Prostanoid Endoperoxide Model Compounds: 1,6-Diradicals in the Thermolysis and Photolysis of 1,2-Dioxanes and Cyclic Peroxalates[1]

Waldemar Adam*[2] and James Sanabia

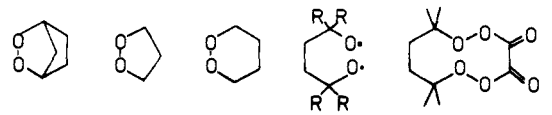
Contribution from the Department of Chemistry, University of Puerto Rico, Río Piedras, Puerto Rico 00931. *Received July 19, 1976*

Abstract: 3,3,6,6-Tetramethyl-1,2-dioxane (**3a**), considered as a prostanoid endoperoxide model compound, was found to afford thermally and photochemically acetone and ethylene in 99 and 96% yield, respectively. Stereochemical studies of deuterium stereolabeled 1,2-dioxanes gave the resulting ethylenes in 70 ± 2% inversion, suggesting olefin genesis from a transoid conformation of the 1,6-dioxahexamethylene diradical (**9**). A negligible secondary deuterium isotope effect of k_H/k_D = 1.03 ± 0.03 was found for the tetradeuterio-1,2-dioxane **3b**. Our present kinetic and stereochemical data provide compelling evidence that the 1,6-dioxahexamethylene diradical (**9**), generated by simple peroxide bond cleavage of the 1,2-dioxane, prefers to fragment concertedly rather than releasing acetone stepwise via a 1,4-diradical. The novel cyclic peroxalate 7,7,10,10-tetramethyl-1,2,5,6-tetroxecane-3,4-dione (**5**) was synthesized and characterized. Its thermolysis and photolysis gave acetone, ethylene, and tetramethyl-1,2-dioxane **3a**. The heat of reaction of the cyclic peroxalate was $\Delta H = -99 \pm 2$ kcal/mol while for its acyclic analogue *tert*-butyl peroxalate, it was $\Delta H = -57 \pm 2$ kcal/mol, both determined by DSC. The kinetic data clearly demonstrate that the cyclic peroxalate **5** has a thermal half-life 3000 times greater than that of its acyclic analogue. Since this enhanced thermal stability is enthalpy controlled, we ascribe it to conformational stabilization of the cyclic peroxide.

In view of the unusual pharmacological activity of the prostaglandins and their endoperoxide precursors in a wide spectrum of physiological functions,[3] it is important to define the chemistry of these intriguing biological intermediates. However, owing to the great thermal lability of the endoperoxide ring system, it has been exceedingly difficult to prepare and isolate these materials for chemical investigations. Since the 2,3-dioxabicyclo[2.2.1]heptane skeleton **1** of the prostanoid endoperoxide system can be viewed as a composite of a 1,2-dioxolane **2** and 1,2-dioxane **3** ring systems, it should be possible to extrapolate the thermal behavior of the endoperoxide system from that of its simpler constituents.

Recently we presented a detailed mechanistic account of the thermolysis and photolysis of 1,2-dioxolanes **2**;[4] but to the best of our knowledge no systematic mechanistic investigation of the thermal and photochemical behavior of 1,2-dioxanes **3** has been reported. Our incentive was to elucidate the mechanism of the thermolysis and photolysis of 1,2-dioxanes **3**.

On the basis of our previous experience with related cyclic peroxides, e.g., β-peroxylactones[5] and γ-peroxylactones,[6] it was expected that relatively high thermal activation would be required to disengage the peroxide bond, leading first to a 1,6-diradical **4**, which would subsequently be degraded into stable products. Since prostanoid endoperoxides exhibit a very low thermal stability, it was relevant to prepare alternative low-temperature precursors to the 1,6-diradicals **4** to serve as more representative model substrates. Peroxalates are exceedingly low temperature sources for alkoxy radicals,[7] compared to dialkyl peroxides,[8] and we anticipated that the cyclic peroxalate **5** could serve as a low-temperature source for the 1,6-diradical **4**. Such materials were unknown prior to our investigation and presently we describe our results for the synthesis, characterization, thermolysis, and photolysis of 7,7,10,10-tetramethyl-1,2,5,6-tetroxecane-3,4-dione (**5**), along with our mechanistic results on the thermolysis and photolysis of 1,2-dioxanes **3**.[9]



1 2 3 4 5

Experimental Section

The refractive indices of all compounds were measured on a Bausch and Lomb refractometer, thermostated by means of a Haake thermoregulator with cryostat. Boiling points and melting points are uncorrected; the latter were determined on a Thomas-Hoover melting point apparatus. The infrared spectra were measured on a Perkin-Elmer 180 and 237-B Infrared. The qualitative and quantitative GLC studies were performed on a Varian Aerograph 202-B, equipped with a disk integrator. Thermokinetic data were obtained on a Perkin-Elmer Model 1B differential scanning calorimeter and the data processed on an IBM-360 computer. The NMR spectra were measured on a Varian T-60 and the mass spectra on a Hitachi Perkin-Elmer RMS-4 spectrometer. All irradiations were conducted in a Rayonet RPR-100 photochemical reactor, supplied with 350- and 310-nm lamps. Quantitative weighings were performed on a Mettler HD-6 analytical balance; but for samples under 5 mg a Cahn electrobalance was used. An Aminco-Bowman spectrofluorimeter, equipped with a high-pressure xenon arc and a 1P28 photomultiplier, was employed for the absorption, fluorescence, and chemiluminescence measurements.

Synthetic Work. All commercially available solvents, starting materials, and authentic samples for product comparison and control experiments were rigorously purified according to reported procedures. The remaining compounds required in this research, except those given below, were prepared and purified according to literature methods and will not be described here.[10]

***meso*-3,3,6,6-Tetramethyl-1,2-dioxane-*4,5-d*$_2$ (3c).** A 25-mL round-bottom flask, provided with spin bar, was charged with 1.50 g (0.01 mol) of *meso*-dihydroxy-2,5-dimethylhexane-*3,4-d*$_2$ (**6c**) and 6.5 mL of 50% H_2O_2 and warmed to 60 °C. While stirring magnetically was added dropwise by remote control using a Cheng tube[12] a mixture of 4.5 mL of 70% H_2SO_4 and 6.5 mL of 50% H_2O_2 (*caution*!). After this mixture was allowed to stir for 1 h at 60 °C, it was cooled to ca. 5 °C by means of an ice bath and then poured into three times the volume of cold water. Extraction with 3 × 25 mL of pentane, drying of the combined pentane extracts with $MgSO_4$, rotoevaporation (ca. 30 °C, 30 mm) of the solvent, and distillation gave the pure 1,2-dioxane **3c** in ca. 20% yield, bp 44–45 °C (11 mm), n^{20}_D 1.4254 (lit.[13] bp 44–45 °C (11 mm), n^{20}_D 1.4251 for the undeuterated substance).

***meso*-2,5-Dihydroxy-2,5-dimethylhexane-*3,4-d*$_2$ (6c).** A 250-mL, three-necked, round-bottom flask, fitted with a mechanical stirrer, pressure-equalizing dropping funnel, nitrogen inlet and outlet, and a dry ice/acetone condenser, was charged with 48 g (0.20 mol) of Mg shavings and flame dried under a N_2 atmosphere. A solution of 19 g (0.20 mol) of methyl bromide in 40 mL of anhydrous ether was added

Table I. Molar Yields[a] of Products and Product Balance of the Thermolysis and Photolysis of 7,7,10,10-Tetramethyl-1,2,5,6-tetroxecane-3,4-dione (**5**) and 3,3,6,6-Tetramethyl-1,2-dioxane (**3**) in Benzene

Substrate	Dec mode	Initial mmol	Molar yields		Product balance, %
			Acetone	1,2-Dioxane	
Tetroxecane **5**	Δ[b]	1.29	0.803 ± 0.023	0.220 ± 0.020	93 ± 2
	$h\nu$[c]	0.43	0.273 ± 0.004	0.077 ± 0.004	92 ± 1
Dioxane **3**	Δ[d]	2.11	1.98 ± 0.04		94 ± 2
	$h\nu$[e]	2.11	3.61 ± 0.10	0.33 ± 0.03[f]	99 ± 2

[a] Determined by GLC on a 4 ft × 0.25 in. copper column, packed with 20% SE-30 and 0.5% Versamid 920 on Chromosorb W with ethylbenzene as internal standard. [b] Heated at 120 °C for 1.25 h. [c] Irradiated at 350 nm for 20 h. [d] Heated at 200 °C for 7 h. [e] Irradiated at 350 nm for 550 h.

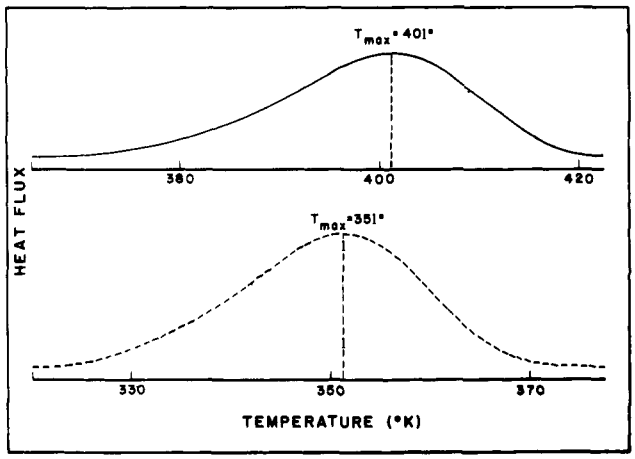


Figure 1. Thermograms for the thermal decomposition of cyclic peroxalate **5** (solid curve) and di-*tert*-butyl peroxalate (broken curve).

at such a rate to maintain a gentle reflux at the Dry Ice condenser, while stirring vigorously at room temperature. When all the magnesium was consumed, a solution of 6.00 g (0.04 mol) of *meso*-dimethyl succinate-*2,3-d*$_2$ (**7c**) in 15 mL of anhydrous ether was added dropwise and stirred for an additional 90 min. Neutralization with 15% aqueous HCl and liquid–liquid extraction for 48 h, drying over $MgSO_4$, rotoevaporation (ca. 30 °C, 25 mm) of the solvent, and recrystallization gave a 55% yield of the diol **6c**, mp 89–90 °C (lit.[14] mp 89–90 °C, for the undeuterated diol).

***meso*-Dimethyl Succinate-*2,3-d*$_2$ (7c).** A 50-mL, round-bottom flask, fitted with a spin bar, a Y-tube, and a dropping funnel, was charged with 5.00 g (0.042 mol) of *meso*-succinic acid-*2,3-d*$_2$ in 10 mL of anhydrous ether. While stirring vigorously, an ethereal solution of diazomethane (prepared freshly from Diazald) was added dropwise until persistence of the yellow color of diazomethane. Rotoevaporation (ca. 30 °C, 15 mm) of the solvent and molecular distillation at 60 °C (0.5 mm) gave the pure diester **7c** in 97% yield.

The remaining deuterated 1,2-dioxanes **3**, diols **6**, and succinates **7** were prepared analogously to the above procedures. Spectral data helped to confirm the respective structures. Extent of deuteration was 90–95%.

7,7,10,10-Tetramethyl-1,2,5,6-tetroxecane-3,4-dione (5) was prepared in 10% yield, mp 108–109 °C, by allowing 3.56 g (0.02 mol) of 2,5-dihydroperoxy-2,5-dimethylhexane and 3.16 g (0.04 mol) of anhydrous pyridine in 250 mL of anhydrous tetrahydrofuran to react with 2.54 g (0.02 mol) of freshly distilled oxalyl chloride in 25 mL of anhydrous tetrahydrofuran at −25 °C. Rotoevaporation of the solvent (ca. 20 °C, 15 mm) and trituration of the pasty residue with 5 × 20 mL of 1:1 pentane/hexane mixture gave the crude cyclic peroxide.[11] The triturates were combined and allowed to crystallize at −10 °C. The pure tetroxecanedione was obtained after five recrystallizations from a 1:1 pentane/hexane mixture. The structure of the tetroxecanedione rests on its molecular weight of 233 ± 1 amu (232 amu calcd for $C_{10}H_{16}O_6$) and on the following spectral data: IR (CCl_4) 2995 and 2950 (aliphatic C–H), 1812 and 1775 (carbonyl stretch), 1375 and 1390 (*gem*-dimethyl), and 1110 cm^{-1} (C–O single bond); NMR (100 MHz) δ (CCl_4, Me_4Si) 1.20 (6, s, CH_3), 1.51 (6, s, CH_3) 1.58 (2, d, J = 12.5 Hz, CH_2), and 2.02 (2, d, J = 12.5 Hz, CH_2); UV (*n*-hexane) λ_{max} 215 nm (ϵ 43).

Table II. *cis*- and *trans*-Ethylene-*1,2-d*$_2$ Ratio in the Thermolysis and Photolysis of *meso*-and *dl*-3,3,6,6-Tetramethyl-1,2-dioxane-*4,5-d*$_2$ (**3c** and **3d**, Respectively), in Benzene

Stereoisomer	Dec mode	Ratio[a,b] (cis/trans)	% isomerization
meso-**3c**	Δ[c]	0.63 ± 0.01	63.1 ± 1.5
	$h\nu$[d]	1.01 ± 0.01	99.3 ± 0.9
dl-**3d**	Δ[c]	1.53 ± 0.03	65.6 ± 1.5
	$h\nu$[d]	1.01 ± 0.01	98.6 ± 0.9

[a] Determined by infrared, measuring the respective absorbances. [b] Ethylene isomerizes under photolysis conditions, but not under thermolysis conditions. [c] Heated at 220 °C for 40 h. [d] Irradiated at 310 nm for 500 h.

Product Studies. The qualitative and quantitative GLC analyses of the thermo- and photoproducts were carried out according to the method outlined by Adam and Rios[15] and the details will not be reproduced here.[10] The molar compositions and total product balance are summarized in Table I.

Stereochemical Studies. A solution of 120 mg (0.82 mmol) of the deuterium-labeled 1,2-dioxetane **3** in benzene was transferred by means of a syringe into three constricted Pyrex test tubes, cooled to −78 °C and sealed. After thermolysis for 40 h at 220 °C in a silicone oil bath or photolysis at 310 nm for 21 days in a Rayonet photoreactor, the ampules were opened on a vacuum manifold and the ethylene product subjected to quantitative infrared analysis in a 10-cm NaCl gas cell. The measured absorbances of *cis*- and *trans*-1,2-dideuterioethylenes, respectively, at 848 and 947 cm^{-1} were calibrated against the infrared spectra of 1:1 mixtures of the authentic ethylenes, which were kindly supplied by Professors P. D. Bartlett (Harvard University) and J. E. Baldwin (University of Oregon). The stereochemical results are given in Table II.

Kinetic and Thermochemical Studies. For the isothermal kinetic work of the cyclic peroxalate **5** and 1,2-dioxane **3a** and **3b** the general procedure described by us previously[16] was used, monitoring the disappearance of the 1812-cm^{-1} carbonyl frequency of the peroxalate **5** or the appearance of the acetone carbonyl frequency at 1710 cm^{-1} by infrared. The rate constants and activation parameters are summarized in Table III.

For the nonisothermal kinetic work of the cyclic and acyclic peroxalates differential scanning calorimetry (DSC) was used. The average temperature calibration of the calorimeter was made with pure samples of acetanilide, indium, tin, vanillin, and benzophenone as standards, while for the differential temperature calibration indium was used. Fresh solutions (ca. 1.0 M) of the peroxides in di-*n*-butyl phthalate were prepared. Aliquots of 25 μL were transferred by means of a 50-μL Hamilton syringe into aluminum capsules, sealed, and placed into the sample pan of the calorimeter, while the reference pan was balanced with an aluminum pan containing an equal amount of pure solvent. When the calorimeter had reached thermal equilibrium, the temperature scan was begun under optimized conditions of scanning rate, range setting, and slope correction. Typical thermograms are shown in Figure 1, in which the solid curve corresponds to the cyclic peroxalate **5** and the broken curve to its acyclic analogue.

Table III. Isothermal and Nonisothermal Rate Data for the Thermolysis of 1,2-Dioxane **3**, Cyclic Peroxalate **5**, and *tert*-Butyl Peroxalate

Substrate	Mode	Temp, K	$k_{arg} \times 10^5$, s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, gibbs/mol	$\Delta G^{\ddagger}$, kcal/mol
1,2-Dioxane **3a**	Isothermal[b]	473.2	2.65 ± 0.10			
	Isothermal[b]	483.2	4.79 ± 0.11	32 ± 1	−13 ± 2	38
	Isothermal[b]	491.2	9.80 ± 0.54			
1,2-Dioxane **3b**	Isothermal[b]	483.2	4.65 ± 0.11			
	Isothermal[c]	362.7	5.29 ± 0.13			
Cyclic peroxalate **5**	Isothermal[c]	382.7	51.5 ± 1.0	31 ± 1	8 ± 1	27
	Isothermal[c]	391.8	147 ± 2			
Cyclic peroxalate **5**	Nonisothermal[d]			30 ± 1	10 ± 2	25
tert-Butyl peroxalate	Nonisothermal[d]			22 ± 1	1 ± 1	22

[a] Isothermal rates were determined by infrared and the nonisothermal rates by DSC. [b] In CCl_4. [c] In cyclohexane. [d] In di-*n*-butyl phthalate.

To determine the activation energy (E_a) and the frequency factor (log A), at regular temperature intervals (about 5 K) to the left and right of the maximum of the peak (a total span of about 50 K) the ordinates (dH/dt) and fractional area ($A - a$) up to that temperature were determined. The first-order rate constants $k(T)$ at these temperatures were calculated as the ratio of the ordinate (dH/dt) and fractional area ($A - a$). From the Arrhenius plot (log $k(T)$ vs. $1/T$) the activation energy (E_a) and the frequency factor (log$A$) were determined. The results are summarized in Table III.

The heats of reaction (ΔH) for the cyclic and acyclic peroxalates were determined from the thermograms (Figure 1), since the area under the peak is proportional to the heat change for the process under examination. The proportionality constant is determined by measuring the area under the peak of a calibration standard whose heat change is known accurately. In this work the heat of fusion of benzoic acid was used as calibration standard ($\Delta H_{fus}^{exp} = 4.97 \pm 0.24$ kcal/mol and $\Delta H_{fus}^{lit.} = 4.25$ kcal/mol).

It was necessary to correct for thermal lag since the sample temperature is lower than the indicator temperature owing to inefficient heat conduction. For example, below 1.0 mg of *tert*-butyl peroxalate and 0.25 mg of cyclic peroxalate **5** the DSC instrument registered zero response. The formula

$$\Delta H_x = \frac{\Delta H_s W_s}{A_s}(m - b/W_x)$$

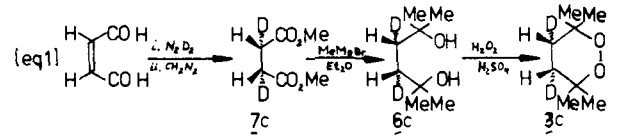
was used to correct for the thermal lag, where ΔH_x is the unknown heat of reaction, ΔH_s is the heat of reaction of the standard, A_s is the area under the thermogram of the standard, W_s is the weight of the standard, m is the slope of the area vs. weight plot, b is the intercept of that slope with the ordinate (dH/dt axis), and W_x is the weight of the unknown. The corrected heats of reaction are −99 ± 2 kcal/mol for the cyclic peroxalate and −57 ± 2 kcal/mol for the acyclic peroxalate.

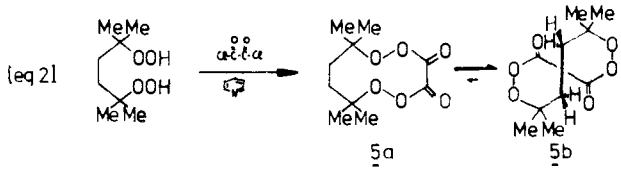
Chemiluminescence Spectra. An *o*-xylene solution, 0.1 M in peroxalate **5** and 0.05 M in rubrene, was transferred by means of a syringe into a 1-cm path length quartz cell and sealed under vacuum. The cell was placed into the sample compartment of the spectrofluorimeter and heated up to the boiling point of the solvent. With the excitation lamp off, the emission spectrum of the sample was recorded, which matched the fluorescence spectrum of rubrene.

Results

Synthesis. The 1,2-dioxanes **3** used in this study were prepared according to the procedure provided by Criegee and Paulig.[13] As an example, the stereospecific synthetic sequence for *meso*-3,3,6,6-tetramethyl-1,2-dioxane-*4,5-d*$_2$ (**3c**) is illustrated in eq 1. The preparation of the *dl-4,5-d*$_2$ stereoisomer **3d** and the tetradeuterio **3b** and tetraprotio **3a** systems followed a similar route, except that fumaric, acetylenedicarboxylic, and succinic acids were used as starting points, respectively. The deuterated compounds showed better than 95% deuteration by NMR and their physical constants and IR and NMR spectral data matched those of the parent 1,2-dioxane **3a**.

The cyclic peroxalate **5** was prepared in 10% yield analogous to Bartlett and Pincock's[7] procedure for the synthesis of *tert*-butyl peroxalate, by treating 2,5-dihydroperoxy-2,5-dimethylhexane with oxalyl chloride (eq 2). In this synthesis a polymeric peroxide is formed as major product which violently explodes when allowed to dry. Thus extreme precautions must be taken when preparing the cyclic peroxalate **5**. The latter is, however, relatively harmless in view of its enhanced thermal stability.





The cyclic peroxalate structure rests on its molecular weight, i.e., 233 ± 1 amu, determined by osmometry in chloroform, compared to 234 amu calculated for $C_{10}H_{16}O_6$. Furthermore, its IR (CCl_4) shows the expected split carbonyl band at 1812 and 1775 cm^{-1} and the *gem*-dimethyl doublet at 1390 and 1375 cm^{-1}. High-resolution NMR (100 MHz) exhibits a pair of methyl groups as a singlet at δ 1.20 ppm and the other pair as a singlet at δ 1.5 ppm, while the methylenic hydrogens occur as a pair of doublets (J = 12.5 Hz) located at δ 1.58 and 2.02 ppm. Examination of molecular models confirms that these spectral data are best accommodated in terms of the folded conformation **5b** rather than the open conformation **5a**, with a considerable barrier separating these conformers. The UV spectrum (EtOH) exhibits a λ_{max} at 215 nm (ϵ 43), with a long tail extending to 350 nm, λ 300 nm (ϵ 1.5). It was not possible to observe a parent ion in the mass spectrum, nor did the material exhibit a reliable iodometric titer, a behavior analogous to that of *tert*-butyl peroxalate.[7]

Products. The sole products of the thermolysis of the 1,2-dioxane **3** at 200 °C for 7 h in benzene were acetone and ethylene. The latter was detected as its 1,2-dibromo derivative by trapping it with bromine and by gas phase IR analysis. On photolysis of **3** at 310–350 nm for 550 h the same products were formed also quantitatively (Table I). Control experiments confirmed that 2,3-dimethyloxetane, a probable decomposition product since it is formed in the thermolysis and photolysis of γ-peroxylactones,[6] is stable under the thermal and photolytic decomposition conditions. Not even traces of this four-membered ring product were formed, suggesting that a 1,4-diradical **4** does not intervene in the thermolysis and photolysis of the 1,2-dioxane **3**.

The cyclic peroxalate **5** gave on thermal and photolytic decomposition acetone and ethylene as the major products and 1,2-dioxane **3a** as the minor product. The thermolysis was

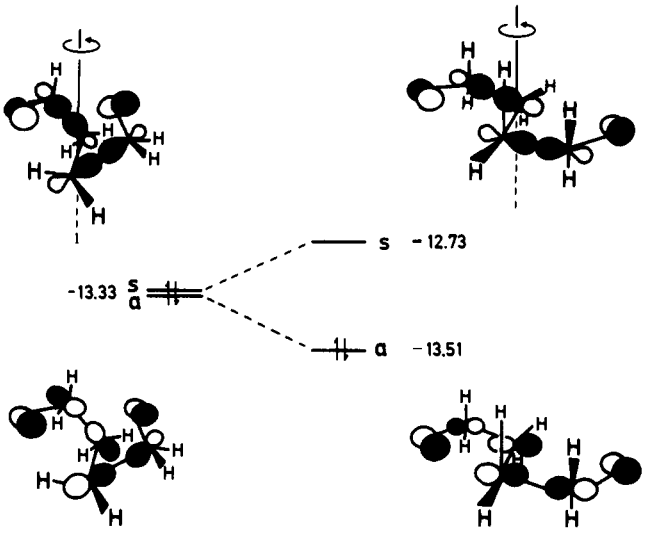


Figure 2. EHT energy diagram of diradical MO's for the 1,6-dioxahexamethylene diradical.

carried out at 120 °C for 1.25 h in benzene and the photolysis at 350 nm for 20 h in benzene, conditions which leave the 1,2-dioxane **3a** and 2,2-dimethyloxetane intact, as confirmed by control experiments. Thus, the acetone and ethylene must be directly derived from the cyclic peroxalate and not by subsequent decomposition of the 1,2-dioxane **3a**. Again, the oxetane is not formed, ruling out 1,4-diradicals as intermediates.[6]

Stereochemistry. Thermolysis of the stereolabeled 1,2-dioxanes **3c** and **3d**, *meso*- and *dl*-3,3,6,6-tetramethyl-1,2-dioxane-*4,5-d*$_2$, respectively, under the same conditions at which the tetraprotio derivative **3a** was decomposed, gave the expected 1,2-dideuterioethylenes **8a** and **8d**, but with inverted configuration (Table II). Thus, the meso isomer **3c** gave predominantly trans olefin **8d**, while the *dl* isomer **3d** gave predominantly cis olefin **8c**. Since a control experiment showed that *cis*-1,2-dideuterioethylene (**8c**) was stable toward the thermolysis conditions, in both cases the inversion process took place with ca. 70% stereospecificity. Mechanistically these results can be reconciled in terms of 1,6-diradical **9**, which fragments preferentially via its trans periplanar conformation **9A** about its C_4–C_5 bond.

The photochemical process of **3c** and **3d** affords 1:1 mixtures of cis and trans ethylenes **8c** and **8d**, respectively. Control experiments indicate, however, that under the photolysis conditions the cis ethylene **8c** is completely isomerized, rendering the stereolabeling experiment mechanistically inconclusive.

Kinetics. The activation parameters for the thermolysis of 1,2-dioxane **3a** are $\Delta H^{\ddagger} = 32 \pm 1$ kcal/mol and $\Delta S^{\ddagger} = -13 \pm 2$ gibbs/mol, corresponding to $\Delta G^{\ddagger} = 38$ kcal/mol at 500 K (Table III). Comparing this with *tert*-butyl peroxide, one of the most stable peroxides ($\Delta G^{\ddagger} = 31$ kcal/mol at 500 K),[8] we observe that the 1,2-dioxane **3a** decomposes by ca. 7 kcal/mol slower than *tert*-butyl peroxide. This corresponds to a significantly enhanced stabilization of the cyclic system; however, the stabilization is entropy rather than energy derived. In fact, on energy grounds the cyclic peroxide **3a** should decompose several magnitudes faster than *tert*-butyl peroxide since $\Delta H^{\ddagger}$ is about 6 kcal/mol lower. Again we are dealing with a case analogous to the 1,2-dioxolanes **2**.[4]

The deuterium isotope effect for the tetraprotio **3a** vs. tetradeuterio **3b** 1,2-dioxanes was 1.03 ± 0.03 (Table III), within experimental error negligible or at best small (ca. 1% per deuterium). This clearly signals that rupture of the peroxide bond in the 1,2-dioxane **3** is unaided by simultaneous C_3–C_4 and/or C_5–C_6 cleavage. Consequently, the kinetics suggest that a 1,6-diradical **9** serves as precursor to the thermoproducts.

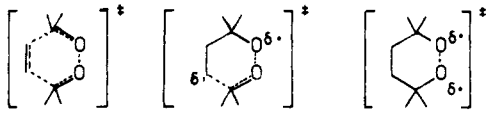
A different situation pertains to the activation parameters of the cyclic peroxalate **5**. As Table III displays, both by isothermal kinetics and by DSC, $\Delta H^{\ddagger} = 30 \pm 1$ kcal/mol and $\Delta S^{\ddagger} = 10 \pm 2$ gibbs/mol, corresponding to $\Delta G^{\ddagger} = 25$ kcal/mol at 500 K. For comparison, the activation parameters for *tert*-butyl peroxalate by DSC are $\Delta H^{\ddagger} = 22 \pm 1$ kcal/mol, $\Delta S^{\ddagger} = 1 \pm 1$ gibbs/mol, and $\Delta G^{\ddagger} = 22$ kcal/mol at 500 K, which are reasonably close to the isothermal data.[7] Clearly, again the cyclic peroxide **5** decomposes significantly slower (ca. 300-fold) than the acyclic analogue. This is dramatically visualized in the thermograms of Figure 1 for the two peroxalates, showing that the acyclic peroxalate is completely destroyed below 370 K, at which point the cyclic peroxalate **5** has barely begun to decompose. However, contrary to the 1,2-dioxane **3** vs. *tert*-butyl peroxide case, the stabilization of the cyclic peroxalate **5** vs. the acyclic analogue is energy derived, i.e., $\Delta H^{\ddagger}$ is ca. 8 kcal/mol higher for the cyclic peroxalate. On entropy grounds, the cyclic peroxalate should decompose faster since its $\Delta S^{\ddagger}$ is ca. 9 gibbs/mol greater compared to the acyclic analogue. Since for *tert*-butyl peroxalate a concerted mechanism with multiple bond fragmentation in the activated complex was demonstrated,[7] we conclude that the cyclic peroxalate **5** suffers stepwise unzipping of the two peroxide linkages. In view of the suggested conformation **5b**, based on the NMR and IR data, the molecule is ideally lined up for the cleavage of one of the peroxide bonds by simple stretching, affording initially a 1,10-diradical **10**. The latter double-decarboxylates into the 1,6-diradical **9**, which serves as precursor to the thermoproducts. The fact that the 1,6-diradical **9** derived from the cyclic peroxalate **5** couples into the 1,2-dioxane **3** suggests that the generation of the 1,6-diradical **6** from the 1,2-dioxane **3** is reversible. On the basis of these intriguing activation parameters, we coin the cyclic peroxalate **5** as "conformationally stabilized" in that lone pair repulsions in the peroxide linkages are minimized in the folded conformation, which increases the bond energy of the peroxide linkage and consequently its thermal stability.

Heats of Reaction and Chemiluminescence. From the DSC thermograms we determined that the heats of reaction (ΔH) for the thermolysis of the cyclic and acyclic peroxalates were -99 ± 2 and -57 ± 2, respectively. Thus, the cyclic peroxalate **5** releases almost twice as much heat as the acyclic analogue. On this basis alone we would expect the cyclic peroxalate to decompose faster were it not for the conformational stabilization. It would be instructive to estimate the heats of reaction from thermochemical group additivities,[17] but insufficient data are on hand. However, in view of the very large exothermicity of the cyclic peroxalate **5**, during thermolysis sufficient energy is being released to expect acetone to be electronically excited.[18] Although the direct chemiluminescence of acetone was too feeble to be picked up, rubrene could be energized by energy transfer. No chemiluminescence could be detected for *tert*-butyl peroxalate even in the presence of rubrene.

Mechanistic Conclusions

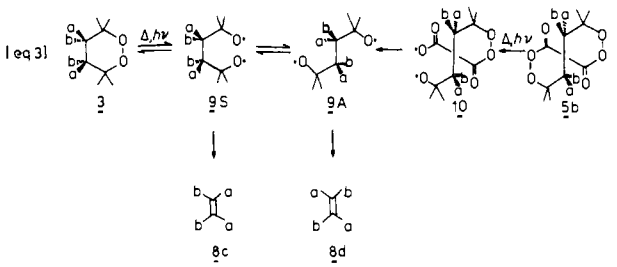
Three activated complexes are likely in the decomposition of 1,2-dioxanes **3**. These are the completely concerted three-bond cleavage via **11A**, the two-bond cleavage via **11B** affording a 1,4-diradical, and the simple one-bond cleavage via **11C** to the 1,6-diradical **19**. Our stereochemical and kinetic results rule out the activated complex **11A** since retention of configuration in the ethylene and an appreciable isotope effect (ca. 10% per deuterium) would be expected. The activated complex **11B** is discarded by the same evidence since the 1,4-diradical would lead to completely isomerized olefin and an appreciable isotope effect. In addition, the 1,4-diradical

would be expected to close up into 2,2-dimethyloxetane,[7] a product that is not even formed in traces.



11A 11B 11C

The most plausible mechanism, which is consistent with the experimental data on hand, involves the 1,6-diradical **9**, produced by simple peroxide bond cleavage via the activated complex **11C** (eq 3). If rotation about the C_4–C_5 bond of the syn 1,6-diradical **9S** into the anti 1,6-diradical **9A** competes favorably with fragmentation, we would expect the observed inversion as the dominant course. Efficient reclosure to the 1,2-dioxane **3** would explain the low $\Delta S^{\ddagger}$ factor. A small or negligible secondary isotope effect is reasonable for the double fragmentation of the 1,6-diradical **9**.



Why should the syn 1,6-diradical **9S** prefer to isomerize into the anti 1,6-diradical **9A** rather than double deketonate directly? Extended Hückel theory (EHT) calculation provided some insight into this question. The most stable conformation of the 1,2-dioxane **3** is a chair conformation since lone pair repulsions in the peroxide bond are minimized. Thus, on thermal activation the shearing motion about the peroxide bond would lead initially to the gauche conformation of the syn 1,6-diradical **9S**. In this gauche conformer the two diradical MO's are degenerate in energy at −13.33 eV by EHT. As the gauche conformer **9S** relaxes to the trans-periplanar conformer **9A** due to steric repulsions, the two diradical MO's split in energy to the extent of ca. 0.8 eV by EHT as the result of bonding and antibonding π character in the incipient olefin (Figure 2). Consequently, fragmentation in the anti conformer **9A** is energetically favored compared to the syn conformer **9S**. Thus, while in the 1,2-dioxane first the peroxide bond is cleaved without any assistance from multiple bond cleavage, the resulting 1,6-diradical suffers concerted fragmentation by double deketonation via a trans-periplanar transition state.

The cyclic peroxalate, especially in its folded conformation **5b**, is lined up for single peroxide bond cleavage, giving initially a 1,10-diradical **10** (eq 3). By double decarboxylation, the 1,6-diradical **5** is generated; some of it cyclizes into 1,2-dioxane **3**, but most of it fragments into acetone and ethylene. In the latter process sufficient energy is made available to produce electronically excited acetone. We are presently investigating the efficiency and selectivity of this chemiluminescent system.

In conclusion, it is interesting to mention that in the biological oxygenation of arachidonic acid into prostaglandins via the endoperoxides **1**, an appreciable amount of malonaldehyde and olefin are formed.[19] This pyrolase activity is analogous to the fragmentation of the 1,6-diradical **9**, generated from 1,2-dioxanes **3** or cyclic peroxalate **5** by thermolysis at photolysis.

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