Synthesis and Thermal Decomposition of *cis*-3,4,5,6-Tetrahydropyridazine-*3,4*-d_2. Relative Rates of Rotation, Cleavage, and Closure for Tetramethylene[1,2]

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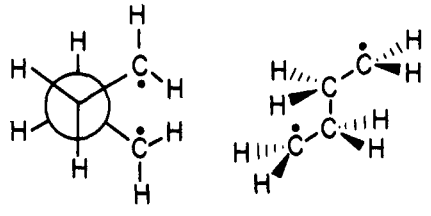
Abstract: The stereospecific syntheses of *cis*-3,4,5,6-tetrahydropyridazine-*3,4*-d_2 (**6**) and *cis*- and *trans*-cyclobutane-*1,2*-d_2 are reported. The thermal decomposition of *cis*-3,4,5,6-tetrahydropyridazine-*3,4*-d_2 (**6**) (gas phase, 439 °C) affords 67.1 ± 0.9% *cis*-ethylene-*1,2*-d_2, 16.1 ± 0.8% *trans*-ethylene-*1,2*-d_2, 9.4 ± 0.4% *cis*-cyclobutane-*1,2*-d_2, and 7.4 ± 0.4% *trans*-cyclobutane-*1,2*-d_2. The relative rates of rotation, cleavage, and closure for this 1,2-diazene generated tetramethylene-d_2 are k(cleavage)/k(closure) = 2.2 ± 0.2 and k(rotation)/k(closure) = 12 ± 3. An extra stereospecific cleavage component (46%) superimposed on the 1,4-biradical pathway (54%) from the parent tetrahydropyridazine was found, similar to that observed in the 3,4-dimethyl-3,4,5,6-tetrahydropyridazine thermal reactions. Finally, the experimental data for the parent 1,4 biradical, tetramethylene, are compared to calculated values in the literature.

Introduction

The only simple 1,4 biradical described by theorists[5] to date is tetramethylene (**1**). Hoffmann's extended Hückel (EH)



1 *gauche* 2 *trans*

calculation for the energy surface between cyclobutane and two molecules of ethylene revealed a rather flat hypersurface.[5b] Segal concluded from an ab initio calculation (SCF at STO-3G level) that there are two well-defined potential energy minima for the gauche and trans conformations of tetramethylene. The barriers ($\Delta H^{\ddagger}$) to cleavage and closure for *gauche*-tetramethylene are 3.6 and ≥2.0 kcal mol^{-1}, respectively.[5f] Benson's thermochemical estimates[6] predict similar differences between the heats of formation of the transition states for cleavage and closure from tetramethylene but a deeper well (Figure 1). Despite the fact that substantial experimental work now exists on 1,4-biradical behavior,[7-12] the relative rates of rotation, cleavage, and closure of the parent system are unknown.

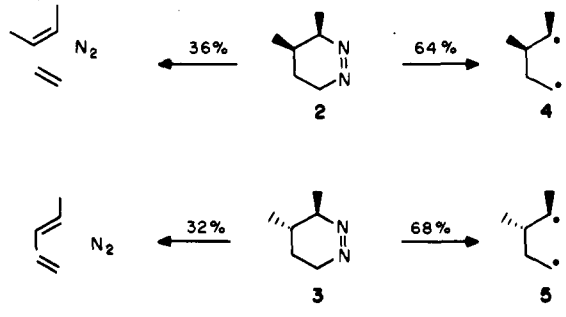
Substituted tetrahydropyridazines have been shown to be excellent sources for the thermal generation of stereospecifically labeled 1,4 biradicals.[9] Recently, the synthesis and study of the product ratios from the thermal decomposition of *cis*- and *trans*-3,4-dimethyl-3,4,5,6-tetrahydropyridazines (**2** and **3**) allowed the experimental determination of the relative rates of rotation, cleavage, and closure for two isomeric 1,4 biradicals with secondary radical centers, 3-methyl-1,4-pentanediyl (**4** and **5**).[9d,e] These substituted six-membered cyclic 1,2-diazenes were shown to undergo a stereospecific fragmentation reaction to olefin (36–32%) in competition with the generation of a 1,4-biradical intermediate(s) (64–68%) which was *identical in behavior* with the intermediate(s) from the pyrolyses of 1,2-dimethylcyclobutanes.[7b]

Recently, Scacchi, Richards, and Bach studied the thermal cycloaddition of ethylene to *cis*- and *trans*-2-butenes (420°C at 12 atm).[8c] Their results show that these cycloaddition reactions are the reverse of the decomposition reactions of 1,2-dimethylcyclobutanes. From these experiments, the relative rates of rotation, cleavage, and closure for 3-methyl-1,4-pentanediyl were determined. Agreement of the relative rates from the cycloaddition route with the 1,2-diazene route is quite good (Table I).[9e,13]

Three different experiments (cyclobutane, 1,2-diazene, [2 + 2] cycloaddition) which characterize the substituted 1,4 biradical, 3-methyl-1,4-pentanediyl, are internally consistent. With the establishment of six-membered cyclic 1,2-diazenes as precursors for the thermal generation of 1,4 biradicals we will apply this method to the parent tetramethylene problem to afford a direct comparison of experiment and theory.

We report the stereospecific synthesis and thermal decomposition in the gas phase (439°C) of *cis*-3,4,5,6-tetrahydropyridazine-*3,4*-d_2 (**6**). In addition, we describe the stereospecific syntheses of *cis*- and *trans*-cyclobutane-*1,2*-d_2 (**7** and **8**).[14] Analyses of the cis/trans stereochemistry in the products from the decomposition of **6** allow an experimental determination of the relative rates of rotation, cleavage, and closure for tetramethylene (**1**). Moreover, a stereospecific cleavage reaction to ethylene and nitrogen in competition with a 1,4-biradical pathway from the thermal decomposition of tetrahydropyridazine becomes evident.

Scheme I



Results and Discussion

Synthesis and Thermal Decomposition of *cis*-3,4,5,6-Tetrahydropyridazine-*3,4*-d_2 (6). The stereospecific synthesis of *cis*-3,4,5,6-tetrahydropyridazine-*3,4*-d_2 (**6**) was accomplished as shown in Scheme II. Successive treatment of 3-butyn-1-ol (**9**) with acetyl chloride, dicyclohexylborane-d_1, and acetic acid-*O*-*d* afforded *cis*-3-buten-1-yl-*3,4*-d_2 acetate (**10**). Conversion of this *cis*-*3,4*-d_2 alkene (**10**) to the corresponding epoxide **11** allowed NMR analysis of the deuterium content of each olefinic position and confirmed the *cis*-*3,4*-d_2 assign-

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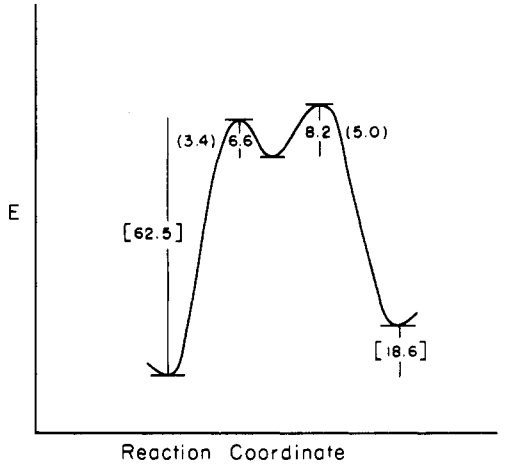
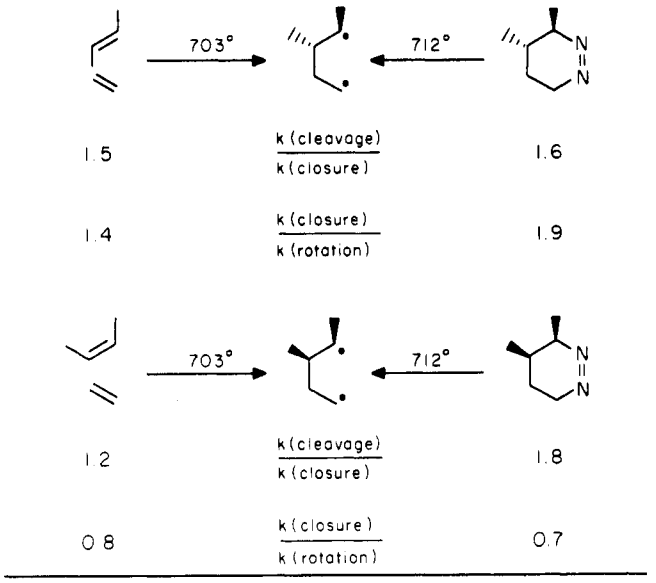
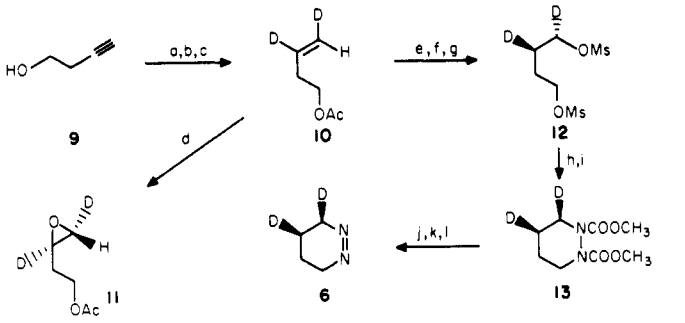


Figure 1. Hypothetical potential energy profile of cyclobutane to ethylene. Energies are in kcal mol^{-1} Experimental values are in brackets. The calculated barriers (E_a) for closure and cleavage of tetramethylene are 3.4 and 5.0 from Segal[5f] and 6.6 and 8.2 from Benson[6] at 723 K.

Table I



Scheme II



a) CH_3COCl b) $(C_6H_{10}D)_2BD$ c) CH_3COOD d) mCPBA e) BH_3 f) H_2O_2 g) MsCl h) $(HNCOOCH_3)_2/NaH$ i) NaH j) $KOH/H_2O/N_2$ k) HCl/N_2 l) O_2/C_6D_6

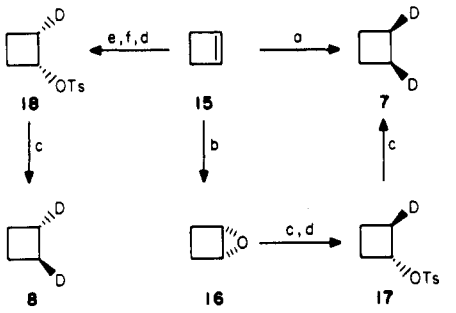
ment of **10** (see Experimental Section). Hydroboration of *cis*-1-butenyl-*3,4-d*$_2$ acetate (**10**), oxidative workup, and reaction with methanesulfonyl chloride afforded *threo*-1,4-butanediyl-*1,2-d*$_2$ dimethanesulfonate (**12**). Reaction of **12** with dimethyl hydrazine-1,2-dicarboxylate and sodium hydride afforded dimethyl *cis*-tetrahydropyridazine-1,2-dicarboxylate-*3,4-d*$_2$ (**13**, 93% d_2, 7% d_1).[15] Hydrolysis of the diurethane **13**, followed by decarboxylation, was carried out under an inert

Table II. Analysis of Ethylene/Cyclobutane Ratios from the Pyrolysis of **6**

reactant	conditions	% yields[a] 2 ethylenes	% yields[a] cyclobutane
6-d_2	*b*	83.5 ± 0.5	16.8 ± 0.5
6-d_0	*b*	84.4 ± 0.5	15.6 ± 0.5
6-d_0	*c*	84.6 ± 1.0	15.4 ± 1.0

[a] Percent yield is the corrected ratio of cleavage pathway (2 mol of ethylene) to closure pathway (1 mol of cyclobutane). Correction for the FID response factors for ethylene to cyclobutane, in addition to the molecular-weight difference, was (1.07 ± 0.02):1.00. Ethylene and cyclobutane accounted for 99.2% of the volatile hydrocarbon yield. Ca. 0.4% of propylene and 0.4% of 1-butene were found by VPC analysis (10 ft × 1/8 in. SE-30; flame ionization detector). Errors are standard deviations for three pyrolyses. [b] Chamber pyrolysis (5 s at 439 ± 5 °C, pressure ~25 mm). [c] Chamber pyrolysis (30 s at 306 ± 5 °C, pressure ~17 mm).

Scheme III



a) N_2D_2 b) mCPBA c) $LiB(C_2H_5)_3D$ d) TsCl e) BD_3 f) H_2O_2/OH^-

atmosphere (N_2) using thoroughly degassed solvents. The *cis*-hydrazine-*3,4-d*$_2$ product **14** was distilled on a vacuum line (10^{-4} Torr). Oxidation of the pure hydrazine **14** in benzene-d_6 to the corresponding *cis-3,4-d*$_2$ azo compound **6** was accomplished by treatment with oxygen and monitored by NMR. This 3,4,5,6-tetrahydropyridazine is an extremely sensitive compound and suffers facile irreversible 1,2-diazene to hydrazone tautomerization in the presence of trace amounts of acid and base. For pyrolyses, this solution was injected into an evacuated Pyrex chamber (preheated to 439 °C) and the products were collected in a trap at −196 °C. The ratio of the two ethylenes/cyclobutane was 83.2/16.8 from analytical VPC analysis (Table II). These products were separated by preparative VPC for infrared analyses of their respective *cis-/trans-d*$_2$ ratios.[16]

Syntheses and Analysis of *cis*- and *trans*-Cyclobutane-*1,2-d*$_2$ (7 and 8). The syntheses of *cis*- and *trans*-cyclobutane-*1,2-d*$_2$ (**7** and **8**) are shown in Scheme III. Treatment of cyclobutene with diimide-d_2 afforded *cis*-cyclobutane-*1,2-d*$_2$ (**7**, >98% cis). An alternate stereospecific route involved successive treatment of cyclobutene with *m*-chloroperbenzoic acid, lithium triethylborodeuteride, tosyl chloride, and lithium triethylborodeuteride (>98% cis). Similarly, successive treatment of cyclobutene with borane-d_3, hydrogen peroxide and base, tosyl chloride, and lithium triethylborodeuteride afforded *trans*-cyclobutane-*1,2-d*$_2$ (**8**, >98% trans).

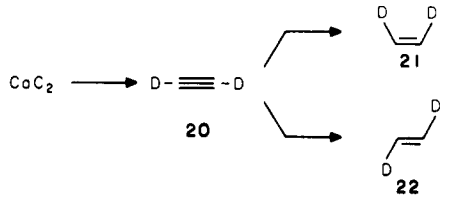
The ratio of *cis-/trans*-cyclobutane-*1,2-d*$_2$ products from the pyrolysis of **6** was determined by measuring the relative ratio of the 1307- (*cis-1,2-d*$_2$) and 1294-cm^{-1} (*trans-1,2-d*$_2$) bands in the infrared[16] and comparing these with those of authentic mixtures. The *cis*-tetrahydropyridazine-*3,4-d*$_2$ (**6**) contains 93% d_2 and 7% d_1 from mass-spectral analysis. Since cyclobutane-d_1 has a band at 1307 cm^{-1} calibration mixtures contained 93% *cis*- and *trans*-cyclobutane-*1,2-d*$_2$ and 7% cyclobutane-d_1. The observed *cis-/trans*-cyclobutane-*1,2-d*$_2$ ratio

Table III. Analysis of Cyclobutane-*1,2-d_2* Products from the Pyrolysis of **6**

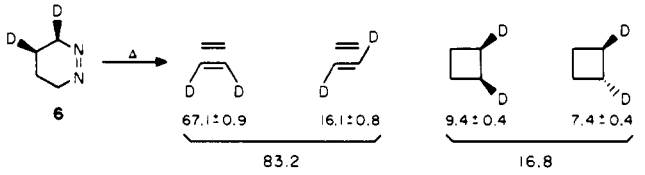
cis-/trans-cyclobutane-*1,2-d_2*[a]	IR peak height ratios (1307/1294 cm^{-1})
1.22 ± 0.01[b]	1.45 ± 0.10
1.01 ± 0.02[b]	1.24 ± 0.06
0.83 ± 0.04[b]	1.06 ± 0.05
pyrolysis of **6**[c]	1.51 ± 0.06[d]

[a] Authentic mixtures contain 92.5 ± 1.0% cyclobutane-d_2 and 7.5 ± 1% cyclobutane-d_1 by ICR.[23] The *cis-* and *trans*-cyclobutane-*1,2-d_2* authentic compounds are each >98% stereochemically pure by IR analysis.[30] [b] These ratios are determined by a MKS pressure gauge. [c] Chamber pyrolysis (5 s at 439 ± 5 °C, pressure ~300 mm). Contains 92.5% d_2 and 7.5% d_1 by ICR.[23] [d] Peak ratio is the average of four spectra. The error is the standard deviation.

Scheme IV



Scheme V



from the pyrolysis of **6** obtained by comparison with authentic mixtures is 1.27 ± 0.06, which corresponds to a 56/44 ratio (Table III).

Synthesis and Analysis of *cis-* and *trans*-Ethylene-*1,2-d_2* (21 and 22). The syntheses of *cis-* and *trans*-ethylene-*1,2-d_2* (**21** and **22**) were carried out using the methods of Nicholas and Carroll (Scheme IV).[17]

The *cis-/trans*-ethylene-*1,2-d_2* ratios from the pyrolysis of **6** can be obtained by measuring the 842- (*cis-1,2-d_2*) and the 724-cm^{-1} (*trans-1,2-d_2*) bands in the infrared[16] and comparing these with those of the authentic mixture (Table IV).

From the pyrolysis of **6** the observed infrared peak height ratio (842/724 cm^{-1}) is 4.9 ± 0.4. By comparison with the authentic mixtures we find that the *cis-/trans*-ethylene-*1,2-d_2* ratio is 4.15. Using the measured relative extinction coefficients of the 842- and 724-cm^{-1} peaks, the *cis-/trans*-ethylene-*1,2-d_2* ratio from the pyrolysis of **6** can be obtained directly, 4.9/1.18 = 4.15, which corresponds to an 80.6/19.4 cis/trans ratio.

A summary of the stereochemical results from the thermal decomposition of *cis*-3,4,5,6-tetrahydropyridazine-*3,4-d_2* (**6**) is shown in Scheme V.

Kinetic Scheme. Examination of the data reveals that the ratio of *cis*-ethylene-*1,2-d_2*/*cis*-cyclobutane-*1,2-d_2* is higher than the ratio of *trans*-ethylene-*1,2-d_2*/*trans*-cyclobutane-*1,2-d_2*. Therefore, there exists an extra component of stereospecific cleavage of retained stereochemistry from the 1,2-diazene **6** thermal decomposition.

By analogy to the previously described decomposition pathways for *cis-* and *trans*-3,4-dimethyltetrahydropyridazines[9d,e] consider the kinetic Scheme VI.

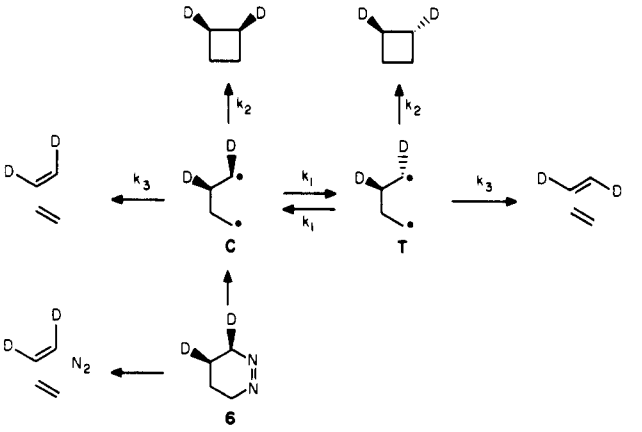
The ratio of k_2(closure)/k_3(cleavage) can be obtained directly. From **6** the ratio of *crossover* products, *trans*-cyclobutane-*1,2-d_2*:*trans*-ethylene-*1,2-d_2*, is equal to the ratio of the rates for closure and cleavage in the unimolecular de-

Table IV. Analysis of Ethylene-*1,2-d_2* Products from the Pyrolysis of **6**

cis-/trans-ethylene-*1,2-d_2*	IR peak height ratio[a] (842/724 cm^{-1})
4.88[b]	5.7
3.76[b]	4.5
2.85[b]	3.7
1:1[c]	1.18
pyrolysis of **6**[d]	4.9 ± 0.4[e]

[a] Infrared mode of operation: absorbance.[16] [b] These authentic mixture ratios are determined by a MKS pressure gauge. Stereochemical purity of each isomer is >99%. The isotopic purities were determined by ICR to ±1%.[23] [c] The relative extinction coefficient of the 842- (*cis-d_2*) and 724-cm^{-1} (*trans-d_2*) bands was determined by comparing the relative extinction coefficient of the 842- and 806-cm^{-1} (ethylene-d_1) bands in isomerically pure *cis*-ethylene-d_2 contaminated with ethylene-d_1 to the relative extinction coefficient of the 724- and 806-cm^{-1} bands in isomerically pure *trans*-ethylene-d_2 contaminated with ethylene-d_1. The ratio of d_2 to d_1 compound in each sample was determined by ICR.[23] [d] Chamber pyrolysis (5 s at 439 ± 5 °C, pressure ~300 mm). [e] Standard deviation of four measurements from two pyrolyses.

Scheme VI



composition of biradical T. From Scheme V, *trans*-cyclobutane-*1,2-d_2*/*trans*-ethylene-*1,2-d_2* = 7.4/16.1 = 0.46 = k_2(closure)/k_3(cleavage). This k_2(closure)/k_3(cleavage) ratio (R_1) and the ratio of *cis-/trans*-cyclobutane-*1,2-d_2* (R_2) allow a determination of k_2(closure)/k_1(rotation) ratio from a simple steady-state analysis of the proposed diradical scheme. Using steady-state approximations:

$$d(T)/dt = k_1(C) - (k_2 + k_3 + k_1)(T) = 0$$

$$(C)/(T) = (k_2 + k_3 + k_1)/k_1$$

$$R_2 = k_2(C)/k_2(T) = k_2/k_1 + k_3/k_1 + 1$$

$$R_2\,(k_2/k_3) = (k_2/k_1)(k_2/k_3) + (k_3/k_1)(k_2/k_3) + k_2/k_3$$

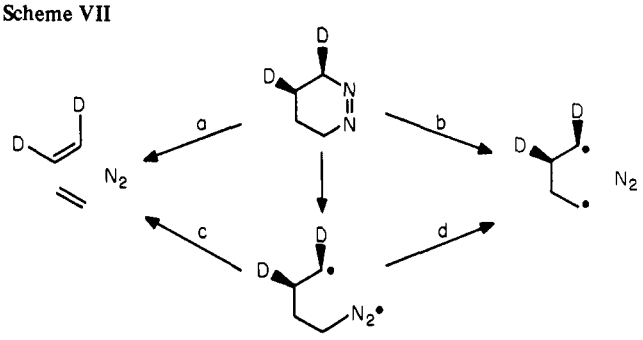
$$R_2R_1 = (k_2/k_1)R_1 + (k_2/k_1) + R_1$$

$$k_2/k_1 = (R_2R_1 - R_1)/(R_1 + 1)$$

From Scheme V, $R_1 = k_2/k_3 = 0.46$ and R_2 = *cis-/trans*-cyclobutane-*1,2-d_2* = 1.27. Substituting R_1 and R_2 from the pyrolysis data, we find k_2(closure)/k_1(rotation) = 0.085. The relative rates of rotation, cleavage, and closure for tetramethylene-d_2 are k_3(cleavage)/k_2(closure) = 2.2 ± 0.2 and k_1(rotation)/k_2(closure) = 12 ± 3.

The amount of stereospecific fragmentation to ethylene and nitrogen from tetrahydropyridazine can be calculated. From Scheme V, the experimental ratio of *cis*-ethylene-*1,2-d_2*/*cis*-cyclobutane-*1,2-d_2* is 67.1:9.4. From k_3/k_2, the amount of *cis*-ethylene-*1,2-d_2* expected from 1,4 biradical C should be 2.2 times the *cis*-cyclobutane-*1,2-d_2* observed (9.4 × 2.2

Scheme VII



= 20.7%). Therefore the *extra stereospecific component* to *cis*-ethylene-*1,2-d*$_2$ is 67.0 − 20.7 = 46.3%. This establishes another example of an extra stereospecific cleavage component superimposed on the 1,4-biradical pathway from a six-membered cyclic 1,2-diazene decomposition.[9d,e] This may be the result of a [2 + 2 + 2] cycloreversion pathway[18] (path a) which is nearly equienergetic with a 1,4-biradical pathway[18] (path b) or the decomposition of a diazenyl biradical that does not lose stereochemical integrity (path c and d) (Scheme VII) or some combination of all four.

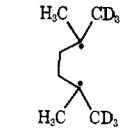
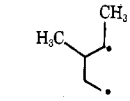
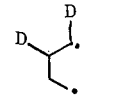
A critical assumption of the analysis is that, if the decomposition of **6** does proceed by a stepwise decomposition to an intermediate diazenyl biradical, then this diazenyl biradical does not lose stereochemical integrity before decomposition to tetramethylene. This assumption appears to be valid in the *substituted* 1,2-diazene fragmentation study, since *identity* with the intermediate from the pyrolysis of 1,2-dimethylcyclobutane was shown.[9d,e] However, it is not known in this case, and we must await an independent check of identity from another precursor, perhaps a study of cyclobutane-*d*$_4$ thermal reactions.[19]

By estimating the structures of the transition states for the cleavage and closure of tetramethylene, Benson used thermochemical estimates[6] to predict entropies of activation for the two processes. Benson estimates that A(cleavage) = $10^{13.07}$ and A(closure) = $10^{12.30}$ from parent tetramethylene. From the k(cleavage)/k(closure) ratio reported here (2.2) one calculates that E_a(cleavage) > E_a(closure) by 1.4 kcal mol^{-1} at 712 K.

The depth of the energy well for tetramethylene is not known. Experimental determination of this value requires the measurement of the absolute rate of one of the 1,4-biradical processes involved, i.e., rotation, cleavage, or closure. Moreover, the rotational barriers even in simple monoradicals are not well known. Experimental measurements of the activation energy for rotation of primary radicals have been reported,[21] and the values range from 0.4 to 3.1 kcal mol^{-1} depending on the method of analysis. Only when reliable Arrhenius parameters for rotational barriers in both radicals and 1,4 biradicals are made available can issues regarding the importance of through-bond and through-space interactions in tetramethylene be resolved.

Factors affecting relative rotational propensities[7e,g,22] of variously substituted biradicals have been of interest but complicated by the scarcity of examples of biradicals *generated under similar conditions*. A comparison of primary, secondary, and tertiary substituted presumed 1,4 biradicals generated under similar conditions is presented in Table V. If the cleavage rate is assumed to be constant, a significant slowing of the rotation rate is observed as one proceeds from primary to tertiary radical centers. One finds that as substitution at the radical center increases (primary → secondary → tertiary) the rotation rate in 1,4 biradicals decreases by more than two orders of magnitude.

Table V. Comparison of the Effect of Substitution on k(rotation)/k(cleavage) for 1,4 Biradicals

			k(rotation)/k(cleavage)	conditions	ref
	tertiary	*dl*	0.02	425/gas	7e
	secondary	*cis*-	0.79	439/gas	9d,e
		trans-	0.33	439/gas	
	primary		5.5	439/gas	this work

3,4,5,6-tetrahydropyridazine-*3,4-d*$_2$, we have measured the relative rates of rotation, cleavage, and closure for tetramethylene-*d*$_2$, k(cleavage)/k(closure) = 2.2 ± 0.2 and k(rotation)/k(closure) = 12 ± 3, and separated a stereospecific cleavage component (46%) in the parent six-membered cyclic 1,2-diazene decomposition. What is needed on both the experimental and theoretical level is more accurate information on the Arrhenius parameters for rotation in both radicals and biradicals. In addition, with regard to the work presented here, a comparison of the relative rates of rotation, cleavage, and closure for tetramethylene from another precursor, e.g., cyclobutane-*d*$_4$, will be of interest.

Summary

In summary, from the thermal decomposition of *cis*-

Experimental Section

Melting points were obtained using a Thomas-Hoover capilliary melting point apparatus and are uncorrected. Elemental analyses were performed by the Caltech Analytical Facility and Spang Microanalytical Laboratory, Ann Arbor, Mich. Infrared spectra (IR) were recorded on a Perkin-Elmer Model 257 infrared spectrophotometer except for gaseous samples, which were recorded on a Beckman IR 42-10 instrument. For quantitative analyses, IR spectra were recorded on a Perkin-Elmer Model 180 infrared spectrophotometer.[16] Nuclear magnetic resonance (NMR) data were recorded on a Varian EM390 NMR spectrometer. Chemical shifts are given as parts per million (ppm) downfield from Me_4Si in δ units and coupling constants in cycles per second (Hz). NMR data are reported in this order: chemical shift; multiplicity, s = singlet, d = doublet, t = triplet, m = multiplet; number of protons; coupling constants; assignment. Electronic spectra were recorded on a Beckman Model 25 spectrophotometer. Mass spectra were recorded on a Du Pont 21-492B mass spectrometer except for ethylene and cyclobutane samples, which were recorded on an ion cyclotron resonance spectrometer (ICR).[23] For analytical vapor-phase chromatography (VPC), a Hewlett-Packard 5700 A gas chromatograph equipped with a flame ionization detector and nitrogen carrier gas was used. The 0.125-in. packed stainless steel columns used in this instrument are listed in Table VI. Quantitative VPC analysis was accomplished using a Hewlett-Packard 3370A electronic digital integrator. For preparative VPC, a Varian Aerograph Model 920 instrument, equipped with a thermal conductivity detector and helium carrier gas, was used. The 0.375-in. packed aluminum columns used are listed in Table VI. Gas samples were separated and collected on a Varian Aerograph Model 90-P instrument equipped with a gas inlet and collection system.

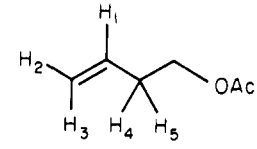
Diglyme and tetrahydrofuran were distilled from sodium metal. Pyridine was distilled from sodium hydroxide and stored over barium oxide.

Dimethyl 3,4,5,6-Tetrahydropyridazine-1,2-dicarboxylate (13-*d*$_0$). A solution of 6 g (30 mmol) of dimethyl 3,6-dihydropyridazine-1,2-dicarboxylate, obtained from Diels-Alder reaction of 1,3-butadiene and dimethyl azodicarboxylate, in 50 mL of ethanol was hydrogenated over 0.1 g of platinum oxide. The solution was filtered, concentrated, and distilled, yielding 5.5 g (90%) of the saturated diurethane **13**-*d*$_0$: bp 90–95 °C (0.3 mm); mp 40.5–41.5 °C; IR (CCl_4) 1710 cm^{-1} (C=O); NMR ($CDCl_3$) δ 1.5–1.9 (m, 4), 2.7–3.2 (m, 2), 3.75 (s, 6), 4.0–4.4 (m, 2); mass spectrum *m/e* 202.

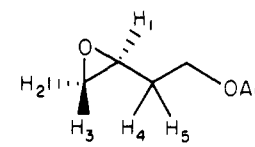
Table VI. VPC Columns

designation	description
SE-30	20 ft × 0.375 in., 25% SE-30 on 100/120 Chromosorb P
Carbowax 20M	10 ft × 0.375 in., 25% Carbowax 20M on 60/80 Chromosorb W
$\beta\beta'$	10 ft × 0.375 in., 25% β,β'-oxodipropionitrile on 60/80 Chromosorb P
FFAP	10 ft × 0.375 in., 25% FFAP on 60/80 Chromosorb W
SF-96	5 ft × 0.375 in., 10% SF-96 on 60/80 Chromosorb W
Pennwalt	5 ft × 0.25 in., glass, Pennwalt 223 amine packing (Applied Sciences Laboratories, Inc.)
SE-30	10 ft × 0.125 in., 30% SE-30 on 100/120 Chromosorb P
Poropak N	6 ft × 0.125 in., Poropak N, 100/120 mesh

Table VII. NMR Integrations of **10** and **11** for the Determination of the Stereochemical and Isomeric Purity of **10**



10



11

compd	H_1	$H_2 + H_3$	$H_4 + H_5$
10-d_0	1.00	2.00	2.00
10		1.06 ± 0.02	2.00

	H_1	H_2	H_3	$H_4 + H_5$
11-d_0	1.00	1.00	1.00	2.00
11	0.02	0.09 ± 0.02	1.00	2.00

Anal. Calcd for $C_8H_{14}N_2O_4$: C, 47.52; H, 6.98; N, 13.85. Found: C, 47.31; H, 6.92; N, 13.52.

***cis*-3-Butenyl-*3,4-d*$_2$ Acetate (10).** Borane-d_3 (0.27 mol) was generated in a flame-dried flask under a nitrogen atmosphere from the dropwise addition of 75 mL (0.61 mol) of boron trifluoride etherate to a stirred slurry of 12.6 g (0.30 mol) of lithium aluminum deuteride (98% *d*) in ether at 0 °C and distilled through a cooled condenser (−78 °C) into 300 mL of dry tetrahydrofuran. To the 0.90 M solution of borane-d_3 in tetrahydrofuran was added 55 mL (0.54 mol) of cyclohexene at 0 °C. A white precipitate formed and the reaction mixture was allowed to stir for 1 h at 0 °C. 3-Butynyl acetate (22 g, 0.19 mol), obtained from the reaction of 3-butyn-1-ol with acetyl chloride in pyridine, was added to the dicyclohexylborane-d_1. The reaction mixture was allowed to stir at 0 °C for 2 h. The solution became clear and 95 mL of acetic acid-*O-d* (98% *d*) was added. This was allowed to stir at 25 °C for 1 h. A solution of 50 g of sodium hydroxide in 150 mL of water was added slowly followed by 100 mL of 30% hydrogen peroxide. After 1 h the tetrahydrofuran layer was separated. The aqueous layer was extracted once with ether. The organic layers were combined, dried (Na_2SO_4), and distilled. One fraction (bp 70–130 °C) was collected. Analytical vapor phase chromatography (Carbowax 20M, 120 °C) indicated that this fraction contained tetrahydrofuran, 3-butenyl acetate (**10**), cyclohexyl acetate, and cyclohexanol and no 3-butynyl acetate, by comparison with authentic samples. This 3-butenyl acetate **10** was purified by preparative vapor phase chromatography (Carbowax 20M, 120 °C) for analysis: IR (CCl_4) 2950 (C—H), 2250 (C—D), 1745 cm^{-1} (C=O); NMR ($CDCl_3$) δ 2.0 (s, 3), 2.3 (broad t, 2, J = 6 Hz), 4.1 (t, J = 6 Hz), 5.0–5.1 (m, 1.06 ± 0.02); mass spectrum *m/e* 116, 115.

***cis*-3,4-Epoxybutan-1-yl-*3,4-d*$_2$ Acetate (11).** To a stirred solution of 10 mL of dichloromethane and 1 g (8.6 mmol) of *cis*-3-buten-1-yl-*3,4-d*$_2$ acetate was added 3 g (19.6 mmol) of *m*-chloroperbenzoic acid in 50 mL of dichloromethane. After stirring for 4 h at room temperature, the solution was washed with saturated aqueous sodium bicarbonate, water, and saturated aqueous sodium chloride. The solution was dried (Na_2SO_4), filtered, and concentrated. The remaining liquid was distilled, bp 48–49 °C (0.5 mm), and further purified by vapor phase chromatography (SF-96, 75 °C) affording 1 g (7.5 mmol) of the epoxide-d_2 **11** (87%): IR (CCl_4) 2940 (C—H), 2210 (C—D), 1740 (C=O), 1350, 1220, 1030, 880 cm^{-1}; NMR ($CDCl_3$) δ 1.7–2.0 (m, 2), 2.0 (s, 3), 2.45 (s, 1), 2.75 (m, 0.09 ± 0.02), 4.2 (t, 2, J = 6 Hz).

3,4-Epoxybutan-1-yl Acetate (11-*d*$_0$). For comparison, the nondeuterated epoxide was prepared in the same manner from 3-buten-1-yl acetate: bp 48–49 °C (0.5 mm); IR (CCl_4) 3030, 2980 (C–H), 1740, 1220, 1050, 900, 830 cm^{-1}; NMR ($CDCl_3$) δ 1.7–2.0 (m, 2), 2.0 (s, 3), 2.40–2.53 (m, 1), 2.67–2.80 (m, 1), 2.82–3.07 (m, 1), 4.2 (t, 2, J = 6 Hz). Anal. Calcd for $C_6H_{10}O_3$: C, 55.37; H, 7.74. Found: C, 55.16; H, 7.59.

The isomeric and isotopic purity of *cis*-3-buten-1-yl-*3,4-d*$_2$ acetate **10** was determined by conversion to the epoxide, which allows the terminal hydrogens to be distinguished.[25] The chemical shifts of H_1, H_2, and H_3 of epoxide-d_0 are δ 2.9, 2.7, and 2.5, respectively. Position 2 contains 0.09 ± 0.02 hydrogen and position 1 contains <0.02 hydrogen for epoxide **11** (standard deviation of ten integrations) (see Table VII).

Dimethyl *cis*-3,4,5,6-Tetrahydropyridazine-1,2-dicarboxylate-*3,4-d*$_2$ (13). The synthesis of butane-1,4-diol-*1,2-d*$_2$ by the hydroboration of **10** was accomplished using the method of Brown and Unni.[26] The aqueous layer was extracted with ether for 4 days by liquid–liquid extraction. Careful addition of sodium bisulfite to the ether extract quenched the excess hydrogen peroxide. The ether solution was dried (Na_2SO_4) and concentrated, affording a mixture of 1,4- and 1,3-diols (4.8/1 ratio, respectively). This was dissolved in 160 mL of dry pyridine and cooled to −42 °C. Methanesulfonyl chloride was added dropwise over 40 min to the cooled reaction mixture with stirring. The reaction mixture was allowed to warm to 25 °C and then stirred for 1 h. This was poured over 250 mL of crushed ice and left to stand for 12 h. A white precipitate formed. This was collected by filtration, dissolved in methylene chloride, washed with aqueous sodium chloride, dried (Na_2SO_4), and concentrated, affording 9.8 g of a white powder. From the ratio of diols, 8.19 (33 mmol) is the desired *threo*-1,4-butanediyl-*1,2-d*$_2$ dimethanesulfonate **12** (17% yield from 3-butynyl acetate): NMR ($CDCl_3$) δ 1.7–1.9 (m, 3), 3.0 (s, 6), 4.1–4.3 (m, 3). The crude dimesylate **12** was used without further purification.

To a solution of 6.0 g (34 mmol) of dimethyl hydrazinedicarboxylate in 50 mL of diglyme was added 1.9 g of sodium hydride (50% mineral oil dispersion, 34 mmol) under a nitrogen atmosphere. After vigorous stirring for 3 h at 25 °C, a solution of 9.8 g of the crude mesylate (containing 33 mmol of *threo*-1,4-butanediyl-*1,2-d*$_2$ dimethanesulfonate **12**) in 30 mL of dry diglyme was added. The reaction mixture was allowed to stir under reflux for 24 h, then allowed to cool. Dry diglyme (50 mL) and 1.9 g of sodium hydride were added.[15] This was allowed to reflux for 24 h and then cooled to room temperature. The reaction mixture was filtered. The filtrate was diluted with 25 mL of water and extracted with 200 mL of ether. The ethereal extract was dried (Na_2SO_4) and concentrated under reduced pressure. The concentrate was extracted with 30 mL of hexane. This was concentrated and distilled, bp 85–95 °C (3 mm). The distillate was further purified by preparative vapor phase chromatography (FFAP, 190 °C) affording 2 g (10 mmol) of the saturated diurethane **13** (30%): mp 40.5–41.5 °C; IR (CCl_4) 2940 (C-H), 2150 (C-D), 1710 cm^{-1} (C-O); NMR ($CDCl_3$) δ 1.6–1.8 (m, 3), 2.8–3.0 (m, 1.5), 3.7 (s, 6), 4.0–4.2 (m, 1.5); mass spectrum *m/e* 204, 203 (d_2/d_1 = 93/7). Anal. Calcd for $C_8H_{12.07}N_2O_4D_{1.93}$: C, 47.07; H, 6.91; N, 13.12. Found: C, 47.44; H, 6.97; N, 13.41.

Hexahydropyridazine and *cis*-Hexahydropyridazine-*3,4-d*$_2$ (14). The undeuterated and *cis-3,4-d*$_2$ diurethane **13** were hydrolyzed in the same manner. The diurethane **13** (0.5 g, 2.5 mmol) was added to 1 g (18 mmol) of potassium hydroxide dissolved in 10 mL of thoroughly degassed water. The reaction mixture was allowed to reflux with stirring for 24 h under a nitrogen atmosphere. The solution was cooled to 0 °C, 4 mL of degassed 6 N HCl was added via syringe, and the reaction mixture was allowed to stir for 0.5 h at 25 °C. Then 12 mL of degassed aqueous saturated potassium carbonate was added, and the reaction mixture was extracted three times with 25-mL portions of ether, which was freshly distilled from calcium hydride under a nitrogen atmosphere and delivered via a double-ended needle. Each extract was transferred by a stream of nitrogen via a double-ended needle to a pressure equalized funnel, containing $MgSO_4$ in a filter thimble attached to the top of a distillation head. After the ether solvent was removed by distillation through a 6-in. Vigreux column, the

remaining oil was distilled on a vacuum line (10^{-4} Torr). The clear, colorless hydrazo distillate was transferred into an NMR tube on the vacuum line and diluted with ca. 0.5 mL of degassed benzene-d_6. The NMR tube was sealed and removed.

Hexahydropyridazine (14-d_0). NMR (C_6D_6): δ 1.3 (quintet, 4, J = 3 Hz), 2.1 (broad s, 2), 2.6 (broad quintet, 4, J = 3 Hz).

***cis*-Hexahydropyridazine-*3,4-d*$_2$ (14).** NMR (C_6D_6): δ 1.3 (broad t, 3, J = 3 Hz), 2.3 (broad s), 2.6 (m, 3).

Preparation of 3,4,5,6-Tetrahydropyridazine and *cis*-3,4,5,6-Tetrahydropyridazine-*3,4-d*$_2$ (6). Both hydrazines **14** were oxidized in the same manner. A solution of the hexahydropyridazine **14** in benzene-d_6 was allowed to stand in the dark under a positive pressure of oxygen for 6 h. The reaction was monitored by NMR. After 6 h, the solution consisted of 50% azo, 30% hydrazo, and 20% of the corresponding hydrazone.

3,4,5,6-Tetrahydropyridazine (6-d_0). UV max (C_6D_6): 375 nm. NMR (C_6D_6): δ 0.8–1.0 (m, 4 H), 3.4–3.6 (m, 4 H).

The corresponding hydrazone was obtained by allowing the azo compound (**6**) to stand for 4 days at room temperature. The hydrazone was isolated by preparative vapor phase chromatography (Pennwalt 22, 170 °C). NMR (C_6D_6): δ 1.5–1.8 (m, 4), 2.5–2.8 (m, 2), 4.3–5.3 (broad s, 1), 6.5–6.7 (m, 1).

***cis*-3,4,5,6-Tetrahydropyridazine-*3,4-d*$_2$ (6).** NMR (C_6D_6): δ 0.8–1.0 (m, 3 H), 3.4–3.6 (m, 3 H).

***cis*-1-Cyclobutanol-*2-d*$_1$ (23).** Cyclobutene (**15**,[27] 1 mL, 13.6 mmol) was bubbled in a stream of nitrogen via a double-ended needle into a flask containing 20 mL of dry tetrahydrofuran at 0 °C equipped with a condenser (−78 °C). Borane-d_3, generated as described previously using 0.25 g (5.9 mmol) of lithium aluminum deuteride (98% d) and 1.5 mL (12.0 mmol) of boron trifluoride etherate, was bubbled into the cyclobutene/tetrahydrofuran solution. This was allowed to stir at 0 °C for 1 h. Water (2 mL) was added to quench excess hydride and the solution was heated to 40 °C. Then 3 mL of 3 N sodium hydroxide was added, followed by 3 mL of 30% hydrogen peroxide. The solution was allowed to stir for 1 h at 40 °C, extracted three times with 30-mL portions of ether, washed with saturated aqueous sodium chloride, dried (Na_2SO_4), and concentrated. The cyclobutanol product **23** (0.6 g, 8.2 mmol, 60%) was isolated by preparative vapor phase chromatography (Carbowax 20M, 140 °C): IR (CCl_4) 3600 and 3300 (O–H), 2970 (C–H), 2190 and 2200 (C–D), 1460 cm^{-1}; NMR ($CDCl_3$) δ 1.2–2.5 (m, 5), 3.3 (broad s, 1), 4.0–4.4 (m, 1).

***cis*-1-Cyclobutanyl-*2-d*$_1$ Tosylate (17).** *cis*-1-Cyclobutanol-*2-d*$_1$ (**23**, 0.3 g, 4.1 mmol) was dissolved in 15 mL of dry pyridine. This was cooled to 0 °C and 3.8 g (20 mmol) of tosyl chloride was added under an inert atmosphere. The reaction mixture was kept at 5 °C for 12 h, diluted with 14 mL of ice-cold water, extracted with 25-mL portions of ether, and washed three times with 20-mL portions of ice-cold 1 M HCl and once with ice-cold water and saturated aqueous sodium chloride. The ether layers were combined, dried (Na_2SO_4), and concentrated, affording 0.4 g (1.65 mmol) of the tosylate **17** (40%): NMR ($CDCl_3$) δ 1.4–2.4 (m, 5), 2.45 (s, 3), 4.5–5.0 (m, 1), 7.2–7.9 (m, 4).

***trans*-Cyclobutane-*d*$_2$ (8).** To 15 mL of a 1 M solution of lithium triethylborodeuteride in dry tetrahydrofuran (Superdeuteride from Aldrich, 98% d_1) at 0 °C was added 0.4 g (1.6 mmol) of *cis*-1-cyclobutanyl-*2-d*$_1$ tosylate (**17**) in 7 mL of dry tetrahydrofuran. The reaction mixture was stirred at 0 °C for 15 min, then at 25 °C for 90 min under a flow of nitrogen gas. The nitrogen carrier gas was passed through a drying tower ($CaCl_2$) into a U-tube cooled to −78 °C. The reaction mixture was heated to 50 °C for 1 h to drive the gaseous products into the U-tube. The products collected were cyclobutane and tetrahydrofuran. No other C_4 gases were formed in the reaction. The *trans*-cyclobutane-*1,2-d*$_2$ was isolated by preparative vapor phase chromatography (SE-30, 25 °C); IR (gas) 2950 (C–H), 2190 (C–D), 1450 (CH_2), 1294 (CHD), 579, 543, (562 < 2%) cm^{-1}; mass spectrum (9.0 eV) m/e 58, 57, 56 (d_2/d_1 = 95.5/4.5 ± 1 by comparison with cyclobutane under the same conditions).

***trans*-1-Cyclobutanol-*2-d*$_1$ (24).** Cyclobutene oxide (**16**), synthesized from cyclobutene as described by Ripoll and Conia,[28] was purified by preparative vapor phase chromatography ($\beta\beta$, 85 °C). To 15 mL of a 1 M solution of lithium triethylborodeuteride in dry tetrahydrofuran (Superdeuteride, 98% d_1) at 0 °C was added 0.5 g (7.1 mmol) of cyclobutene oxide in 5 mL of dry tetrahydrofuran. Excess hydride was quenched with water after 2 h. Hydrogen peroxide solution (30%, 3 mL) was added until no reaction occurred. Then 10 mL of ether was added followed by potassium carbonate until the two layers separated. The aqueous layer was extracted with two 10-mL portions of ether, and the ether layers were combined with the ether/tetrahydrofuran layer, dried (Na_2SO_4), and concentrated. The cyclobutanol product **24** was further purified by preparative vapor phase chromatography (Carbowax, 140 °C) affording 0.5 g (6.9 mmol) of *trans*-1-cyclobutanol-*2-d*$_1$ **24** (96%): IR (CCl_4) 3600 (O–H), 2980 (C–H), 2200 (C–D), 1460 cm^{-1}; NMR ($CDCl_3$) δ 1.1–2.4 (m, 6), 1.6 (broad s), 3.9–4.4 (m, 1).

***cis*-Cyclobutane-*1,2-d*$_2$ (7). Method A.** Successive treatment of *trans*-1-cyclobutanol-*2-d*$_1$ (**24**) with tosyl chloride and lithium triethylborodeuteride (as reported above for *cis*-1-cyclobutanol-*2-d*$_1$ (**23**)) afforded *cis*-cyclobutane-*1,2-d*$_2$ (**7**), which was isolated by preparative vapor phase chromatography (SE-30, 25 °C): IR (gas) 2990 (C–H), 2220 (C–D), 1450 (CH_2), 1207 (CHD), 569, 562 (1294 < 2%) cm^{-1}; mass spectrum (90 eV) m/e 58, 57, 56 (d_2/d_1 = 95.4/4.5 ± 1 by comparison with cyclobutane under the same conditions).

***cis*-Cyclobutane-*1,2-d*$_2$ (7). Method B.** Cyclobutene (**15**, 1 mL, 13.6 mmol) was added via a condenser (−78 °C) to 40 mL of ethanol-*O-d* and 9.0 g (56 mmol) of potassium azodicarboxylate.[29] Acetic acid-*O-d* (98% d) was added dropwise via a dropping funnel and the reaction mixture was maintained at 0 °C for 90 min. The reaction mixture was heated slowly to 50 °C over 90 min and then cooled. The −78 °C condenser was replaced with a 25 °C condenser and the ethanol was refluxed for 1 h under a stream of nitrogen gas which was passed through a U-tube cooled to −78 °C in order to collect the volatile products. Analytical vapor phase chromatography (SE-30, 25 °C) indicated the products (~2 mL) to consist of a 90/10 mixture of cyclobutane and cyclobutene, relative retention times 1.0 and 0.81, respectively. The *cis*-cyclobutane-*1,2-d*$_2$ (**7**) was isolated by preparative vapor phase chromatography (SE-30, 25 °C). The spectral properties were identical with those of the *cis*-cyclobutane-*1,2-d*$_2$ (**7**) obtained by method A. Mass spectral analysis revealed a d_2/d_1 ratio of 89.3/10.7 ± 1.

Cyclobutane-d_1 (26). Similar to procedures described above, reaction of cyclobutanyl tosylate (**25**) with lithium triethylborodeuteride (Superdeuteride, 98% d_1) afforded cyclobutane-d_1 (**26**): IR (gas) 2990, 2200, 1450, 1307 cm^{-1}.

***cis*-Ethylene-*1,2-d*$_2$ (21).**[17] Acetylene-d_2 (**20**) was synthesized by the reaction of calcium carbide (Fisher 20–30 mesh) and deuterium oxide. Reduction of this acetylene-d_2 (**20**) with zinc–copper couple, from the reaction of zinc dust and an aqueous solution of cupric sulfate, in the presence of HCl afforded *cis*-ethylene-*1,2-d*$_2$ (**21**). The *cis*-ethylene-*1,2-d*$_2$ (**21**) was further purified by preparative vapor phase chromatography (SE-30, 25 °C): IR (gas) 842, (987 and 724 < 1%) cm^{-1}; mass spectrum (12 eV) m/e 30, 29, 28 (ratios 72.6, 21.0, 6.4 ± 1%). The mass spectrum was run under conditions where ethylene gave only one peak at m/e 28. Analysis by analytical VPC (Poropak N, 70 °C) revealed 2.1% acetylene present which accounts for 33% of the m/e 28 peak.

***trans*-Ethylene-*1,2-d*$_2$ (22).**[17] Reduction of acetylene-d_2 (**20**) by aqueous chromous chloride afforded *trans*-ethylene-*1,2-d*$_2$ (**22**). This was purified by preparative vapor phase chromatography (SE-30, 25 °C): IR (gas) 987, 742, (842 < 1%) cm^{-1}; mass spectrum (12 eV) m/e 30, 29, 28 (ratios 56.4:30.9:12.7 ± 1%). Analysis by analytical VPC (Poropak N, 70 °C) revealed 0.3% acetylene present.

Thermal Reactions. The pyrolyses were carried out in a 2.8 × 30 cm cylindrical Pyrex tube, equipped with a 0.6 × 3 cm injector port, serum cap, mounted in a Hoskins Type FD 303 A tube furnace. The other end of the tube was connected via a 6-mm bore stopcock (A) to a high-vacuum line equipped with two liquid nitrogen cooled U-shaped traps plus a small receiving tube equipped with a stopcock and a side arm sealed with a serum cap. The temperature was measured with an Omega digital thermometer with an iron–constantan thermocouple. Before pyrolysis, the tube was evacuated and stopcock A was closed. In a typical run for analytical VPC analyses, 10 μL of the 1,2-diazene in solution (10% in C_6D_6) was injected through the serum cap via a gas-tight syringe. For infrared analyses, 150-μL injections were made. Ethylene/cyclobutane product ratios were unchanged. After pyrolyses times of 5 or 30 s, stopcock A was opened and the pyrolysate was collected in the liquid nitrogen cooled traps. The hydrocarbon contents of the traps were transferred into a receiving tube, sealed, and removed from the vacuum line for VPC analysis. Upon warming to room temperature, the entire sample vaporized in the tube. Using a gas syringe (precision Sampling Model "Pressure-lok" series A) the products were analyzed by VPC (SE-30, 25 °C). Assignments of the product peaks were made by coinjection techniques using authentic

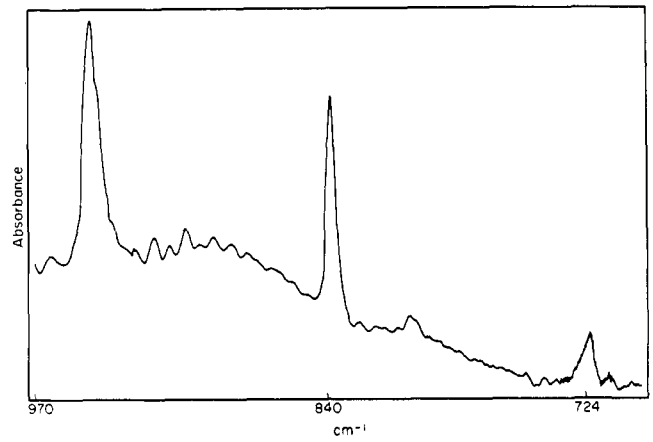


Figure 2. Infrared spectra of the ethylene products from the pyrolysis of **6**.

samples. The response factors for ethylene and cyclobutane were found to be 1.07 ± 0.02 to 1.00, respectively by calibration with authentic mixtures. Relative retention times (SE-30, 25°C): ethylene (0.181), propylene (0.295), 1-butene (0.595), cyclobutane (1.00) (Table II).

For infrared analyses, ethylene and cyclobutane products were separated by preparative gas chromatography (SE-30, 25 °C) on a Varian Aerograph Model 90-P instrument equipped with a gas inlet and collection system. The IR analyses of the products are described below.

Infrared Analysis of Pyrolysis Products.[30] The ethylene and cyclobutane samples, purified by preparative VPC as described above, were analyzed by infrared spectroscopy with a Perkin-Elmer Model 180 infrared spectrometer in the absorbance mode.[16] The wavelengths were not calibrated. The cell used for gas sampling had a path length of 8 cm and a volume of 8 mL and was equipped with a cold finger.

Ethylene was analyzed using the 842-cm^{-1} band for *cis*-ethylene-*1,2*-d_2 and the 724-cm^{-1} band for *trans*-ethylene-*1,2*-d_2. Ethylene-d_1 has a band at 809 cm^{-1}, and ethylene (half of the ethylene product from the pyrolyses of **6** is nondeuterated) has a band at 945 cm^{-1}. These peaks did not interfere with the analyses, although use of the 987-cm^{-1} band from *trans*-ethylene-*1,2*-d_2 was precluded. A sample for IR analysis (Figure 2) was prepared by pyrolyzing the 1,2-diazene **6** synthesized from 0.5 g of the diurethane. Three samples were analyzed.

Two methods were used to obtain the relative ratio of *cis*-/*trans*-ethylene-d_2 (**21**/**22**). Because the relative amount of d_2 to d_1 compound in the authentic samples was known by mass spectrometry, the relative extinction coefficients between *cis*-ethylene-*1,2*-d_2 and ethylene-d_1 and between *trans*-ethylene-*1,2*-d_2 and ethylene-d_1 could be determined. From this, the relative extinction coefficient between *cis*- and *trans*-ethylene-d_2 could be calculated. In addition, known mixtures of authentic samples were made up using an MKS vacuum transmitter Type 221 pressure gauge. The pressure (±0.005 Torr) of a fixed volume of sample was measured and the sample transferred into a bulb followed by a measured amount of another sample. The mixture was vacuum transferred into the gas cell for infrared analysis. This sample was collected again, measured, and more of one isomer was added, etc. (Table IV).

The cis/trans ratios of the cyclobutane products (**7** and **8**) from the pyrolysis were analyzed by measuring the relative ratios of the 1307-(*cis*-**7**) and 1294-cm^{-1} (*trans*-**8**) bands. The sample analyzed was obtained from the total pyrolysis of the 1,2-diazene synthesized from two 0.5-g samples of the diurethane. The total pyrolysis required six ca. 150-μL pyrolyses. Infrared spectra are given in Figure 3. Mass-spectral analysis showed the cyclobutane from pyrolysis to be 92.5% d_2 and 7.5% d_1 ± 1%. Since cyclobutane-d_1 has a band at 1307 cm^{-1}, calibration mixtures of authentic samples contained 7.5% cyclobutane-d_1.

The mixtures were prepared in the same manner as described for ethylene. The results are given in Table III. The spectrum of each mixture was taken three times and the spectrum of the pyrolysis product was taken four times. The spectra were enlarged five times for analysis.

Complete error analyses for the various ratios presented in this paper as well as spectra of the authentic mixtures of deuterated

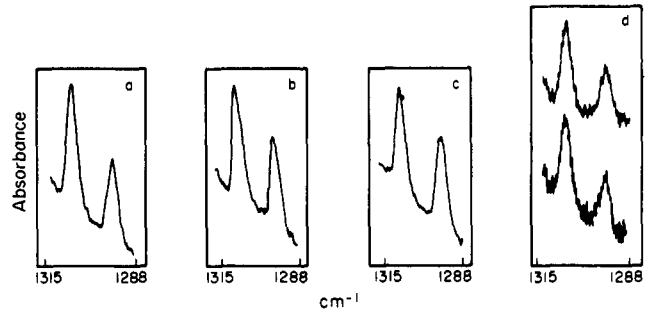


Figure 3. Infrared spectra of authentic samples of *cis*-/*trans*-cyclobutane-*1,2*-d_2 in ratios of (a) 55/45, (b) 50.3/49.7, (c) 45.5/54.5, and (d) from the pyrolysis of **6**.

compounds can be found elsewhere.[31]

Controls. (a) The hydrazone and the hydrazine **14** afforded ethylene and cyclobutane under identical pyrolysis conditions for **6** in less than 1% yield. (b) *trans*-Ethylene-*1,2*-d_2 was shown to be stable under the pyrolysis conditions. (c) Cyclobutane gave no ethylene under the pyrolysis conditions. (d) The presence of ethylene-d_0 in the pyrolysis product mixture was shown not to affect the 842- to 724-cm^{-1} peak height ratio, by adding nearly equivalent amounts of ethylene to the authentic mixtures. (e) Surface effects were checked by repeating the pyrolyses with a tube filled with glass chips. None were found. Also, pressure effects were absent since 150-μL injections (ca. 300 Torr) gave the same ethylene/cyclobutane product ratios as 10-μL injections (ca. 20 Torr). (f) The ratio of 1,2-diazene **6** to internal standard (ethyl ether) in benzene-d_6 was determined by NMR. After pyrolysis, the ratio of hydrocarbon products/ethyl ether afforded an approximate estimate of mass balance. The 1,2-diazene **6** decomposed to ethylene and cyclobutane in ~60% yield.

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(13) The headings for this table are reversed in ref 9e. The table is correct as

it appears here.
(14) For an alternate synthesis and thermolysis of *cis*- and *trans*-cyclobutane-*1,2-d*$_2$, see ref 7].
(15) This reaction has been shown to be 95% stereospecific inversion for secondary centers, i.e., *threo*-3-methyl-1,4-pentanediyl 1,4-dimethanesulfonate affords dimethyl *cis*-3,4-dimethyltetrahydropyridazine-1,2-dicarboxylate and *erythro*-dimethanesulfonate affords trans 3,4-disubstituted diurethanes.[9e]
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Regioselectivity in Cycloadditions of Singlet 2-Methylenecyclopenta-1,3-diyl Species[1]

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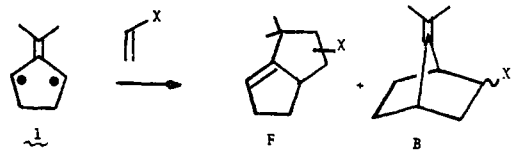
Abstract: The regioselectivity for fused adduct in the cycloaddition of singlet 2-methylenecyclopenta-1,3-diyls to olefins can be explained either as an orbital overlap effect in a reaction of a bisected singlet trimethylenemethane (TMM) or as an orbital symmetry effect in a reaction of a planar singlet TMM. The first hypothesis predicts the same regioselectivity in 1,2 and 1,4 cycloadditions to conjugated dienes (fused adducts), but the second hypothesis predicts a switch in regioselectivity, in which 1,2 addition should give fused adduct and 1,4 addition should give bridged adduct. In the latter case, a further prediction of the orbital symmetry model is that the adduct with the syn relationship between the exocyclic double bond and the newly developing ring double bond should be favored over its anti isomer. The predictions of the orbital symmetry model are confirmed in every instance in the cycloaddition of 2-methylenecyclopenta-1,3-diyl to cyclopentadiene. The dominant products are fused 1,2 and syn-bridged 1,4 adducts.

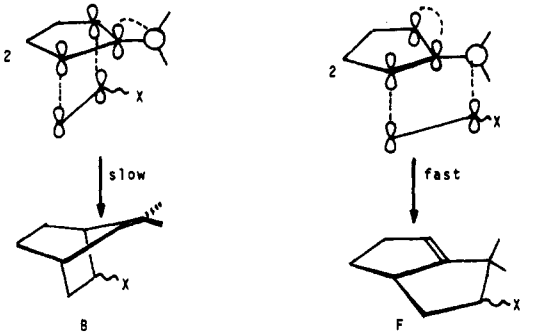
The trimethylenemethane (TMM) biradical 2-isopropylidenecyclopenta-1,3-diyl (**1**) reacts with olefins to give [3 + 2] cycloadducts[3] by pathways involving two mechanistically distinguishable forms, a singlet and a triplet.[4] Such cycloadditions should be capable of forming both fused (F) and bridged (B) adducts, a prediction verified by experience[4] with the *triplet* diyl **1**. This species gives F and B with little or no



preference for either. It is therefore remarkable that the cycloadditions of the *singlet* are highly regioselective and give largely the fused isomer.[4]

Our first attempt[4] to rationalize the behavior of the singlet invoked the bisected TMM **2** as the reactive species. Theory[5] suggests that in the singlet manifold the bisected configuration should be readily accessible by twisting one methylene group of TMM out of the plane of the other two. Moreover, there is ample experimental support for the occurrence of this process.[6] From the strict syn stereoselectivity of the singlet cycloaddition, we also infer that the singlet + olefin reaction probably is concerted. Concerted reaction at the potential bridgehead sites (**2** → B) generates a twisted π bond in the transition state, whereas reaction at one ring site and the exocyclic site (**2** → F) does not. This would tend to retard the formation of bridged cycloadduct.

An alternative rationale for regioselective formation of fused adduct can be constructed on the basis of orbital-symmetry[7] relationships in the diyl and diylophile. Frontier orbital theory[8]



provides a simple way to present the argument. Thus, a concerted, orbital symmetry allowed cycloaddition could occur only at the TMM sites at which the orbital phase properties of the TMM's highest occupied molecular orbital (HOMO) match those of the olefin's lowest unoccupied MO (LUMO), normally the antisymmetric π^* MO.

The TMM's HOMO must be one of the two nominally degenerate nonbonding orbitals **3**-S or **3**-A (Figure 1),[9] since four electrons must be accommodated in the π system. In a planar TMM, these MOs are truly degenerate at the level of simple Hückel theory, even when, as in **1**, the D_{3h} structure of the parent compound is distorted to C_{2v}. We defer a discussion of more sophisticated theory which rationalizes a splitting of the degenerate Hückel MOs, and for the purpose of argument we examine the corollaries of the hypotheses that the *reactive* singlet is planar, that the S level is below the A by a large enough gap to make S the HOMO, and that the regioselectivity of cycloaddition is frontier orbital controlled. The ordering S below A is chosen to make the hypothesis conform to the experimentally observed regioselectivity.

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