Oxygen Diradicals Derived from Cyclic Peroxides[1]

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Received May 10, 1979

The first systematic attempts to generate carbon diradicals and explore their chemical behavior and physical properties date back about 50 years to Wittig's work.[2] He dubbed this class of reactive intermediates "diyls". Subsequently, excepting sporadic efforts, for several decades this challenging field of mechanistic organic chemistry lay essentially dormant. With the advent of the Woodward–Hoffmann theory of orbital symmetry conservation,[3] fresh interest in these fascinating species was kindled. In the interim there has appeared an avalanche of papers on diradicals, as well as numerous reviews.[4]

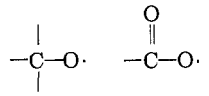
The major impetus for this renaissance in diradicals derives from the logical expectation that orbital symmetry forbidden reactions may occur stepwise. Consequently diradicals are probable intermediates in homolytic bond fission or bond fusion. It is, therefore, not surprising that deliberate and intensive efforts ensued to generate and detect diradical intermediates and elucidate their structures and behavior. Most of these efforts have been directed toward carbon-centered diradicals, only few toward heteroatom-centered derivatives. This Account focuses on the latter type of diyls, specifically the oxygen-centered diyls or dioxyls, i.e., oxygen diradicals.

For the generation of simple oxyl radicals, the appropriate acyclic peroxides are thermally or photolytically decomposed, forming first a solvent-caged radical pair. Diffusion out of the solvent cage leads to the free oxyl radicals (eq 1). For example, in this way alkyl

$$\mathrm{RO\text{-}OR} \xrightarrow[\text{or } h\nu]{\Delta} \overbrace{\mathrm{RO\cdot \quad \cdot OR}} \longrightarrow 2\mathrm{RO\cdot} \qquad (1)$$

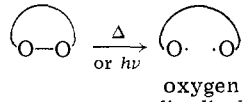
caged oxyls free oxyls

peroxides afford alkoxy radicals **1**,[5a] diacyl peroxides acyloxy radicals **2**,[5b] and peroxyesters a pair of alkoxy



1 **2**

and acyloxy radicals.[5c,d] It follows that on enclosure of the peroxide linkage into a cyclic structure, thermal and photochemical activation should afford dioxyls (eq 2)

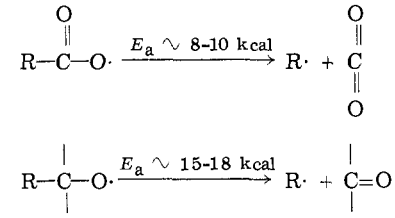


oxygen diradical (2)

as intermediates. Consequently, cyclic peroxides should be convenient precursors to the little explored oxygen diradicals.

From the point of view of chemical behavior, the fundamental difference between an oxygen diradical and a caged pair of oxyl radicals is that the latter can diffuse apart to become statistically free radicals. Of course, if the intervening carbon chain between the two oxyl termini in the diradical is infinitely long, for all practical purposes each oxyl site will behave independently. In such a case it should be possible to infer the chemistry of the dioxyls directly from that of the statistically free oxyl radicals.

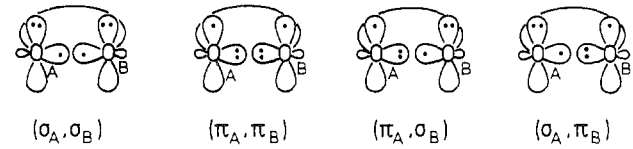
For example, an acyloxy radical site will decarboxylate, while an alkoxy radical site will suffer β scission (eq 3), but usually decarboxylation will outweigh β



(3)

scission since the activation energies are significantly lower.[5] However, when the intervening carbon chain is short, typically two to four atoms, the electrons of the two oxyl ends interact appreciably. Such interactions are expected to lead to new electronic states. Thus, the unpaired spins can align parallel (a triplet state) or antiparallel (a singlet state). In contrast, two noninteracting spins exist as a pair of doublet states.

Furthermore, because each oxyl center carries a lone pair and an unpaired spin, the spatial accommodation of these six electrons leads to four distinct electronic configurations. The designations σ(in-plane) and π-



(σ_A,σ_B) (π_A,π_B) (π_A,σ_B) (σ_A,π_B)

(out-of-plane) refer to the spatial assignments of the unpaired spins on oxygen atoms O_A and O_B.[6] Conse-

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(1) This paper, No. 100 in the Cyclic Peroxide Series, I dedicate with gratitude to Professor Frederick D. Greene, III, Massachusetts Institute of Technology.

(2) Wittig, G. *Acc. Chem. Res.* **1974**, *7*, 6.
(3) Hoffmann, R.; Woodward, R. B. *Acc. Chem. Res.* **1968**, *1*, 17.
(4) (a) Bergman, R. G. "Free Radicals"; Kochi, J. K., Ed.; Wiley-Interscience: New York, 1973; Vol. I, p 191. (b) Salem, L.; Rowland, C. *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 92.
(5) (a) Hiatt, R. In "Organic Peroxides"; Swern, D., Ed.; Wiley: New York, 1972; Vol. 3, Chapter 1. (b) *Ibid.*; Vol. 2, Chapter 8. (c) Singer, L. A. *Ibid.*, Vol. 1, Chapter 5. (d) Kochi, J. K. In "Free Radical"; Kochi, J. K., Ed., Wiley: New York, 1973; Vol. 2, Chapter 23.
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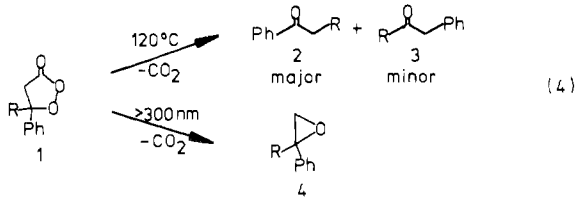
Table I
Alkyl to Phenyl Rearrangement Ratios in the Thermolysis of the β-Peroxylactones 1

	1a	1b	1c	1d	1e	1f	1g
R	Me	Et	*i*-Pr	Bz	Bz	Bz	Bz
a	H	H	H	H	H	Me	Me
b	H	H	H	H	Me	H	Me
R/Ph	5.6	14.5	55	36.5	21.0	12.2	6.4

quently, we expect novel chemistry from the oxygen diradicals, dependent on the electron configuration and the spin multiplicity of these intriguing reaction intermediates.

Numerous examples of oxygen diradicals have been postulated in thermal and photochemical transformations of cyclic peroxides, but only in a few cases have such claims been mechanistically scrutinized. Our intensive study of some instances demonstrates that these reactive intermediates exhibit unusual and entertaining chemistry.

For illustration, let us consider the thermal[7] and photochemical[8] decarboxylation of β-peroxylactones 1 (eq 4). That this case conforms to the above premises



(4)

is immediately apparent from the products. First, in the thermal process alkyl migration which affords ketone **2** outweighs the normally expected phenyl migration[9] which leads to ketone **3**. Second, the photoextrusion of CO_2 leads to epoxide **4** as the major product rather than to ketones **2** and **3**. Indeed, if it could be demonstrated that diradicals intervene in eq 4, then such diradicals represent a class of bona fide reaction intermediates.

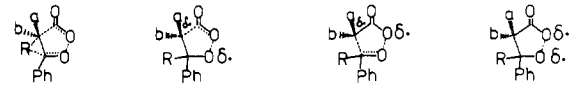
Thermolysis of β-Peroxylactones

Product Studies. The β-peroxylactones **1** were prepared by acid-catalyzed cyclization of β-hydroxy acids with 98% H_2O_2[10] or by perhydrolysis of β-lactones.[11] Thermolysis of the β-methyl-β-phenyl derivative **1a** at moderate temperatures, ca. 120 °C, afforded rearranged ketones **2a** and **3a** (eq 4) as the major products (Table I), along with minor amounts of acetophenone, but only traces of epoxide **4a**. Control experiments confirmed that epoxide **4a** is stable under the reaction conditions. Furthermore, the respective enol ethers did not lead to the observed products.[10] Since the ca. sixfold preference for alkyl migration over aryl shift is rare in free-radical rearrangements,[9] we examined other β-alkyl substituents. In all cases (Table I) alkyl migration is preferred over phenyl, the actual ordering being *i*-Pr > Bz > Me > Ph.[7] Interesting are the erythro and threo isomers[12] whose behavior shows a conformational effect on the migratory aptitude.

Table II
Activation Parameters for the Thermolysis of β-Peroxylactones

	R	a	b	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu	ΔG_{400}, kcal/mol
1a	Me	H	H	31.7	+0.1	31.7
1b	Et	H	H	31.2	+0.3	31.1
1c	*i*-Pr	H	H	31.1	−1.0	31.5
1d	Bz	H	H	31.0	−0.8	31.3
1e	Bz	H	Me	28.0	−1.3	28.5
1f	Bz	Me	H	28.2	−1.5	28.8
1g	Bz	Me	Me	28.4	+1.2	27.9

Mechanistic Preview. Before devising experiments to scrutinize the mechanism of this thermal decarboxylation, let us consider the four possible but reasonable activated complexes **1A**‡ through **1D**‡, which exhibit

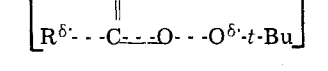


1A‡ **1B**‡ **1C**‡ **1D**‡

varying degrees of multiple bond breakage. For example, in **1A**‡ three-bond scission leads to ketone **2** via the most concerted path. In **1B**‡ and **1C**‡ we consider two-bond cleavages of which **1B**‡ ultimately leads to 1,3-diradical **6** and CO_2 and **1C**‡ to an α-lactone fragment and ketone. This latter path represents only a very minor product-forming step and will be discarded. Finally, **1D**‡ represents the least concerted path which leads ultimately to the 1,5-diradical **5** prior to CO_2 formation.

Activation Parameters. To distinguish between the alternatives **1D**‡ (1,5-diradical pathway) and the various concerted ones, we examined[7,13] the effect of β and α substitution on the $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ parameters (Table II). Clearly, variation of the migrant structure, i.e., R = Me, Et, *i*-Pr, and Bz, does not affect significantly the $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values.

This is to be contrasted with acyclic peroxyesters[14] in which variation of the R structure of the acyl moiety from Me through Bz causes a ca. 10-kcal drop in the $\Delta H^{\ddagger}$ values and a ca. 15-eu decrease in the $\Delta S^{\ddagger}$ values. The activated complex



accounts for these trends. This implies that our kinetic data (Table II) are not consistent with the activated complexes **1A**‡ and **1C**‡.

α-Substitution (last four entries in Table II) does suggest some multiple bond cleavage, but the effect is small and irregular. In view of the difficulty in acquiring accurate activation parameters and the problem of conformational effects, we investigated the kinetic isotope effect.

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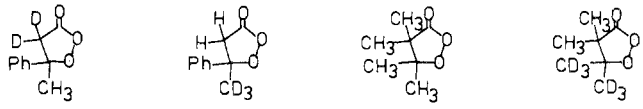
Table III
Solvent Effects on the Activation Parameters in the Thermal Decarboxylation of β-Peroxylactone 1j

solvent	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu	ΔG_{383}, kcal/mol
CCl_4	28.7 ± 0.3	1.7 ± 0.4	28.0 ± 0.4
c-C_6H_{12}	28.6 ± 0.2	1.4 ± 0.3	28.1 ± 0.5
C_6H_6	28.3 ± 0.4	1.0 ± 1.2	27.9 ± 0.5
CH_3CN	26.7 ± 0.2	1.8 ± 0.6	27.4 ± 0.6

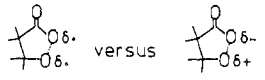
Secondary Deuterium Isotope Effects. For this purpose the deuterium-labeled β-peroxylactones **1h**, **1i**, and **1k** were prepared and their thermolysis kinetics



1h 1i 1j 1k

studied.[15] The k_H/k_D values were 0.99 ± 0.03, 1.01 ± 0.03, and 0.99 ± 0.03, respectively, for β-peroxylactones **1h**, **1i**, and **1k**. Clearly, there is no secondary isotope effect at the β-carbon, e.g., **1i** and **1k**, nor at the α-carbon, e.g., **1h**. For comparison, an appreciable secondary isotope effect (k_H/k_D = 1.17) has been reported[16] for thermolysis of *tert*-butyl phenylperacetate on deuteration of the benzylic position.

The isotope effect and the activation parameter data rule out activated complexes **1A‡**, **1B‡**, and **1C‡** as major pathways in the thermal decarboxylation of the β-peroxylactones 1. Therefore, we postulate the activated complex **1D‡**, ultimately leading to 1,5-diradical **5**, as the reaction path to rationalize our results.

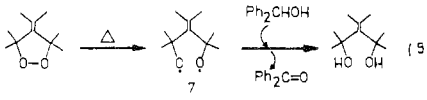


1D‡ versus 1E‡

Solvent Effects. One mechanistic feature that needed to be explored concerned the polar character of the thermal decarboxylation. We had to consider the possibility that the peroxide bond cleaved heterolytically via activated complex **1E‡**. We therefore probed the solvent effect for the β-peroxylactone **1j**.[15] The results are given in Table III. It is obvious from the data that the dipolar structure **1E‡** cannot accommodate our results because the rate difference between cyclohexane and acetonitrile should have been several powers of ten rather than threefold, as observed.

It is of interest to mention that β-peroxylactone **1j** affords essentially quantitatively (ca. 99%) pinacolone in all four solvents. Therefore, there exists no solvent effect in conversion of the postulated 1,5-diradical **5** into products.

Trapping Experiments. The most convincing technique to establish the intermediacy of diradicals is either through matrix isolation[17] or through trapping.[18] Since benzhydrol proved successful[19] for trapping the 1,5-dioxyl **7** (eq 5), we applied it to thermolysis of the



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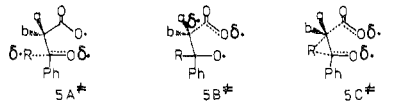
β-peroxylactone **1j**. Under all conditions, avoiding induced decomposition, we observed only ketones **2** and **3** with no traces of the β-hydroxy acid that would be formed from the tetramethyl dioxyl diradical (**5j**) by transfer of two hydrogens from benzhydrol. This suggests that if this diradical (**5j**) indeed exists, to have evaded trapping its lifetime must be shorter than 10^{-7} s.

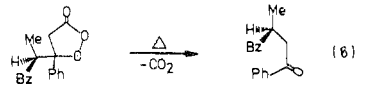
Fate of the Postulated 1,5-Diradical 5. Accepting the intervention of a short-lived 1,5-diradical in the thermolysis of β-peroxylactones, let us ask what is its mechanistic fate during its decarboxylation into ketones **2** or **3**? Again it is instructive to entertain plausible alternatives, as illustrated in activated complexes **5A‡**, **5B‡**, and **5C‡**. Thus, based on what we know about the



5A‡ 5B‡ 5C‡

chemistry of oxyl and carbonyl radicals,[20] in **5A‡** β-scission at the oxyl site precedes decarboxylation, leading eventually to a radical pair. The latter on decarboxylation and coupling should afford rearranged ketone **2**. In **5B‡** the contrary occurs, i.e., decarboxylation at the carboxyl site affords 1,3-diradical **6**; subsequent R migration leads to ketone **2**. Finally, in **5C‡** β scission and decarboxylation occur essentially simultaneously.

Stereochemical labeling experiments are best suited to sort out these mechanistic alternatives. For example, **5A‡** generates on β scission an essentially free R radical. Consequently, an optically labeled R group should tell us how free R becomes in **5A‡** during its migration. For this purpose the resolved β-peroxylactone **1l** was synthesized and thermally decarboxylated into ketone **2l** (eq 6).[21] Within experimental error, R migrates with

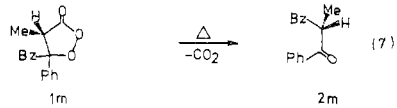


(6)

1l 2l

complete retention of configuration. Such perfect stereochemical control cannot be reconciled in terms of a pair of caged radicals derived from **5A‡** since substantial, but not necessarily complete,[22] racemization of the asymmetric migrant is expected.

In **5B‡** decarboxylation frees the α carbon once the 1,3-diradical **6** is attained. We would expect again extensive racemization at an optically labeled α carbon prior to 1,2-shift of the β-alkyl group. To probe this possibility, the optically active β-peroxylactone **1m** was prepared and decarboxylated into ketone **2m** (eq 7).[23]



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1m 2m

The stereolabeling experiment revealed that the migration terminus inverts essentially quantitatively. This stereospecificity defies the 1,3-diradical route via **5B‡**.

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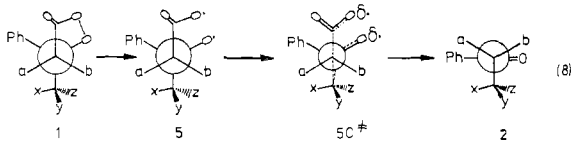
Table IV
Product and Quantum Yields for the Decarboxylation of β-Peroxylactone 1j

process	conditions	yields, % 3j	4j	$Me_2C=O$	total
thermolysis	125 °C, c-C_6H_{12}	100 ± 0.5	-	-	100 ± 0.5
TMD-energized	60 °C, n-C_6H_{12}	0.9 ± 0.1	97 ± 2	a	98 ± 2
photolysis (direct)	355 nm, n-C_6H_{12}	49 ± 3	22 ± 1	26 ± 4	97 ± 4
photolysis (1.0 M Pip)[b]	355 nm, n-C_6H_{12}	50 ± 2	20 ± 2	25 ± 5	95 ± 5
photolysis (sensitized)	313 nm, acetone	32 ± 1	44 ± 1	a	76 ± 2

[a] Acetone yield could not be determined. [b] Pip = piperylene.

Consequently, the fully concerted 1,2 shift shown in **5C**‡, i.e., concurrent β scission and decarboxylation, best reconciles our experimental findings.

Mechanism of Thermal Decarboxylation. The complete mechanistic drama is displayed in eq 8. With



(8)

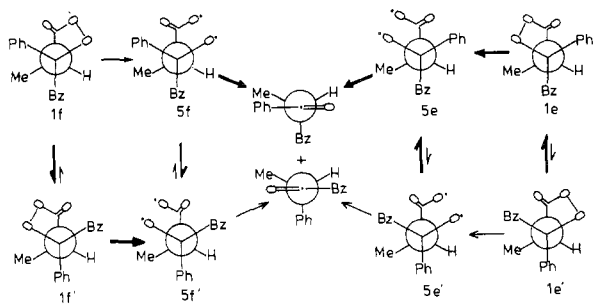
the help of Newman projections, we focus on the trans-periplanar arrangement of the migrant (β substituent) and leaving group (CO_2), retention of configuration of the migrant and inversion of configuration of the migration terminus. Thus, transposition of the R migrant and detachment of the CO_2 leaving group take place essentially concurrently, but they become initiated only after breaking of the peroxide bond via the activated complex **1D**‡ into 1,5-diradical **5**. That the activation barrier for the β-alkyl migration in the 1,5-diradical **5** must be low is supported by the negligible secondary deuterium isotope effect on the Me/Ph migration ratio. For example, the β-peroxylactone **1a** and its deuterated analogue **1i** gave Me/Ph ratios of 5.92 ± 0.10 and 5.85 ± 0.15, respectively, leading to $k_H/k_D = 1.02 \pm 0.02$.[15] This negligible isotope effect implies that bond-breaking at the β carbon and bond-making at the α-carbon must take place essentially concurrently.

Such a tight lineup of migrant and leaving group in the activated complex **5C**‡ implies that steric interactions exerted by the β substituents **a** and **b** should affect the alkyl/phenyl migratory aptitudes. For this purpose the *erythro*- and *threo*-β-peroxylactones **1e** and **1f** were prepared and their Bz/Ph migration ratios were determined as 21.0 ± 0.3 and 12.2 ± 0.2 (Table I).[12] These results are rationalized in Scheme I, in which we emphasize the interactions between the α and β substituents as the result of conformational effects. Such steric factors make it plausible why **1f** prefers conformation **1f′** (bold arrows), while **1e** does not prefer conformation **1e′**. Also for the 1,5-diradical conformation **5f′** should predominate over **5f** and a low Bz/Ph ratio should be expected. However, the intrinsic preference for benzyl over phenyl migration as the result of electronic factors overrides the steric factor in such 1,5-diradicals.

Photolysis of β-Peroxylactones

Product Studies. The photolysis of the β-peroxylactones takes a different course. For example, the β-methyl-β-phenyl derivative **1a** gave 50% α-methylstyrene oxide, 11.5% acetophenone (fragmentation ketone), 7.1% propiophenone (β-methyl migration), and 7.6% phenylacetone (β-phenyl migration) on irradiation at λ >300 nm in benzene in a Pyrex vessel.[8] Piperylene

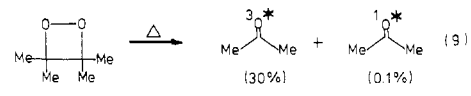
Scheme I



in concentrations up to 1 M has little effect on the photoproduct composition; this implies that the initial singlet excited β-peroxylactone leads faster to product-forming intermediates than to intersystem crossing.

Quantum Yields. The tetramethyl derivative **1j** was examined in greater detail, with use of the usual photomechanistic tools.[24] The quantum yield of disappearance of **1j** was found to be 100%. Furthermore, the ketone products (pinacolone and acetone) sensitized the photodecarboxylation of **1j**. Therefore, quantum yields were determined up to 15–20% β-peroxylactone consumption and irradiations were performed at long wavelengths (>350 nm) to minimize sensitization by products. The results are summarized in Table IV, together with those from the thermal and tetramethyl-1,2-dioxetane (TMD) energized decompositions.

Formation of pinacolone (**3j**) as the major product in the thermolysis of β-peroxylactone **1j** was expected, but what was surprising was the very high product specificity, i.e., 100% ketone **3j**. Not even traces of tetramethyloxirane (**4j**) could be detected. Still more unusual is the chemienergized decarboxylation by tetramethyl-1,2-dioxetane (TMD). Since the latter is known[25,26] to generate efficiently (ca. 30%) triplet excited acetone (eq 9), the TMD-energized photo-



(9)

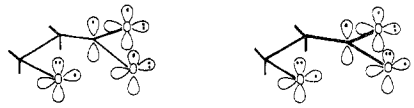
decarboxylation of β-peroxylactone **1j** must be brought about by the triplet excited acetone. To explain these results, a triplet state tetramethyl 1,5-dioxyl (**5j**) could be postulated in the TMD-energized process and a singlet state in the thermolysis. However, the full mechanistic picture is definitely more complex.

For example, in the direct photolysis at 355 nm (Table IV) both pinacolone (49 ± 3%) and epoxide (22 ±

(24) Adam, W.; Cueto, O.; Guedes, L. N., unpublished results.
(25) Turro, N. J.; Lechtken, P. *J. Am. Chem. Soc.* **1972**, *94*, 2886.
(26) Adam, W.; Cheng, C.-C.; Cueto, O.; Sakanishi, K.; Zinner, K. *J. Am. Chem. Soc.* **1979**, *101*, 1324.

1%) are formed. Assuming that a singlet excited (n → π*) β-peroxylactone **1j** decarboxylates predominantly into pinacolone, presumably via singlet-state 1,5-dioxyl **5j**, and the remainder intersystem-crosses to give triplet excited **1j**, which decarboxylates into epoxide **4j** presumably via triplet-state 1,5-dioxyl **5j**, would rationalize the direct photolysis results. But this does not make sense if we inspect the piperylene-quenching data (Table IV). The photoproducts remain unaltered[27] up to 1.0 M piperylene concentration. If singlet excited **1j** were long-lived enough to intersystem-cross into triplet excited **1j**, then an effective triplet-state quencher such as piperylene should have altered the product composition. Moreover, the lack of fluorescence and the 100% quantum yield for consumption of β-peroxylactone **1j** imply that in the photoenergized singlet excited state of **1j** the weak peroxide bond rapidly ruptures to afford a singlet 1,5-diradical and that there is not sufficient time for intersystem crossing. However, how do we account for the epoxide **4j** product in the direct photolysis which is clearly triplet state derived (cf. TMD-energized results)?

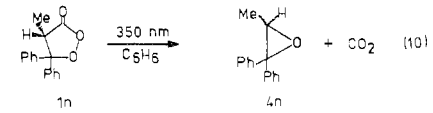
A reasonable but not necessarily the only way out of this mechanistic deadlock is to postulate that, depending on the mode of activation, the 1,5-dioxyl **5j** exists in two distinct electronic configurations, each exhibiting its specific chemistry. Such theoretical predictions have been made for the acyloxy[28] and succinimidyl[29] radicals and experimentally confirmed[30] for the latter. Therefore, we propose that a more stable and selective π-type 1,5-dioxyl (**5π**) is produced in the thermal process and



a more labile σ-type 1,5-dioxyl (**5σ**) is generated in the photolysis. Of course, allowance must be made for the spin states of these electronic isomers, depending on singlet or triplet sensitization.

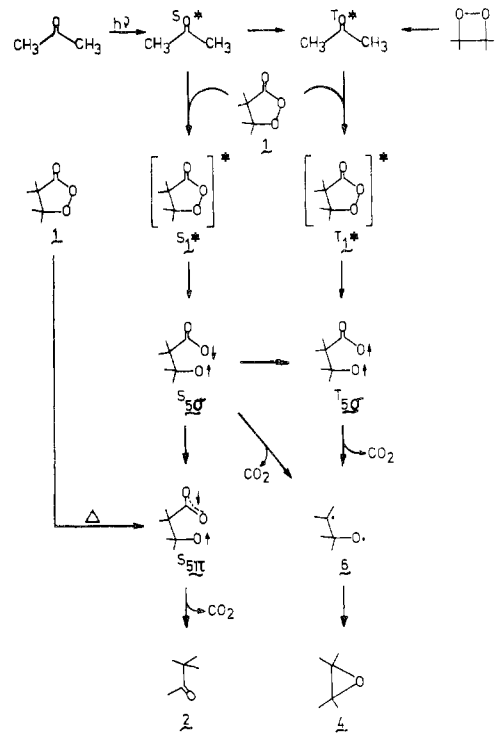
In that respect the acetone sensitized results are informative (Table IV). Using acetone as solvent and irradiating at 313 nm, we obtain from β-peroxylactone **1j** again pinacolone (32%) and epoxide (44%), the latter now predominating. If this reaction were strictly triplet acetone sensitized as in the TMD-energized process, then the exclusive product should have been the epoxide. We suspected that the β-peroxylactone is an efficient quencher of singlet excited acetone and thus intercepts in part the intersystem crossing into triplet excited acetone. Indeed, when we varied **1j** by 10-fold, i.e., from 0.01 to 0.10 M, the pinacolone/epoxide product ratio **3j**/**4j** increased from ca. 0.08 to 0.70. Clearly, at the higher β-peroxylactone concentration more singlet excited acetone was intercepted. Unfortunately, the quenching process did not follow linear Stern–Volmer kinetics to permit quantitative analysis.

Stereochemistry. Here it was of interest to test the stereochemical course of epoxide formation in the photodecarboxylation. For this purpose optically active β-peroxylactone **1n** was prepared and photodecarboxylated at 350 nm in benzene, affording totally racemized epoxide **4n** (eq 10).[8] The optically active



epoxide **4n** was prepared via a stereospecific route and shown not to photoracemize under the photodecarboxylation conditions of **1n**. We assume that the 1,5-dioxyl radical **5n**, presumably of σ-type electronic configuration at the acyloxy site, first decarboxylates into 1,3-diradical **6n**, from which subsequently the epoxide product **4n** is derived by cyclization. A theoretical analysis predicts[28] that a σ-type acyloxy radical should efficiently decarboxylate.

Scheme II



Mechanism of Photodecarboxylation. In Scheme II are summarized our mechanistic interpretations of the direct, acetone-sensitized, and TMD-energized photodecarboxylation of β-peroxylactones. In view of the complete lack of optical activity in the epoxide product, the 1-oxatrimethylene diradical **6** must be the immediate precursor to this photoproduct.

The genesis of this 1,3-diradical intermediate is obviously complex. For example, the direct photolysis (355 nm) gives both ketone **3** and epoxide **4**. Since the intersystem crossing step ^{S}**1*** → ^{T}**1*** is unlikely, the singlet excited β-peroxylactone ^{S}**1*** formed initially on photoexcitation suffers immediate peroxide bond rupture to afford the 1,5-dioxyl ^{S}**5**σ. The electronically excited ^{S}**5**σ diradical must somehow relax to the ground state ^{S}**5**π diradical to afford ketone **3**, which is the exclusive product in the thermolysis. In competition with this relaxation process is the production of epoxide **4**, presumably derived from the 1,3-diradical **6**. Whether the 1,3-diradical **6** is formed via ^{S}**5**σ → **6** + CO_2 or via ^{S}**5**σ → ^{T}**5**σ → **6** + CO_2 cannot be answered with the data

(27) At [Pip] > 1.0 M, e.g., neat piperylene, a very complex chemical reaction is observed, leading to intractable products. We suspect chemical trapping of diradical intermediates.
(28) Koenig, T.; Wielesek, R. A.; Huntington, J. G. *Tetrahedron Lett.* **1974**, 2283.
(29) Koenig, T.; Wielesek, R. A. *Tetrahedron Lett.* **1975**, 2007.
(30) Skell, P. S.; Day, J. C. *Acc. Chem. Res.* **1978**, *11*, 381.

on hand. Similarly, it cannot be decided whether in the triplet-sensitized process the triplet excited β-peroxylactone affords the 1,3-diradical **6** directly via $^T\mathbf{1}^* \rightarrow \mathbf{6} + CO_2$ or via the alternative diradical path $^T\mathbf{1}^* \rightarrow {}^T\mathbf{5}\sigma \rightarrow \mathbf{6} + CO_2$. We favor the latter path.

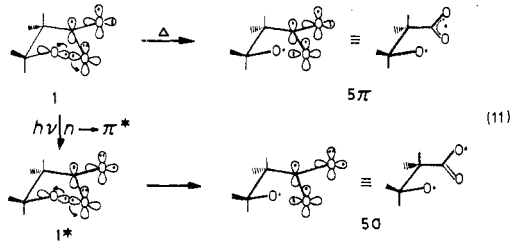
It should be apparent that the postulated mechanistic picture in Scheme II is complex and speculative and will require further scrutiny and verification, but it does offer an internally consistent interpretation of our data.

Genesis of 1,5-Dioxyls

Accepting our postulate that 1,5-diradicals are bona fide reaction intermediates in the decarboxylation of β-peroxylactones, then we require a π-type 1,5-diradical in the thermolysis and σ-type 1,5-diradical in the photolysis in order to reconcile our experimental findings. It is important to emphasize that the structures **5σ** and **5π** are electron isomers of one another, **5σ** being the electronically excited species of the more stable **5π** 1,5-dioxyl. Theoretical work[28] suggests that the π-type acyloxy radical is by ca. 37 kcal/mol more stable than the σ-type. Furthermore, decarboxylation of a π-type acyloxy radical should lead to electronically excited CO_2, which is energetically prohibitive, while decarboxylation of a σ-type acyloxy radical should afford ground-state CO_2. Therefore, the more stable **5π** diradical should be quite sluggish, while the labile **5σ** diradical should be quite eager to expel CO_2.

These theoretical notions permit us to rationalize the astounding observation that alkyl migration outweighs phenyl migration in the thermal decarboxylation. The 1,5-dioxyl **5π** that is formed in the thermolysis is quite selective in its decarboxylation and must derive considerable assistance from the oxyl site to push the alkyl group over to the α-carbon prior to any significant decarboxylation at the acyloxy site. Activation energies definitely would favor decarboxylation over β scission by at least 5–8 kcal/mol, but the electronic barrier in the π-type structure more than offsets this apparent advantage. Since the driving force is principally oxyl center derived, it is not surprising that alkyl migration wins out over aryl migration.[31]

Why should, however, the thermal process lead to a π-type and the photolytic process to a σ-type 1,5-dioxyl, i.e., **5π** and **5σ**, respectively? In eq 11 we attempt to



(11)

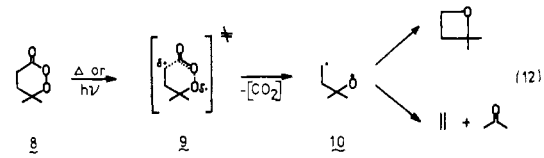
answer this query. In the thermal mode the already tense five-membered ring, shown in the conformation with an optimal dihedral angle of the peroxide linkage, must twist rather than stretch apart the oxygen–oxygen bond. This twisting motion is illustrated by the arrows. Such vibrational deformation seems to be quite suitable to overlap the odd-electron orbital with the π-orbital of the carbonyl double bond. This adiabatic path should favor the more stable and selective **5π** diradical.

On the other hand, the photochemical mode appears to be n–π* derived.[32] Suitable lineup of the odd-electron orbital developing at the carboxylate oxygen through the twisting mode in the n–π* excited **1** should lead to the more labile **5σ** diradical. Therefore, the divergent chemical behavior of the β-peroxylactones on thermal and photochemical activation can be rationalized in terms of the postulate that 1,5-dioxyls of distinct electronic configuration intervene.

Related Work and Outlook

This detailed discussion of the mechanism of decarboxylation of the β-peroxylactones suggests that cyclic peroxides in general should offer a fruitful and challenging opportunity for the exploration of the chemistry of diradicals. In fact, a number of related cyclic peroxides have been mechanistically scrutinized and are briefly discussed below.

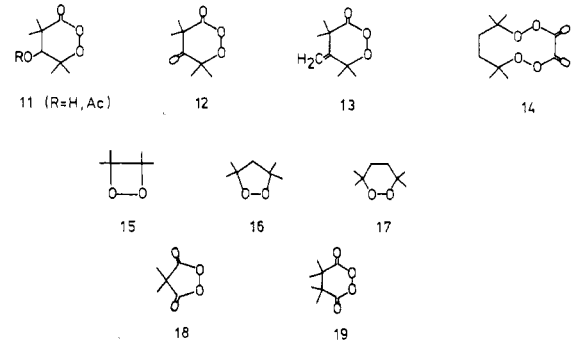
By employing the mechanistic tools utilized in the β-peroxylactone study, we showed[33] that the related γ-peroxylactones **8** on thermal and photolytic activation expel CO_2 via a concerted two-bond cleavage transition state, **9**, leading first to the 1,4-diradical **10**. Subsequently the 1,4-diradical **10** fragments or cyclizes (eq 12).



(12)

8 **9** **10**

More recently the mechanism of decarboxylation of the γ-peroxylactone derivatives **11**–**12** have been re-



11 (R=H, Ac) **12** **13** **14**

15 **16** **17**

18 **19**

ported.[34] Unlike the γ-peroxylactone **8**, derivative **11** prefers to deketonate rather than decarboxylate, leading to β-lactone products. On the other hand, the γ-peroxylactones **12** and **13** prefer again to decarboxylate to give dimethylketene (isolated as dimer) and allene, respectively, as major products. Neither dimethylmalonyl anhydride nor tetramethyl-3-oxetane was detected, although both are stable under the thermolysis conditions. The low activation enthalpy ($\Delta H^{\ddagger}$ = 27 kcal/mol) and entropy ($\Delta S^{\ddagger}$ = 5.3 eu)[34] imply a three-bond cleavage; however, more mechanistic scrutiny will be necessary to substantiate these interesting results.

Adam and Sanabia[35] have investigated the photolysis of the cyclic peroxalate **14** and shown that it is a con-

(31) (a) Martin, J. C.; Hargis, J. H. *J. Am. Chem. Soc.* **1970**, *92*, 5399. (b) Sheldon, R. A.; Kochi, J. K. *Ibid.* **1970**, *92*, 4395, 5175.

(32) Photoelectron spectroscopy shows that the lowest energy ionization is out of the carbonyl oxygen lone pair. We are grateful to Professor Dr. Rolf Gleiter (Heidelberg) for this measurement.

(33) Adam, W.; Szendrey, L. M. *J. Am. Chem. Soc.* **1974**, *96*, 7135.

(34) Gibson, D. H.; Joseph, J. T. *J. Am. Chem. Soc.* **1978**, *100*, 3641.

(35) Adam, W.; Sanabia, J. *J. Am. Chem. Soc.* **1977**, *99*, 2735.

venient low-temperature source for 1,6-dioxyl radicals. The thermal and photochemical products were carbon dioxide, ethylene, and acetone (60–65%) and 3,3,6,6-tetramethyl-1,2-dioxane (18%).

The cyclic dialkyl peroxides which have received considerable attention are the 1,2-dioxetanes **15**,[36] the 1,2-dioxolanes **16**,[37] and the 1,2-dioxanes **17**.[35] With the help of the mechanistic tools that were described in the elucidation of the β-peroxylactones, the respective diradicals were postulated as reaction intermediates.

Among the cyclic diacyl peroxides, the malonyl peroxides **18**[38] and the succinyl peroxides **19**[39] have been worked on. The thermal and photochemical decarboxylation of the malonyl peroxides **18** gave cleanly the elusive α-lactones. Consequently, these substrates seem to be of little use for the generation of oxygen diradicals.

The succinyl peroxide **19**, on the other hand, was a fruitful system for mechanistic elucidation of dioxyl radicals. Using the *meso*- and *dl*-dimethylsuccinyl derivatives, it was shown[39] that the same ratio of *cis*- and *trans*-2-butenes, 61% and 28%, respectively, and the same ratio of *meso*- and *dl*-β-lactones, 10% and 3%, respectively, were formed from both diacyl peroxides **22a,b**. A 1,4-diradical was proposed to account for these interesting experimental data.

Finally, work on the thermal decomposition of bicyclic dialkyl peroxides is beginning to appear.[40] However, rigorous mechanistic studies seem to be in order for the full exploration of the conformationally anchored dioxyl intermediates. Such mechanistic investigations are timely, urgent, and important. We foresee a great deal of mechanistic activity on the versatile and fascinating dioxyl intermediates and certainly encourage it.

I wish to express my gratitude to my students, whose names are referenced in the bibliography, for their enthusiastic and dedicated collaboration. Without their diligent efforts there would be no Account. Our work was supported by the National Institutes of Health, National Science Foundation, the Petroleum Research Fund, administered by the American Chemical Society, the Guggenheim Foundation, the Sloan Foundation, Research Corporation, Western Fher Company, Eli Lilly Company, and the University of Puerto Rico.

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(37) Adam, W.; Duran, N. *J. Am. Chem. Soc.* **1977**, *99*, 2929.
(38) Adam, W.; Rucktäschel, R. *J. Org. Chem.* **1978**, *43*, 3886.
(39) Dervan, P. B.; Jones, C. R. *J. Org. Chem.* **1979**, *44*, 2116.
(40) (a) Coughlin, D. J.; Salomon, R. G. *J. Am. Chem. Soc.* **1977**, *99*, 655. (b) Salomon, R. G.; Salomon, M. G.; Coughlin, D. J. *Ibid.* **1978**, *100*, 660. (c) Schuster, G. B.; Bryant, L. A. *J. Org. Chem.* **1978**, *43*, 521.

Alkaloids from Nitrones

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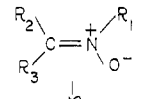
Received March 8, 1979

Although the education of the organic chemist has traditionally involved an exposure to the chemistry of a plethora of functional groups, only recently has significant attention been focused on the important chemistry of certain 1,3-dipolar functionalities.[1-3] Indeed, applications of these dipolar substrates to the synthesis of natural products has been a very recent development.[4,5] Noteworthy is the elegant application of nitrile oxide chemistry to the synthesis of corrins.[4] We have been long convinced that nitrones, in particular, offer unique advantages in total synthesis. The nitrone functionality (cf. 1), so designated because of an ob-



served chemical relationship to ketones,[6] is a 4-π-electron system capable of undergoing reaction with other multiply bonded systems in a process not unlike the Diels–Alder reaction. Although the addition of nitrones to phenyl isocyanate was described in the last century,[7] their additions to alkenes were reported relatively recently and independently by three separate groups.[8-10] The brilliant efforts of Huisgen[1,11] are largely responsible for the important and systematic exploration of intermolecular 1,3-dipolar cycloadditions to afford five-membered heterocycles ([3 + 2] cycloadditions),[3,11] while LeBel[12] is responsible for the pioneering investigations of the factors influencing intramolecular nitrone–alkene cycloadditions.

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