the process:



The boat cyclohexane-1,4-diyl (**2**) appears to be a required intermediate in order to account for the ring inversion.[3] A key element of the process is the conformational change from the boat of the chair diyl (**3**), and the orbital symmetry allowed cleavage of the latter to the product diene.[4]

The thermolysis of the known [2.2.2]propellane derivative (the *N*,*N*-dimethylamide) leads to the same overall process and has a remarkably low activation energy, E_a = 22 kcal/mol, which allows the reaction to occur at room temperature with a half-life of less than an hour.[5] It has been proposed that the reaction proceeds as follows:[6]



Here, the initial cleavage of the central bond of **4** leads to the symmetric diyl, **5S**. It has little through-space interaction because of the flexibility of the ring system which allows the bridgehead carbons to be fairly far apart. The antisymmetric diyl, **5A**, may now have the lower energy because of the interaction of the bridgehead orbitals with the σ* orbitals of the ethano bridges.

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(1) For a review of cyclobutane thermolyses, see: Berson, J. A. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 1.

(2) Steel, C.; Zand, R.; Hurwitz, P.; Cohen, S. G. *J. Am. Chem. Soc.* **1964**, *76*, 679. Srinivasan, R. *Int. J. Chem. Kinet.* **1969**, *1*, 133.

(3) Goldstein, M. J.; Benzon, M. S. *J. Am. Chem. Soc.* **1972**, *94*, 5119.

(4) Paquette, L. A.; Schwartz, J. A. *J. Am. Chem. Soc.* **1970**, *92*, 3215. Sinnema, A.; Rantwijk, F. v.; De Konig, A. T.; Wijk, A. M. v., Bekkum, H. v. Tetrahedron **1973**, *32*, 364. Wehrli, R.; Bellus, D.; Hansen, H.-J.; Schmid, H. *Chimia* **1976**, *30*, 416.

(5) Eaton, P. E.; Temme, G. E., III *J. Am. Chem. Soc.* **1973**, *95*, 7508.

(6) (a) Stohrer, W.-D.; Hoffmann, R. *J. Am. Chem. Soc.* **1972**, *94*, 779. (b) Newton, M. D.; Schulman, J. M. *Ibid.* **1972**, *94*, 4391.6.

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Scheme I

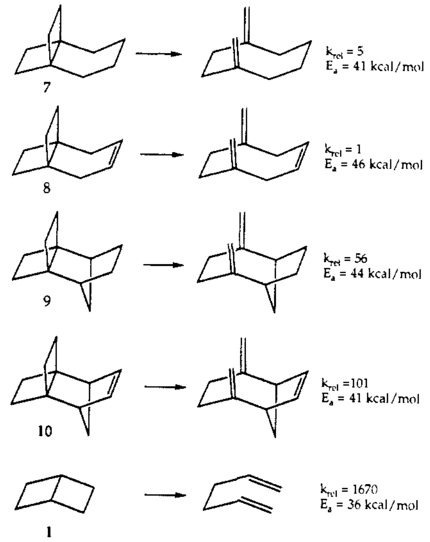

Table I. Kinetics of Thermolysis of Propellanes **7–10**

compd	T, °C	$k \times 10^3$, s^{-1}	activation parameters
7	303.8	1.88 ± 0.02	ΔH = 39.6 ± 1.0
	324.4	5.52 ± 0.05	ΔS = −3.7 ± 1.7
	345.4	20.1 ± 0.08	E_a = 40.9 ± 1.0
	366.9	60.6 ± 0.7	log A = 12.7
8	324.8	1.27 ± 0.09	ΔH = 45.0 ± 1.1
	335.4	3.14 ± 0.16	ΔS = 2.2 ± 2
	345.9	4.75 ± 0.22	E_a = 46.3 ± 1.3
	355.6	7.10 ± 0.25	log A = 14.0
	367.2	15.0 ± 0.4	
	376.6	29.2 ± 1.1	
	383.8	44.8 ± 1.3	
	394.8	84.1 ± 2.2	
9	255.3	0.53 ± 0.07	ΔH = 43.0 ± 1.4
	270.1	1.62 ± 0.08	ΔS = 6.8 ± 1.8
	290.1	7.92 ± 0.40	E_a = 44.3 ± 1.4
	310.8	27.9 ± 0.7	log A = 15.0
10	250.1	0.870 ± 0.024	ΔH = 40.3 ± 1.0
	260.6	1.65 ± 0.02	ΔS = 3.2 ± 2
	274.7	4.74 ± 0.28	E_a = 41.4 ± 1.0
	294.9	17.4 ± 0.4	log A = 14.2
	309.3	49.6 ± 2.0	

A conversion of **5S** to **5A** would be followed by an orbital symmetry allowed conversion of **5A** to the product, **6**.

Both mechanistic hypotheses appear quite reasonable, but lead to rather different mechanisms for the reactions of compounds which are chemically quite similar and which lead to similar products. Our interest in these reactions, as well as those of propellanes having cyclopropane rings, has led us to carry out a study of the kinetics of the thermolysis of a number of related compounds, **7–13**. The first four, **7–10**, are bicyclo[2.2.0]hexanes containing bridges larger than that in [2.2.2]propellane (Scheme I). [3.3.2]Propellane (**11**) provides an example of a cyclobutane having relatively little extra strain and with the same substitution pattern as the other propellanes. [4.2.1] and [3.2.1]Propellanes, (**12** and **13**, respectively) are compounds in which the bridgehead carbons would remain relatively close to each other in the diyl formed by stretching the central bond. Here, the symmetric diyl would be expected to be lower in energy than the antisymmetric form because of the greater through-space interaction and also because of the smaller number of potentially stabilizing through-bond interactions (e.g., there is now only one ethano bridge). All of the compounds were prepared via previously reported procedures.[7]

Scheme II

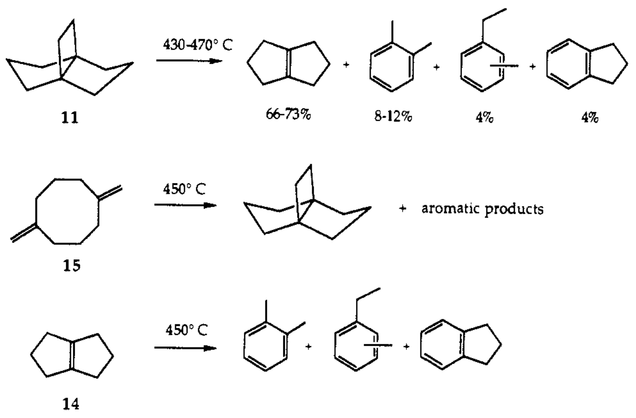

Table II. Kinetics of Thermolysis of [3.2.2]Propellane[a]

T, °C	$k_{obs} \times 10^5$, s^{-1}
430.2	2.09 ± 0.01
450.2	6.28 ± 0.20
469.9	21.3 ± 0.7

[a] $\Delta H^* = 59.3 \pm 3.0$ kcal/mol, $\Delta S^* = 2.5 \pm 4.1$ eu, $E_a = 60.7 \pm 3.0$ kcal/mol, log $A = 14.1 \pm 0.8$.

The thermolyses of **7–10** were studied with use of a stirred flow reactor.[8,9] In each case, the reaction occurred cleanly and gave a single product derived by cleavage of one of the cyclobutane rings (Scheme I).[10] The rate constants and derived activation parameters are given in Table I, and the latter are included in Scheme I for convenience. The contrasting effects of fusing a four-membered ring onto bicyclo[2.2.0]hexane leading to a large rate increase and of larger rings leading to a large rate decrease is striking.

The structure of **7** permits the bridgehead carbons to move relatively far apart in the possible diradical intermediate formed by cleaving the central C–C bond. It also has two ethano bridges which could help stabilize the diradical via a through-bond interaction. Despite these similarities to [2.2.2]propellane, the reaction of **7** is retarded with respect to **1** rather than being accelerated. Why should **7** have such a low reactivity?

The proposed mechanism for the thermolysis of **1** bypasses an orbital symmetry forbidden process (the cleavage of the boat diyl to hexadiene) by having a conformational change to the chair diyl which may then cleave in a symmetry allowed process. The stereochemistry of the cleavage is in accord with such a process.[4] The addition of a third ring, as in going from **1** to **7**, prevents the conformational change. The reaction must now proceed directly from the boat diyl via the forbidden process which has a higher activation energy. It can be seen that the thermolyses of **7–10** are in good accord with the proposed mechanism for the cleavage of **1**.

If this view is correct, it would be less likely that **4** reacts via a different mechanism. The low activation energy would then be ascribed to ground-state destabilization, and there is good reason to think that **4** has a much larger strain energy than any of the other compounds.[11]

In order to have a relatively unstrained propellane for comparison, we studied [3.3.2]propellane (**11**). It has the same

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(7) Compounds **7–10**: Wiberg, K. B.; Matturro, M. G.; Okarma, P. J.; Jason, M. E.; Dailey, W. P.; Burgmaier, G. J.; Bailey, W. F.; Warner, P. *Tetrahedron* **1986**, *42*, 1895.

(8) A preliminary account of the thermolyses of **7–10** has been presented: Wiberg, K. B.; Matturro, M. G. *Tetrahedron Lett.* **1981**, *22*, 3481.

(9) Lewis, E. S.; Herndon, W. C. *J. Am. Chem. Soc.* **1961**, *83*, 1955. Herndon, W. C.; Henly, M. B.; Sullivan, J. M. *J. Phys. Chem.* **1963**, *67*, 2842. Herndon, W. C.; Lowry, L. L. *J. Am. Chem. Soc.* **1964**, *86*, 1922. Herndon, W. C. *J. Chem. Ed.* **1964**, *41*, 425.

(10) The compounds were identified by comparison with the spectra previously reported: Tatarsky, D.; Kaufman, M.; Ginsberg, D. *Isr. J. Chem.* **1971**, *9*, 715. Dean, C. S.; Jonas, D. A.; Graham, S. H.; Lewis, D. O. *J. Chem. Soc. C* **1968**, *24*, 3045. Beckhaus, H.-D.; Heller, C.; Mayer, B. *Chem. Ber.* **1980**, *11*, 2589.

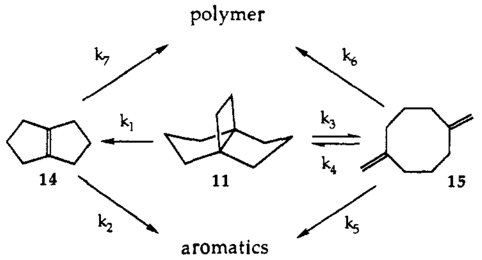
(11) Wiberg, K. B. *J. Am. Chem. Soc.* **1983**, *105*, 1227.

Table III. Kinetics of Thermolysis of 1,5-Dimethylenecyclooctane

T, °C	$k_{obs} \times 10^4$, s^{-1}	$k_{prop} \times 10^4$,[a] s^{-1}	$k_{arom} \times 10^4$,[b] s^{-1}
415.1	9.1 ± 0.39	2.9 ± 0.13	6.2 ± 0.27
450.1	6.1 ± 1.0	13.9 ± 0.2	55.2 ± 0.8
470.2	185.7 ± 2.9	25.4 ± 0.4	160.2 ± 2.5

[a] Propellane formation: $\Delta H^\ddagger = 39.1 \pm 1.9$ kcal/mol, $\Delta S^\ddagger = -19.4 \pm 2.8$ cal deg^{-1} mol^{-1}, $E_a = 40.6 \pm 1.9$ kcal/mol, log $A = 9.4 \pm 0.6$. [b] Aromatic hydrocarbon formation: $\Delta H^\ddagger = 58.9 \pm 1.9$, $\Delta S^\ddagger = 10.6 \pm 2.8$ cal deg^{-1} mol^{-1}, $E_a = 60.3 \pm 1.9$ kcal/mol, log $A = 16.0 \pm 0.6$.

Scheme III



substitution pattern as the other compounds, but only the strain inherent in one cyclobutane ring. Its low reactivity made it impractical to study it by using the stirred-flow reactor, and therefore it was studied in the gas phase in a static system. Unlike **7**–**10**, its thermolysis at 450 °C led to a complex mixture of products (Scheme II). The major product was bicyclo[3.3.0]-oct-1(5)-ene (**14**) and other products were found. The first order rate constants are given in Table II. The activation energy was 61 kcal/mol, similar to that for the thermolysis of cyclobutane (63 kcal/mol)[12]

The product that would correspond to the mode of reaction of the other propellanes is 1,5-dimethylenecyclooctane (**15**). The thermolysis of **15** was found to proceed at a somewhat lower temperature than **11** and led to **11** along with **14** and aromatic hydrocarbons (Scheme II). The thermolysis of **15** was studied with use of a stirred-flow reactor, giving the first-order rate constants shown in Table III. The rate constants were partitioned into the rates of formation of **11** and of aromatic hydrocarbons by using the observed product ratios.

The facile conversion of **15** to **11** ($E_a = 39$ kcal/mol) is remarkable in that it is the reverse of the usually observed process. It is interesting to note that the dimerization of ethylene giving cyclobutane would have a favorable equilibrium constant at room temperature and that the unfavorable entropy term is the factor which leads to the unfavorable equilibrium at temperatures at which the reaction could be observed. In the present case, no loss of translational entropy occurs, and the smaller negative $\Delta S^\ddagger = -19$ cal deg^{-1} mol^{-1} arises from the constraint of internal motion on going to the relatively rigid activated complex.

The rate of thermolysis of **14** also was determined in a static system at 450 °C, giving the first-order rate constant, 5.1×10^{-5} s^{-1}. With the assumption that the initial reaction of **11** gave only **14** and **15**, it was possible to simulate the course of the reaction via the reactions in Scheme III. Here, the rate constants k_3, k_4, k_5, and k_6 were set at the values formed in independent studies of **14** and **15** under the same conditions. The constants k_1 and k_2 were varied with use of a Runge–Kutta numerical integration scheme to yield changes in concentration with time which agreed with the experimental data. The rate constants thus obtained at 450 °C are (s^{-1}): $k_1 = 4.4 \times 10^5$, $k_2 = 1.3 \times 10^{-5}$; $k_3 = 2.1 \times 10^{-5}$; $k_4 = 1.4 \times 10^{-3}$; $k_5 = 5.5 \times 10^{-3}$; $k_6 = 5.0 \times 10^{-3}$; $k_7 = 3.8 \times 10^{-5}$.

The thermolyses of [4.2.1]- and [3.2.1]propellanes (**12** and **13**, respectively) could be studied with use of the stirred-flow reactor, and under these conditions the reactions were first order. The reaction of **12** gave mainly 1,3-dimethylenecycloheptane (Scheme IV) along with 7% of a mixture of three other compounds. The product ratio was essentially independent of temperature. The rate constants and activation parameters are given in Table IV. The thermolysis of **13** formed mainly 1,3-dimethylenecyclohexane along with about 2% of other products.[13] The kinetic data for this compound are given in Table V. The activation energy for **12** (61 kcal/mol) was considerably higher than that for **13** (54 kcal/mol) as might be expected for the difference in strain energies. Both reactions had a relatively large preexponential factor corresponding to $\Delta S^\ddagger \approx +10$ cal mol^{-1} deg^{-1}.

Scheme IV

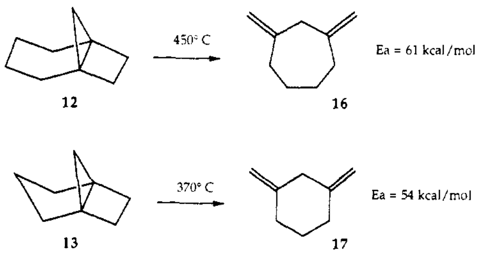


Table IV. Rate Constants for the Thermolysis of [4.2.1]Propellane (**12**)

	$k_{obs} \times 10^3$, s^{-1}	
T, °C	loss of **12**	form of **16**[a]
420.0	1.12 ± 0.02	0.91 ± 0.02
433.1	2.29 ± 0.02	1.99 ± 0.02
446.7	4.56 ± 0.10	4.11 ± 0.09
458.0	9.14 ± 0.04	8.47 ± 0.04
470.5	19.8 ± 1.1	18.3 ± 1.0

[a] Formation of **16**: $\Delta H^\ddagger = 59.1 \pm 2.0$ kcal/mol, $\Delta S^\ddagger = 11.0 \pm 3.0$ cal deg^{-1} mol^{-1}, $E_a = 60.5 \pm 2.0$ kcal/mol, log $A = 16.0 \pm 0.6$.

Table V. Rate Constants for the Thermolysis of [3.2.1]Propellane (**13**)

	$k_{obs} \times 10^4$, s^{-1}	
T, °C	loss of **13**	form of **17**[a]
348.8	7.1 ± 0.2	6.6 ± 0.2
361.5	15.9 ± 0.7	15.3 ± 0.7
373.8	35.3 ± 1.1	34.0 ± 1.1
387.8	84.7 ± 1.6	82.8 ± 1.6
400.4	195 ± 5	191 ± 5

[a] Formation of **17**: $\Delta H^\ddagger = 52.8 \pm 1.2$ kcal/mol, $\Delta S^\ddagger = 10.3 \pm 2.2$ cal deg^{-1} mol^{-1}, $E_a = 54.1 \pm 1.2$ kcal/mol, log $A = 15.8 \pm 0.4$.

A reasonable working hypothesis to explain all of the data is that the initial rate-determining reaction leads to bond cleavage, giving a diyl, which is followed by cleavage of the second bond to form the product diene. Then the mechanism, at least as far as the rate-determining step is concerned, would be the same for all of the compounds. Since the closure of the diyl would be expected to have a small activation energy, there should be a relationship between the activation energy for the reaction and the strain energy relief in going from the hydrocarbon to the diyl.

There are some problems associated with estimating the changes in strain energy. First, the heats of formation of the reactants are needed. Then, some way must be found in order to estimate the heats of formation of the diyls. We have chosen to use ab initio MO theory to provide estimates of the heats of formation of the propellanes since simpler methods such as molecular mechanics are not appropriate for cases in which the hybridization differs significantly from normal values. The heats of formation of the diyls were estimated by using molecular mechanics. It is well recognized that the heats of formation of most alkanes can be satisfactorily estimated via molecular mechanics.[14] We have developed parameters suitable for the description of tertiary

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(12) Genaux, C. T.; Kern, F.; Walters, W. D. *J. Am. Chem. Soc.* **1953**, *75*, 6196.

(13) The thermolysis of **13** also has been studied by Aue and Reynolds (Aue, D. H.; Reynolds, R. N. *J. Org. Chem.* **1974**, *39*, 2315), but detailed kinetic data have not been presented.

(14) Burkert, U.; Allinger, N. L. *Molecular Mechanics*; ACS Monograph 177; American Chemical Society: Washington, DC, 1981.

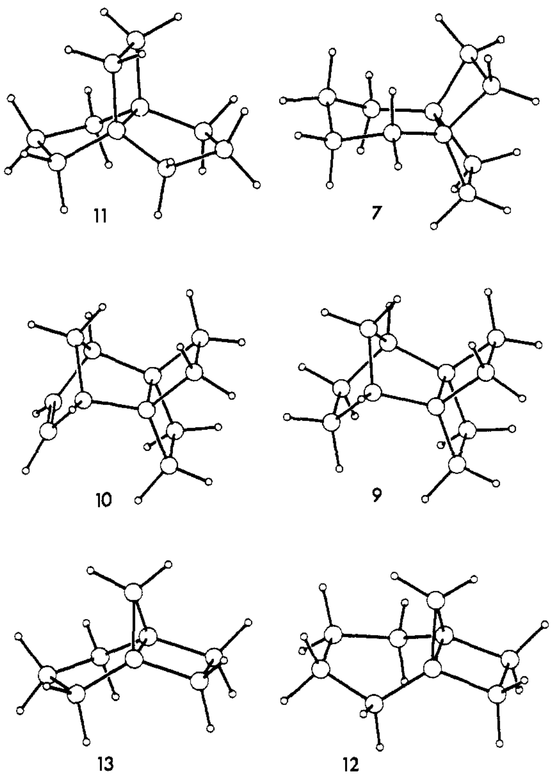
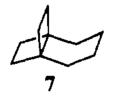
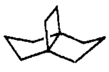
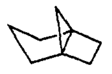


Figure 1. Calculated structures of propellanes.

radicals, and have used them along with the normal alkane parameters to estimate the energies of the diyls. It should be noted that this procedure neglects all through-bond interactions and through-space interactions in the diyls.

The geometries of some of the propellanes were calculated with use of the 3-21G basis set, and then the 6-31G* energies were obtained at those geometries. The results are shown in Figure 1 and Table VI. The calculated energies were converted to heats of formation by using the group equivalents we have developed for this purpose.[15] Because of the size of these molecules, it was necessary to employ some symmetry element in the ab initio calculations. This does not present much of a problem with most of the molecules since they would be expected to either have a plane of symmetry or to be energetically close to such a structure. [4.2.2]Propellane (**7**) would be expected to have a structure based on cyclohexene, and a C_2 axis was used. [4.2.1]Propellane (**12**) would be expected to have a similar structure, but this would have no symmetry. The energy of the structure with C_s symmetry was calculated (Figure 1). It was estimated via molecular mechanics that its energy would be 4.5 kcal/mol larger than that of the lower energy structure, and this correction is noted in Table VI.

Table VI. Calculated Energies for the Propellanes

compd	E(H) 3-21G	E(H) 6-31G*	ΔH_f, kcal/mol	strain energy, kcal/mol
 **4**	-308.089 43	-309.807 07	69.3	97
 **10**	-422.243 15	-424.585 94	74.5	79
 **9**	-423.437 79	-425.782 38	43.2	78
 **7**	-385.798 31	-387.942 73	17.7	56
 **11**	-385.836 38	-387.974 93	-2.6	40
 **12**	-346.952 53	-348.894 23	31.4 (26.9)[a]	64 (59)[a]
 **13**	-308.122 21	-309.848 35	43.4	71

[a] The values in parentheses are corrected to correspond to a cyclohexene-like structure for the six-membered ring (cf. the text).

Table VII. New Molecular Mechanics Parameters

a. Force Constants

term	f	r_0 or θ_0
C—C· stretch	4.70	1.50
C═C—C (>111°) bend	0.62	124.7
C═C—C (<111°) bend	0.35	124.7
C—Ċ—C bend	1.08	118.4
C—C—C (<102°) bend	0.60	109.5
C—Ċ—C—C torsion	V_3 = 0.0037	

b. Group Increments, kcal/mol

tertiary radical	286.89
═C—	222.3
C3 ring	-29.51
C4 ring	-23.09

Parameters for molecular mechanics modeling of tertiary radicals were obtained by using the known geometry, vibrational frequencies, and energy of the *tert*-butyl radical.[16] The normal hydrocarbon parameters were those of Boyd.[17] The new parameters are shown in Table VII.[18] The vibrational frequencies derived from this force field were calculated. Here, we do not expect to reproduce the frequencies accurately because all interaction terms are left out. Rather, one expects to find the appropriate number of frequencies in the low-, mid-, and high-frequency ranges,[16] and this was the case. The observed spectrum leads to a zero-point energy of 71.7 kcal/mol and $S°$ = 76.0 eu at 25 °C,[15] and the calculated spectrum gives a zero-point energy of 70.6 kcal/mol and $S°$ = 76.0 eu. The results appear to be satisfactory.

The estimated energies of the diyls are given in Table VIII. A comparison with the parent bicycloalkanes leads to C–H bond dissociation energies which appear to be reasonable. The relatively unstrained bicycloalkanes give bond dissociation energies close to that of isobutane (96 kcal/mol),[19] and it is known that angular distortion at the bridgehead carbons, such as in norbornane, increases the bond dissociation energies.[20] The last column of the table gives the calculated change in energy on going from the propellane to a "classical" diyl having no through-bond or through-space interactions. These data are for 25 °C and would change somewhat on going to the higher reaction temperatures. However, it would be reasonable to expect that the changes in heat capacities for the reactions would be small and approximately the same for all of the propellanes. Therefore, little error should

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(15) Wiberg, K. B. *J. Org. Chem.* **1985**, *50*, 5285.

(16) Yoshimine, Y.; Pacansky, J. *J. Chem. Phys.* **1981**, *74*, 5168. Schrader, B.; Pacansky, J.; Pfeiffer, U. *J. Phys. Chem.* **1984**, *88*, 4069. Pacansky, J.; Chang, J. S. *J. Chem. Phys.* **1981**, *77*, 5539.

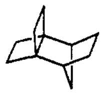
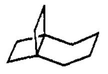
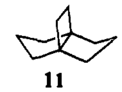
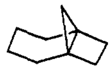
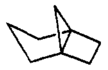
(17) Chang, S.; McNally, D.; Shary-Tehrany, S.; Hickey, M. J.; Boyd, R. H. *J. Am. Chem. Soc.* **1970**, *92*, 3109.

(18) The full set of parameters which were used are given in the Ph.D. thesis of J. Caringi, Yale, 1989.

(19) Tsang, W. *J. Am. Chem. Soc.* **1985**, *107*, 2872. With the parameters given herein, the calculated bond dissociation energy of isobutane is 95 kcal/mol.

(20) Walling, C.; Mayahi, M. H. *J. Am. Chem. Soc.* **1959**, *81*, 1485.

Table VIII. Molecular Mechanics Calculations for Diyls, kcal/mol

	bicycloalkane, ΔH_f	diyl, ΔH_f	diyl, SE	diyl[a] dist, Å	BDE[b]	propellane, ΔH_f	$\Delta\Delta H_f$[c]
 **4**	-22.8	79.5	24.8	2.42	103.2	69.3	10.2
 **10**	15.5	109.6	38.2	2.54	99.1	74.5	35.1
 **9**	-10.9	82.3	38.0	2.51	98.6	43.2	39.1
 **7**	-24.9	57.5	13.6	2.63	93.2	17.7	39.8
 **11**	-26.6	55.6	11.6	2.70	93.1	-2.6	58.2
 **12**	-25.0	68.1	18.3	2.22	98.6	26.9	41.2
 **13**	-22.7	78.8	24.3	2.16	102.8	43.4	35.4

[a] Calculated distance between bridgehead carbons in the diyls. [b] Calculated C–H bond dissociation energies for the parent hydrocarbons. [c] Change in ΔH_f on going from the propellane to the diyl.

be introduced in using the 25 °C data in a comparison with the activation energies.

With these data in hand, the activation energies may be compared with the estimated changes in enthalpy on going to the diyls. The correlation is shown in Figure 2. In the case of the propellanes with the bicyclo[2.2.0]hexane structural unit, there is an excellent correlation with a slope of 0.8. This result confirms our conclusion that all of the bridged bicyclo[2.2.0]hexanes, including [2.2.2]propellane, react via the same mechanism, i.e. the "forbidden" mechanism for bicyclo[2.2.0]hexane. The high reactivity of **4** results from its high ground-state strain, most of which may be relieved on going to the stretched diyl.

In this connection, it is interesting to reexamine the calculations of Newton and Schulman[6b] for the thermolysis of **4**. They confirmed Hoffman's suggestion concerning the diyls **5S** and **5A**.[6a] However, a careful examination of their data suggests that the transformation of **5S** to **5A** occurs *after* the rate-determining step. Thus, it would not affect the rate of reaction. It can be seen that the basic idea presented by Hoffman, the calculations of Newton and Schulman, and the present data are all in good accord.

In contrast to the bicyclo[2.2.0]hexane derivatives, the propellanes based on the bicyclo[2.1.0]pentane ring system, **12** and **13**, reacted at a slower rate than expected from the correlation in Figure 2. A reason for the difference may be found in Table VIII which gives the calculated bridgehead–bridgehead distances for the diyls. With the compounds based on the bicyclo[2.2.0]hexane ring system, the distances were about 2.5 Å, which is long enough to minimize through-space interactions. However, with **12** and **13** the calculated distances were only about 2.2 Å. It would seem reasonable to propose that the diyls formed from these compounds would have to be stretched further before the transition state is reached and that the calculated diyl energies are significantly lower than the transition-state energies. An estimate was made via molecular mechanics of the change in energy in stretching the diyls derived from **12** and **13** to 2.5 Å, giving a value of 18 kcal/mol. When this was added to the $\Delta\Delta H_f$ values in Table VIII, both **12** and **13** move close to the correlation line (Figure 3). The remarkably good fit is surely fortuitous, but the result does suggest that essentially the same process is operative with all of the compounds.

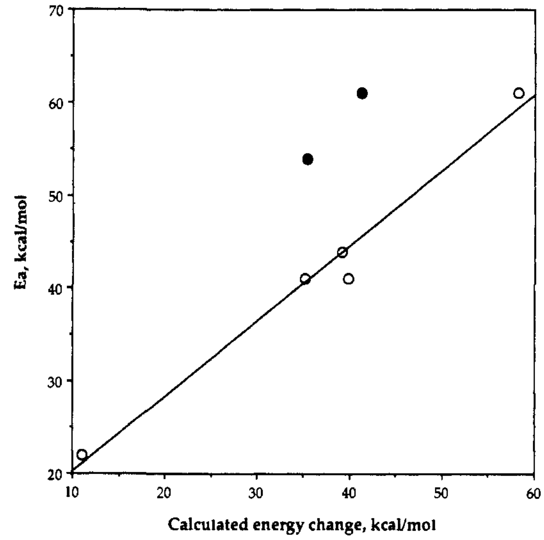


Figure 2. Correlation of activation energies with calculated energy changes for propellanes going to the corresponding diyls. The open circles are for the compounds having only cyclobutane rings, whereas the closed circles are for those based on the bicyclo[2.1.0]pentane ring system.

Calculations

The programs GAMESS[21] as well as GAUSSIAN-82[22] were employed for the ab initio calculations. Input geometries for optimization

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(21) Dupuis, M.; Spangler, D.; Wendoloski, J. J. *GAMESS*. NRCC program QG01, 1980.

(22) Binkley, J. S.; Frisch, M. J.; DeFrees, D. J.; Raghavachari, K.; Whiteside, R. A.; Schlegel, H. B.; Fluder, E. M.; Pople, J. A. *GAUSSIAN-82*; Department of Chemistry, Carnegie-Mellon University: Pittsburgh, PA, 1982.

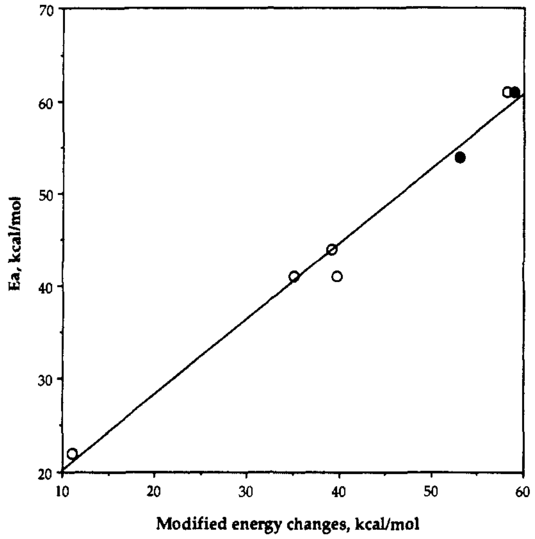

Figure 3. Correlation of activation energies with calculated energy changes. Here, the energy changes for the bicyclo[2.1.0]pentane based propellanes (**12** and **13**) are those for going to diyls with a 2.5 Å distance.

with the 3-21G basis set were provided by MOLBLD[16] optimizations. Single-point calculations at the 6-31G* level on the 3-21G geometries were carried out to obtain energies. Empirical force field calculations were performed with MOLBLD.[16]

Experimental Section

Materials. The propellanes **7–10** were prepared via cycloaddition reactions of bicyclo[2.2.0]hex-1(4)-ene.[7] [3.2.1]- and [4.2.1]Propellanes were prepared by the addition of methylene to the corresponding alkenes.[23] 1,5-Dimethylenecyclooctane was prepared by the procedure of Bishop and Landers.[24]

Tricyclo[3.3.2.$0^{4,8}$]decan-1-one. Bicyclo[3.3.0]-7-octen-1-one[25] (1 g), purified by passage through basic alumina (60% ether/40% hexane), was added to 180 mL of dry methylene chloride (distilled from calcium hydride) in a photolysis well equipped with a quartz probe, vycor filter, 450-W Hanovia medium-pressure mercury lamp, reflux condenser, and nitrogen inlet. The well was cooled by immersion in a Dewar flask containing dry ice/acetone and by circulation of ethanol at −60 °C through the probe. The solution was degassed by bubbling nitrogen through the system for 1 h, ethylene was bubbled in, and the solution was photolyzed. Progress of the reaction was monitored by UV spectroscopy by using the disappearance of the λ_{max} at 240 nm of the enone. After 18 h the reaction was judged to be complete, and the solution was dried over magnesium sulfate, filtered, and evaporated. Thin-layer chromatography (20% ether/80% hexane) indicated the presence of some starting material. The mixture was separated on a silica gel column (same solvent system) to provide 1 g of tricyclo[3.3.2.$0^{4,8}$]decan-1-one. ^{1}H NMR ($CDCl_3$, 60 MHZ): δ 1.0–2.3 (12 H, m), 2.3–3.1 (2 H, m). ^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 25.1, 28.3, 29.5, 32.5, 33.5, 40.1, 50.0, 51.4, 57.0, 221.0.

[3.3.2]Propellane (11). To a 25-mL flask equipped with a magnetic stir bar and a reflux condenser were added 300 mg of tricyclo-[3.3.2.$0^{4,8}$]decan-1-one, 1.6 g of potassium hydroxide, 1.2 g of 95% hydrazine, and 5 mL of diethylene glycol. The mixture was stirred and heated at 110 °C for 1 h, then at 180 °C for 4 h. A white solid collected on the inside of the condenser during this time. The reaction was cooled, and the solid was washed out of the condenser with pentane. This solution was dried over magnesium sulfate, filtered, and concentrated by distillation. Preparative gas chromatography (12 ft × $^1/_4$ in. 20% SE-30 on Chromosorb W) of the remaining solution provided 180 mg (66%) of tricyclo[3.3.2.$0^{1,5}$]decane, which sublimed over a range of 98–103 °C (lit[20] 94–102 °C). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.21–1.37 (4 H, m), 1.58–1.70 (4 H, m), 1.65 (4 H, s), 1.71–2.01 (2 H, m), 2.01–2.22 (2 H, m). ^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 27.6, 30.8, 39.1, 55.1.

Gas-Phase Stirred-Flow System. A flow system with a conventional design was constructed.[9] Modifications were made to accommodate higher reaction temperatures of over 400 °C and oxygen sensitive substrates. A stream of helium carrier gas, controlled by a Nupro needle valve, passed through a constant temperature sample vaporizer. Transfer lines were warmed to 40 °C with heating tape. The gas mixture then entered the reactor immersed in a constant temperature molten salt bath. From there the stream passed through a sample loop in a gas chromatograph, a cold trap, a room temperature equilibration tower, and a soap film flow meter. In order to obtain consistent results for **12** and **13**, it was necessary to install a Matheson model 6406 gas purifier in the line before the sample.

The main body of the reactor was made from a 50-mL round-bottomed Pyrex flask. Its 33-cm stem was constructed from concentric 5-, 8-, and 10-mm Pyrex tubing. The 5-mm tube extended into the flask and was sealed ~3 mm above the bottom; it served as a thermocouple well. The 8-mm tube terminated ~3 mm higher; it was between these two tubes that gas entered. The 10-mm tube emanated vertically from the top of the flask; gas exited between it and the 8-mm tube. The vessel was immersed in the Hitec salt bath up to the point at which the 10-mm tube rose from the flask. This point was used to delimit the volume of the reactor. The vessel was weighed, filled with mercury, and weighed again. The temperature of the mercury was measured, and with use of the known density, the volume was calculated as the average of three measurements. This method resulted in errors of less than 0.5%.

The entire vessel was then cleaned with nitric acid, nitric and sulfuric acid, alcoholic KOH, NH_4OH, and water and dried. It was silylated with *N*,*O*-bis(trimethylsilyl)acetamide, washed with CCl_4, and dried. Once the reactor was inserted in the flow system it was maintained under helium. Interruptions in the stream of carrier gas were held to a minimum.

The bath was of molten Hitec, a mixture of 53% potassium nitrate, 40% sodium nitrite, and 7% sodium nitrate available from Costal Chemical Co., contained in a 12 in. diameter dia × 12 in. Pyrex battery jar which was insulted with vermiculite. The salt was heated with two custom made stainless steel immersion heaters (38 in. × 0.315 in., 115 V, 1000 W) from Waage Electric, Inc. They were bent to form a circle at the bottom of the bath and extend up the sides of the battery jar. One was heated constantly through a Variac; the other was controlled by a Bayley Instrument Co. Model 124 precision temperature controller. An electric motor drove a one-piece, welded centrifugal stirrer at 1725 rpm.

Temperature measurements were made with chromel–alumel thermocouples which were positioned in a 0 °C reference bath, in the reactor, in a Pyrex tube in the bath, and next to a gas transfer line. Voltages were measured with a Leeds and Northrup Co. Model 8687 volt potentiometer. Over the course of a 10-h kinetic run, the reactor temperature was typically constant to ±0.2 °C.

The gaseous product mixture flowed from the reactor to a Valco Instruments no. CV6HTA six-port sampling valve located in the oven of a Hewlett-Packard F and M Scientific series 700 flame-ionization gas chromatograph. The valve allowed continuous passage of gas through both the flow system and the GC, while alternately opening either stream to a small sample loop. GC conditions were determined prior to the kinetic experiment. Peak areas were measured with a Varian CDS-11 digital integrator. Response factors were not measured.

Gas passed from the sample valve through a dry ice/acetone trap, where organic material was condensed. The contents of this trap could be removed from preparative isolation and further analysis. Next the helium was brought to ambient temperature by flowing through an equilibration tower, a long glass coil immersed in a Dewar flask of water. Finally, gas exited through a vertical soap film flow meter constructed from a 50-mL buret. The temperature of the gas was measured with a thermometer hung inside the buret. The time required for the soap film to be displaced by 10 mL of gas was measured with a digital timer.

General Experimental Procedure. The salt bath was equilibrated overnight at the desired reaction temperature. Between 30 and 100 mg of a compound was transferred to the appropriate sample vaporizer and immersed in a cold bath of the minimum temperature which would allow adequate detection. A flow rate of helium carrier gas was established between 0.05 and 0.33 mL/sec. Rates beyond this range proved difficult to control or measure. Intentional changes in flow rate were followed by 30 min of equilibration. Reaction temperatures and flow rates were chosen to allow 20–80% conversion of starting material. GC analysis of the gas stream was performed three to six times. From four to eight measurements of flow rate and the temperatures of the reactor, salt bath, and flow meter were made. This process was carried out at a total of four or five flow rates. Less than 5 mg of material was necessary for the determination of a rate constant.

Calculations. The observed rate constant for the conversion of A to products P via unimolecular processes may be extracted from the mass balance equation for an equilibrated flow system of volume *V*:

$$U^\circ[A]^\circ = U[A] + Vk_{obs}[A]$$

where U° is the entering flow rate, $[A]^\circ$ the entering reactant concen-

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[23] Warner, P.; LaRose, R. *Tetrahedron Lett.* **1972**, 2141. Wiberg, K. B.; Burgmaier, G. J. *J. Am. Chem. Soc.* **1972**, *94*, 7396.

[24] Bishop, R.; Landers, A. E. *Aust. J. Chem.* **1979**, *32*, 2675.

[25] Cooke, F.; Moerck, R.; Schwindeman, J.; Magnus, P. *J. Org. Chem.* **1980**, *45*, 1046.

tration, U the exiting flow rate, and [A] the exiting reactant concentration. U° rigorously equals U when $[A]^\circ = [A] + \sum[P_n]$, so the equation above may be rearranged to give

$$k_{obs} = \frac{U}{V}\frac{([A]^\circ - [A])}{[A]} = \frac{U}{V}\frac{\sum[P_n]}{[A]}$$

The flow rate measured is corrected to the flow rate in the reactor by the ratio of reactor temperature to flow meter temperature, T_2/T_1, so

$$k_{obs} = \frac{T_2}{T_1}\frac{U}{V}\frac{\sum[P_n]}{[A]}$$

The observed rate constant was calculated by least-squares treatment as the slope of the line formed by plotting the corrected flow-to-volume ratio against the product-to-reactant ratio. The theoretical point 0,0 was included in the data. Errors in k_{obs} were given as the percent error in the slope. Errors in ΔH and ΔS were calculated on the basis of an estimated 5% uncertainty in the rate constants.[26] The flow system could consistently duplicate rate constants to within 5%, known activation enthalpies to within 1 kcal/mol, and known activation entropies to within 2 cal mol^{-1} deg^{-1}.

Thermolysis of [3.2.1]Propellane (13). Approximately 100 mg of **13** was purified by preparative gas chromatography and collected in a tube fitted with a rubber septum, stopcock, and ground glass joint. The propellane was attached to a vacuum line, freeze degassed, and transferred to a sample holder with Teflon stopcocks. As an internal standard, 30 μL of *n*-nonane was degassed and added to the propellane. The evacuated bulb was opened to argon, attached to the flow system under a positive pressure of helium, and immersed in a dry ice/*m*-xylene bath. Purity of the sample was found to be ~99% by GC analysis of the gas stream at a bath temperature of 200 °C.

Reaction occurred in the vicinity of 360 °C. The product mixture was separated on a 10 ft × $^1/_8$ in. 10% SE-30 column: (6.8 min), major product (4.8 min), minor products (3.6 and 4.1 min), *n*-nonane (9.7 min). The major product was identical with authentic 1,3-dimethylenecyclohexane (**17**). In order to obtain reproducible results, it was necessary to install a Matheson model 6406 gas purifier in the carrier gas line to remove water and oxygen.

The two peaks of earliest retention time comprised ~2% of the reaction mixture. To determine their origin, authentic 1,3-dimethylenecyclohexane (**17**) was subjected to the reaction conditions. It produced a trace of material at 4.1 min, and about 1% each of peaks at 6.0, 6.5, and 6.9 min. It was found that less than 10% of the minor products of propellane thermolysis could be accounted for by reactions of **17**. Consequently, the major products were treated as being derived from **13** by unimolecular processes. Rate constants for the conversion of **13** to all products were determined at five temperatures over a 52-deg range. The rate constants were determined with use of the flow system equation employing the ratio of propellane to products. The observed rate constants were partitioned into rate constants for the formation of **17** and the formation of minor products. The ratio of the partitioned rate constants was taken to be the slope of the line formed by plotting the concentration of 1,3-dimethylenecyclohexane against that of the minor products, as they varied with flow rates. The rate constants are given in Table VI.

Thermolysis of [4.2.1]Propellane (12). The air-stable propellane **12** was purified by preparative gas chromatography (12 ft × $^1/_4$ in. 20% SE-30 on Chromosorb W). This material was found to be completely homogeneous in the 500-MHz proton NMR, GC/MS, and capillary GC (retention time 52 min). a 50-mg sample was placed in a 5-mL pear-shaped flask, attached to the flow system, and thermostated by a dry ice/*o*-xylene bath. At a bath temperature of 430 °C, gas chromatographic analysis (10 ft × $^1/_8$ in. 10% SE-30) indicated several products, of which 97% was found to be the diene, **16**. This distribution was unaffected by treatment of the reactor with triethylamine or ethylene. All products were considered to be derived from **12** by unimolecular processes. For the purposes of the kinetic experiments, the product mixture was better separated with a 7 ft × $^1/_8$ in. 3% $AgBF_4$/10% Carbowax 400 on Chromosorb P column, oven temperature 50 °C. The major product was isolated by preparative gas chromatography (4 ft × $^1/_4$ in. 3% $AgBF_4$/10% Carbowax 400 on Chromosorb P) of a pentane solution of the flow system's trap contents. Its identity as 1,3-dimethylenecycloheptane (**16**) was confirmed by its NMR and mass spectra. ^1H NMR ($CDCl_3$, 250 MHz: δ 1.6 (4 H, b quint), 2.17 (4 H, b m), 3.01 (2 H, b s), 4.75 (4 H, s). Mass spectrum, *m/e* (relative intensity): 122 (42), 107 (43), 94 (27), 93 (76), 91 (41), 79 (100), 77 (35), 67 (27), 53 (16), 39 (27).

The observed rate constants were partitioned into rate constants for the formation of **16** and the formation of minor products. The ratio of the partitioned rate constants were taken to be the slope of the line formed by plotting the concentration of 1,3-dimethylenecycloheptane against that of the minor products, as they varied with flow rates.

Thermolysis of Propellanes 7–10. Each of the propellanes were purified by preparative gas chromatography. Approximately 50 mg of the hydrocarbon was transferred to a 5-mL flask which was attached to the above apparatus. In each case the propellane was found to be homogeneous by GC at a temperature lower than that required for reaction, and at the temperatures used for the kinetic experiments, only the propellane and the derived diene were observed. The rate constants were derived as described above and are given in Table I.

Thermolysis of [3.3.2]Propellane (11). The low reactivity of **11** made it impractical to carry out kinetic studies in the flow system. Static pyrolyses were carried out in Pyrex tubes sealed under diffusion pump pressure. The tubes were then clamped to steel rods and held below the surface of the flow system salt bath. After a tube was removed from the bath, it was allowed to cool to room temperature. The contents were condensed by immersion of the bottom of the tube in liquid nitrogen. The neck was scored, broken, and plugged with a rubber septum, and the tube was warmed to room temperature. The contents were washed out with a small amount (~0.5 mL) of pentane, and this solution was used for gas chromatographic analysis.

In this manner, 7 mg of **11** in each of four 8-mL tubes was pyrolyzed at 450 °C for 4, 7, 10, and 12 h. At the higher conversions achieved, a complex reaction mixture was produced. This result was consistently reproduced when base-washed and silylated tubes, as well as untreated tubes, were used. Tubes for all further pyrolyses were washed with chromic acid cleaning solution, deionized water, concentrated ammonium hydroxide, and deionized water, dried, silylated with *N*,*O*-bis(trimethylsilyl)acetamide, washed with CCl_4, and dried.

Identification of Products of [3.2.2]Propellane Thermolysis. **11** (300 mg) in a 300-mL tube was pyrolyzed for 11 h at 450 °C. The products were washed out in ~2 mL of pentane. This solution was separated into eight fractions on a 12 foot × $^1/_4$ in. 20% SE-30 on Chromosorb W column, oven temperature 90 °C. The components of each fraction were identified by their NMR and mass spectra: fraction 1, benzene; fraction 2, toluene; fraction 3, *m*- and *p*-xylene, ethylbenzene; fraction 4, *o*-xylene; fraction 5, bicyclo[3.3.0]oct-1(5)-ene; fraction 6, 1,3,5-trimethylbenzene, *m*- and *p*-ethyltoluene; fraction 7, [3.3.2]propellane; fraction 8, indan.

No 1,5-dimethylenecyclooctane (**15**) was detected in this way. In another experiment, 7 mg of **11** in each of two tubes was pyrolyzed for 1 and 4 h at 450 °C. Careful search of the product mixture by GC/MS also indicated that **15** was absent.

Thermolysis of Bicyclo[3.3.0]oct-1(5)-ene (14). A 7-mg sample of **14** was pyrolyzed for 8 h at 450 °C. Some **14** remained after this time. The GC trace for the products of this pyrolysis was remarkably similar to that of **11**. A 30-mL tube containing 25 mg of **14** was pyrolyzed for 12 h at 450 °C. Products were washed out with 1 mL of pentane and separated into six fractions by employing the GC conditions used for **11**. The components of each fraction were identified by their NMR spectra: fraction 1, benzene; fraction 2, toluene; fraction 3, *m*- and *p*-xylene, ethylbenzene; fraction 4, *o*-xylene; fraction 5: bicyclo[3.3.0]octene (**14**); fraction 6, indan.

Thermolysis of 1,5-Dimethylenecyclooctane (15). In a similar fashion, 100 mg of **15** was pyrolyzed for 8 h at 450 °C. All starting material was consumed. The GC trace for the products of this pyrolysis was remarkably similar to that of **14**; together, they accounted for all peaks seen in the pyrolysis of **11**. The pentane solution of the products of **14** was separated into six fractions by GC and analyzed by NMR: fraction 1, benzene; fraction 2, toluene; fraction 3, *m*- and *p*-xylene; fraction 4, *o*-xylene; fraction 5, *m*- and *p*-ethyltoluene, 1,3,5-trimethylbenzene; fraction 6, 1,2,3-trimethylbenzene.

Four tubes each containing 7 mg of **15** were pyrolyzed at 450 °C for 0.5, 1.5, 3, and 6 h. Analysis by GC/MS revealed that all starting material had been consumed after 0.5 h. A new, intermediate peak with retention time of the ethyltoluenes and mass spectrum similar to starting material was present at 0.5 h and had disappeared by 6 h. This peak was identified as [3.3.2]propellane, having mass spectrum and retention time identical with authentic material under a variety of GC conditions.

Kinetics of Thermolysis of 1,5-Dimethylenecyclooctane (15). **15** (100 mg) and 30 μL of *n*-undecane as internal standard were placed in a 5-mL pear-shaped flask and attached to the flow system. The temperature of the sample was maintained at 0 °C. Observed rate constants for the conversion of starting material to all products were obtained at 415.1, 450.1, and 470.2 °C. At each temperature, five flow rates were established and sampled four times for analysis, except at 470.2 °C where four flow rates were used. Over the course of a kinetic run, the percentage of internal standard in the gas stream remained constant. Least-squares

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[26] Petersen, R. C.; Markgraf, J. H.; Ross, S. D. *J. Am. Chem. Soc.* **1961**, *83*, 3819.

J. Am. Chem. Soc. **1990**, *112*, 5861–5865

treatment of the data provided the rate constants in Table III.

The observed rate constants were partitioned into rate constants for the formation of [3.3.2]propellane (**11**), k_{prop}, and the formation of the remaining aromatic products, k_{arom}. The ratio of these rate constants at each temperature was calculated by least-squares treatment as the slope of the line formed by plotting the concentration of **11** against that of aromatic products, as they varied with flow rates. The calculated, partitioned rate constants are given in Table III.

Gas-Phase Static Kinetics of [3.3.2]Propellane (11). A nearly saturated solution of **11** in *n*-octane as internal standard was prepared. Observed rate constants based on disappearance of starting material relative to internal standard were obtained at 430.2, 450.2, and 469.9 °C. At each temperature, four tubes containing about 10 mg of solution was pyrolyzed for four different lengths of time. Pentane solutions of the products were prepared, and their composition determined by GC analysis (10 ft × $^1/_8$ in. 10% SE-30, oven temperature 80 °C). Four or five injections were made of each time. Plots of natural log of concentration of **11** vs time were linear, and the first-order rate constants were calculated by least-squares treatment of the data.

Gas-Phase Static Kinetics of Bicyclo[3.3.0]oct-1(5)-ene (14). To approximately 60 mg of **14** was added 20 μL of *n*-octane as internal standard. Four samples were pyrolyzed at 450.4 °C for 2, 4, 6, and 8.5 h. Four injections for each tube were made. A plot of natural log of the concentration of **14** vs time was linear and gave a rate constant of $5.13 \pm 0.15 \times 10^{-5}$ sec^{-1}.

Determination of Rate Constants for [3.3.2]Propellane (11) Pyrolysis. Rate constants at 450 °C for the formation of **14** and **15** from **11** were estimated by Runge–Kutta integration of the rate equations. The kinetic scheme used for the fit is shown in Scheme III.

Loss of volatile mass was observed in the pyrolyses of **11**, **14**, and, when carried out in sealed tubes, **15**. The observed rate constant for the disappearance of **11** was partitioned into rate constants for product formation and polymerization, k_{prod} and k_{poly}, by a Runge–Kutta calculation. The best fit for the observed product formation, while maintaining $k_{\text{prod}} + k_{\text{poly}} = k_{\text{obs}}$, occurred with $k_{\text{prod}} = 1.32 \times 10^{-5}$ and $k_{\text{poly}} = 3.81 \times 10^{-5}$. k_2 and k_7 were fixed at these values for the tricyclo[3.3.2.0^{1,5}]decane calculation. Considerable loss of volatile mass for **15** was observed in sealed tubes, but due to the speed of this reaction at 450 °C, no attempt was made to quantify it. k_6 was included as a variable in the calculation, while k_4 and k_5 were fixed at the experimentally determined values. Separate static pyrolyses of toluene, ethylbenzene, the xylenes, and indan showed the aromatic products were stable to the reaction conditions.

The concentrations of **11**, **14**, and **15** and aromatic products as a function of time were calculated by integrating the rate equations and varying k_1, k_3, and k_6. Care was taken to match the experimental half-life of **11**, the time and value of the maximum concentration of **14**, and overall volatile mass.

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Integer-Spin EPR Studies of the Fully Reduced Methane Monooxygenase Hydroxylase Component

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Abstract: The hydroxylase component of methane monooxygenase contains a binuclear iron cluster in which the iron appears to be oxo or R-oxo bridged. Mössbauer and EPR studies have demonstrated antiferromagnetic coupling for the [Fe(III)Fe(III)] and [Fe(II)Fe(III)] states of the cluster. In the [Fe(II)Fe(II)] form the cluster exhibits an intense X-band EPR signal with zero crossing near $g = 16$, which originates from an electronic system with integer spin. We have studied this signal from 2 to 20 K using a cavity that allows modes where the microwave magnetic field fluctuates either parallel or perpendicular to the static field. We have analyzed the line shapes and the temperature dependence of the spectra with a spin Hamiltonian containing zero-field splitting (D, E) and exchange (J) terms for a pair of $S = 2$ spins. Two coupling schemes, both involving *ferromagnetic* coupling, are compatible with the data. In the scheme for strong coupling ($|J| \gg D$ and $D = 1.2$ cm^{-1}), the $g = 16$ signal results from $\Delta M = \pm 1$ transitions between the two lowest levels of an $S = 4$ multiplet. In the scheme for weak coupling ($J = -0.75$ cm^{-1} and $D_1 = D_2 = -5$ cm^{-1}), the resonance is assigned to $\Delta m_i = 0$ transitions. Simulation of the observed spectra has allowed quantitation of the $g = 16$ signal. This signal represents the majority of the iron in the hydroxylase regardless of the spin-coupling model assumed. Our results demonstrate that integer spin systems with large zero-field splittings are amenable to reliable quantitative analysis.

Soluble methane monooxygenase (EC 1.14.13.25) isolated from *Methylosinus trichosporium* OB3b is a three-component enzyme composed of a reductase (40 kDa, containing one FAD and one [2Fe 2S] cluster), component B (16 kDa, no cofactors or metal ions), and hydroxylase (245 kDa, containing four non-heme iron atoms).[1] The function of the enzyme system in vivo is to catalyze the O_2– and NADH-dependent oxidation of methane to methanol.[2] This is the first step in the catalytic pathway utilized by methanotrophic bacteria to provide carbon and energy for growth. The enzyme system adventitiously catalyzes the oxidation of many other saturated, unsaturated, and cyclic hydrocarbons, some at rates comparable to that of methane turnover.[3] While all three protein components are required for NADH-dependent substrate oxidation, we have recently shown that the hydroxylase alone will

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