CIDNP experiment, was carried out on a Waters Associates high-pressure liquid chromatograph equipped with a μBONDAPAK C-18 column using 50% CH_3CN–H_2O eluent at a flow rate of 1 mL min^{-1}. This analysis revealed nitrobenzene (0.066 mmol, 26.2%), **3b** (0.015 mmol, 11.6%), *p*-nitrophenyl azide (0.023 mmol, 9.1%), *p*-nitroaniline (0.026 mmol, 10.3%), and *p*-nitrophenylhydrazine (0.043 mmol, 16.9%).

Effect of Aryldiazonium Salt Concentration on ^1H CIDNP Intensity. Four solutions of **2a** or **2b** (0.056, 0.12, 0.18, and 0.27 M in CH_3CN) were prepared. A suspension of $NaBH_4$ (30 mg, 0.790 mmol) in 0.3 mL of CH_3CN was added. The spectra of each solution was recorded as soon as possible after mixing and the intensity of the strongest emission peak measured. The emission intensity in centimeters plotted as a function of the square of concentration of **2a** or **2b** is shown in Figure 3.

Decarboxylation of Aryldiazenecarboxylates. Potassium *p*-nitrophenyldiazenecarboxylate (**4b**, 60 mg, 0.26 mmol) and 0.4 mL of CH_3CN were placed in an NMR tube. Glacial acetic acid (0.3 mL, 5.25 mmol) was added and the ^1H NMR spectra immediately recorded. Emissions for the protons of nitrobenzene were observed (δ 7.57, 8.20 ppm). For ^{13}C studies, 200 mg (0.86 mmol) of **4b** in 1.0 mL of CH_3CN and 1.0 mL of glacial acetic acid (17.5 mmol) were employed. Emissions for the ortho and para carbons of nitrobenzene (δ 123.7, 134.3 ppm, Figure 2) and an enhanced absorption for C_1 (δ 154.5 ppm, Figure 2) of **4b** were observed.

The decarboxylation of phenyldiazenecarboxylate (**4a**) was investigated by mixing 50 mg (0.27 mmol) of the salt with 21 mg (0.26 mmol) of dimethylamine hydrochloride in 0.5 mL of Me_2SO and recording the ^1H NMR spectrum at 90 °C. These conditions resulted in an emission for the protons of benzene (δ 7.23 ppm).

Reduction of 2a and 2b with Cycloheptatriene. This reaction was initially investigated by preparing solutions containing equimolar amounts of **2a** or **2b** and cycloheptatriene. The ^1H NMR spectrum indicated that reduction was taking place as evidenced by the appearance of signals for tropylium ion (δ 9.3 ppm) and for the arene. When an acetonitrile solution of **2b** and cycloheptatriene was placed in the probe at 80 °C, emission for the ortho and meta protons of nitrobenzene was observed.

UV Spectrum of *p*-Nitrophenyldiazene (1b). A solution containing equimolar quantities of **2b** and cycloheptatriene in CH_3CN (1.3×10^{-4} M) was prepared. The UV spectrum of this solution, recorded 24 h after preparation on a Cary 17 spectrometer, showed a peak at 274 nm attributed to **1b**.

A similar experiment was conducted using excess sodium borohydride in place of cycloheptatriene. Identical peaks for **1b** were observed at 274 nm in both studies.

Acknowledgment. We are grateful to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for the support of this research.

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Oxygenation of 3-Aryl-2-hydroxyacrylic Acids. The Question of Linear Fragmentation vs. Cyclization and Cleavage of Intermediates

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Abstract: Radical-initiated autoxidation of the enolic tautomer of 4-hydroxyphenylpyruvic acid (**6**) gives the β-hydroperoxy-α-ketocarboxylic acid **9**, which decomposes in inert solvents producing 4-hydroxybenzaldehyde (**8**), carbon monoxide, and carbon dioxide. Base-promoted decomposition of **9** depends on the base used. Nucleophilic bases such as methoxide ion add to the ketone function of **9** creating a tetrahedral intermediate which cleaves to **8** and monomethyl oxalate. *tert*-Butoxide ion, a bulky base, generates the peroxide ion of **9**, which cyclizes onto the ketone function giving the 1,2-dioxetane **7**, which spontaneously cleaves to **8** and oxalic acid. In the absence of base, **9** does not cyclize to **7**. Dye-sensitized photooxygenation of **6** in inert solvents gives oxalic acid and carbon monoxide and dioxide. Quenching studies reveal that oxalic acid results from addition of singlet oxygen to give **7**, whereas "ene" reaction of singlet oxygen and free-radical, type I processes lead to **9**, which collapses to the oxides of carbon. The ratio of the two pathways is dye dependent. Mechanisms are discussed together with their relevance to bioluminescent processes and the cleavage of phenols by dioxygenases.

Whether or not α-hydroperoxycarbonyl compounds cyclize to dioxetanes is of crucial importance in understanding the mechanisms of phenol cleavage by dioxygenases[1] and certain bioluminescent processes.[2] Depending on the nature of the terminal carbonyl substituent (X), cyclization can occur with or without the loss of acid (HX). Subsequently, the

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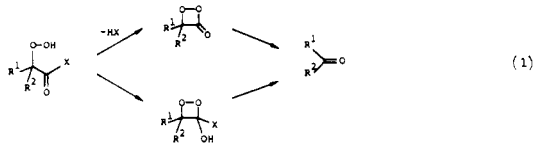
dioxetane so formed can cleave to give the ketone (eq 1). Such cyclizations have been frequently proposed to account for the base-catalyzed fragmentation of α-hydroperoxy ketones [3a]

Recently, however, product and kinetic studies have demonstrated that an acyclic mechanism (eq 2) can compete with and may eventually predominate over the cyclic alternative (eq 3).[4] In principle, a base of the alkoxide type (RO^-) can either



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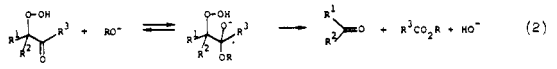

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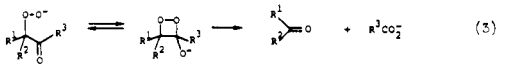
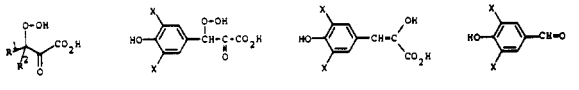


(3)

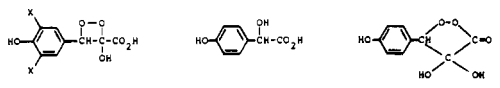
add to the carbonyl function or abstract a proton from the hydroperoxy group. In the first event, fragmentation to ester, ketone, and hydroxide ion is the logical outcome (eq 2), whereas in the second, the peroxide anion can cyclize to a dioxetane which will cleave to carboxylate and ketone (eq 3).

Convincing evidence, however, for the spontaneous cyclization of α-hydroperoxy ketones in the absence of base has not been forthcoming. This may be simply due to insufficient activation of the carbonyl function in the particular molecules studied.[3] In view of the readiness shown by α-keto acids to form hydrates and to add hydrogen peroxide, β-hydroperoxy-α-keto acids (**1**) should be excellent candidates for spontaneous cyclization.

The diiodophenylhydroperoxypyruvic acid (**2**) obtained from autoxidation of the enol tautomer of the corresponding arylpyruvic acid **3** represents the only member of this class to have been detected so far.[5,6] Unfortunately, **2** is too unstable to be isolated and it decomposes to give the arylaldehyde **4** and oxalic acid via the supposed intermediacy of the dioxetane **5.** Similar dioxetane intermediates have also been proposed to account for the chemiluminescent, base-catalyzed autoxidation of other arylpyruvic acids.[7]



1 — 2 X=I, 9 X=H — 3 X=I, 6 X=H — 4 X=I, 8 X=H



5 X=I, 7 X=H — 10 — 11

Prompted by a recent report of the dye-sensitized photooxygenation of the enolic arylpyruvic acid **6** in which the dioxetane **7** was postulated as an intermediate,[8] we have investigated the oxygenation of the enol **6** under a variety of conditions[9] and now give an account of our findings.

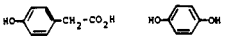
Results and Discussion

Autoxidation of 6 in Aqueous Solution. Nishinaga et al.[5] have reported that the diiodoarylpyruvic acid **3** is completely oxygenated after 1 h in aerated borate buffer (pH 7.4). Under identical conditions, we found that the nonhalogenated acid **6** was significantly less reactive in that approximately 50% had reacted after 7 days. Still longer periods led to the isolation of the arylaldehyde **8,** thereby indicating that rates of both formation and decomposition of the supposed intermediate hydroperoxy keto acid **9** are similar. Attempts to isolate and purify **9** were thwarted by its rapid decomposition on extraction with organic solvents.

Good evidence for the intermediacy of **9** was obtained, however, from several sources. NMR spectroscopy of partially reacted solutions of **6,** which had been concentrated in vacuo, showed a singlet at 6.1 ppm attributable to the benzylic proton in **9** which was readily distinguishable from the singlet at 6.5 ppm due to the vinylic proton in **6.**

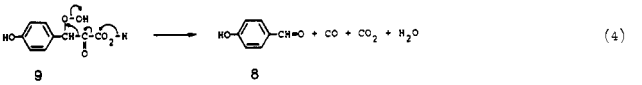
Acidification and concentration of partially oxygenated solutions of **6** in borate buffer permitted the isolation of a mixture of unreacted **6,** the aldehyde **8,** and 4-hydroxymandelic acid **10.** A likely explanation for the appearance of the last product is that the proposed hydroperoxy keto acid **9** has undergone oxidative decarboxylation with accompanying reduction of the hydroperoxy group.[10] One could imagine this redox process occurring either intermolecularly or even intramolecularly by excision of a molecule of carbon dioxide from the lactone hydrate **11.**

Additional evidence for the hydroperoxy keto acid **9** was obtained by adding excess hydrogen peroxide to a partially oxygenated solution of **6.** A clean mixture of the arylacetic acid **12** and hydroquinone **13** was obtained. The former product



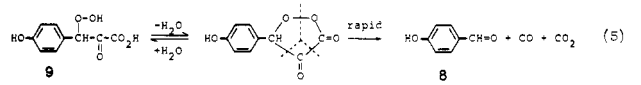
12 — 13

results from the action of hydrogen peroxide on the keto tautomer of the starting material **6,** which simply undergoes oxidative decarboxylation.[11] Of course, it could be argued that any process leading to **8** would account for hydroquinone (**13**). Nevertheless, there is circumstantial evidence that **9** is the precursor to **13.** In borate buffer the decomposition of **9** is slow, allowing it to be identified by NMR spectroscopy (cf. eq 4). Acidification accelerates its decomposition, presumably through the intermediacy of the peroxylactone which promptly splinters to the oxides of carbon and aldehyde **8** (eq 5).[12a]



(4)

9 — 8



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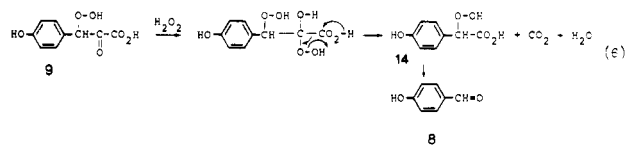
9 — 8



(6)

9 — 14 — 8

Significantly, the addition of hydrogen peroxide to **9** in borate buffer also causes rapid decomposition by successive decarboxylation, passing through the α-hydroperoxy acid **14** to give **8** by Grob fragmentation[12b] (eq 6). The aldehyde **8** is then oxidized via the Dakin reaction[13] with hydrogen peroxide yielding hydroquinone (**13**).

Autoxidation in Acetonitrile. Azobis(isobutyronitrile)-initiated autoxidation of **6** in boiling acetonitrile gave a number of products. Their relative proportions are listed in Table I (entry 1). Oxalic acid was not detected, although independent experiments have shown that it would have been stable under the reaction conditions. Evolution of carbon monoxide and dioxide presumably accounts for the loss of this two-carbon fragment. A mechanism which explains the formation of these gases is that in acetonitrile the intermediate hydroperoxy keto acid **9** undergoes a linear fragmentation similar to that of oxalic acid monochloride[14] (eq 4) or that the peroxylactone intervenes (eq 5).

Table I. Products Obtained from the Oxygenation of the Enolic Tautomer of 4-Hydroxyphenylpyruvic Acid (**6**)

entry	conditions[a]	aromatic products[b] 8	10	12	oxalic[c] acid	gaseous products[d] CO	CO_2[e]	oxalic acid % CO %
1	In·, O_2	62[f]	10	3		71	95	0
2	RF*, O_2	86	tr	14	8	74	100	0.10
3	RB*, O_2	90	4	6	21	66	65	0.31
4	TPP*, O_2	85		14	40	41	80	0.98
5	MB*, O_2	82	11	7	38	40	72	0.95
6	RB*, O_2, Dabco[g]	78	tr	11		60	104	0
7	RB*, O_2, β-car[h]	71		8	tr	45	31	0
8	RB*, O_2, DBPC[i]	36		29	18	30	51	0.60

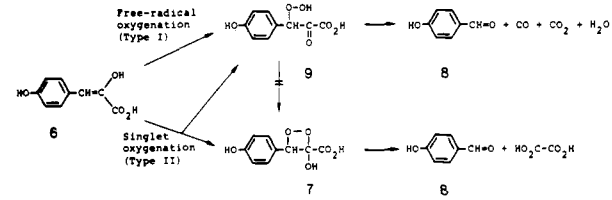
[a] See Experimental Section. All reactions were carried out on 5.5 mmol of 4-hydroxyphenylpyruvic acid (**6**) in 50 mL of CH_3CN; In· = azobis(isobutyronitrile), 10^{-3} M at 78 °C for 6 h. Dye* = irradiation with visible light for 6 h at 5 °C (ref 31) in the presence of dye, 10^{-3} M (RF = riboflavin, RB = rose bengal, TPP = tetraphenylporphine, and MB = methylene blue). Reactions 6, 7, and 8 were performed with Dabco (1,4-diazabicyclo[2.2.2]octane, 10^{-3} M), β-car (β-carotene, 10^{-3} M), and DBPC (2,6-di-*tert*-butyl-*p*-cresol, 5.5 mmol). [b] Percentage yields from GLC of trimethylsilyl derivatives based on molar response ratios and adjusted to 100% for total aromatic products (tr = trace, estimated error ±5%). [c] Percentage yield from GLC of bistrimethylsilyl ester relative to total aromatic products. [d] Yield as percentage of 5.5 mmol of $BaCO_3$ precipitated from aqueous $Ba(OH)_2$ solution by effluent gases before (for CO_2) and after oxidation by I_2O_5/H_2SO_4 (for CO). [e] Often in excess of prediction owing to additional unspecified oxidations. [f] 4-Hydroxybenzoic acid (20%) and various unidentified minor products (total 5%) also obtained. [g] 11%, [h] 20%, and [i] 35% unreacted starting material.

Dye-Sensitized Photooxygenation in Acetonitrile. Dye-sensitized photooxygenation of **6** in acetonitrile was found to be essentially complete after 4 h. No reaction occurs in the absence of either light or dye. The distribution of products was found to be extremely sensitive to the nature of the dye (entries 2–5, Table I). This was most evident for the relative yields of oxalic acid and the oxides of carbon which, as alternative ways of eliminating the two-carbon fragment, are representative of two competing processes. Strictly speaking, the ratio of oxalic acid to the sum of carbon monoxide and dioxide would be a proper index of these two processes. However, as carbon dioxide can be liberated by unspecified side reactions (e.g., entry 6, Table I), we have chosen as a surer guide the ratio of oxalic acid to carbon monoxide alone (Table I).

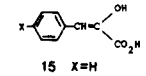
It is widely recognized that dye-sensitized photooxygenation can either occur by free-radical reactions between excited sensitizer, substrate, and triplet oxygen or through the intervention of singlet oxygen as the discrete reactant. These processes have been classified as type I and type II, respectively,[15] and numerous examples are known in which both compete.[16] In fact, the distribution of nonaromatic products in Table I shows a decreasing resemblance to free radical initiated autoxidation (entry 1) in descending order (entries 2–5). We interpret this trend as reflecting the increasing ability of sensitizers to favor type II processes. This variation in behavior correlates reasonably well with our expectations based on sensitizer properties. Photoexcited riboflavin, for instance, is a poor sensitizer of oxygen, and is known to undergo free-radical reactions.[17] Although rose bengal is regarded as a good sensitizer of oxygen, CIDNP studies[18] have shown that similar xanthene dyes cause type I processes in the photooxygenation of phenols. We have also noticed a spectral change in rose bengal when α-keto acids are present,[19] which is probably due to partial protonation of the dye, thereby diminishing its ability to promote type II, but not necessarily type I, processes. Experiments, in which type I or type II processes were selectively inhibited, support this proposal. When concentrations of either 1,4-diazabicyclo[2.2.2]octane or β-carotene were sufficiently low to significantly quench singlet oxygen, but not the excited dye[20] (entries 6 and 7), formation of oxalic acid was completely suppressed. On the other hand, the presence of a known terminator of chain autoxidation, 2,6-di-*tert*-butyl-*p*-cresol, produced the opposite effect and enhanced the yield of oxalic acid (entry 8, Table I).

We believe that the foregoing observations can be adequately rationalized as follows (Scheme I). Free-radical oxygenation of **6** (type I or radical initiated) appears to lead only to the hydroperoxy keto acid **9**, whereas singlet oxygen adds to the electron-rich double bond of **6** to give **9** by the "ene" reaction and the dioxetane **7** by [2 + 2] cycloaddition. In acetonitrile, the hydroperoxy keto acid **9** collapses to the oxides of carbon, water, and the arylaldehyde **8**, while the dioxetane **7** neatly cleaves to oxalic acid and **8**. The inability of free-radical oxygenation to generate oxalic acid clearly demonstrates that the hydroperoxy keto acid **9** cannot spontaneously cyclize to the dioxetane **7**.

Scheme I



Changing the para substituent of the arylpyruvic acid does not affect the overall reaction course, but merely alters the balance between the various pathways. Rose bengal sensitized photooxygenation of phenylpyruvic acid (**15**) gave an oxalic acid/carbon monoxide ratio of 1.2 (cf. 0.32 for **6**, entry 3, Table I). Benzoic acid from further oxidation of benzaldehyde (88%) and phenylacetic acid (12%) were also obtained. Similar treatment of 4-methoxyphenylpyruvic acid (**16**) gave 4-



15 X=H
16 X=OCH_3

methoxybenzaldehyde (90%), 4-methoxybenzoic acid (5%), 4-methoxymandelic acid (trace), and an oxalic acid/carbon monoxide ratio of 0.1. It is difficult to say whether these variations are due to the effect of substituent on the relative proportions of type I and type II processes or on the relative amounts of "ene" and [2 + 2] modes of singlet oxygenation.

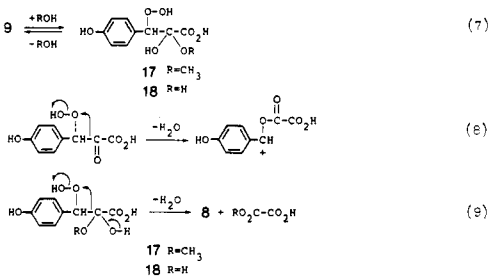
Effect of Solvent and Bases. The products of methylene blue sensitized photooxygenation are not altered substantially when the solvent is changed from acetonitrile to methanol (entries 1 and 2, Table II); however, the formation of free oxalic acid rather than its monomethyl ester in methanol is interesting. We have observed that a number of α-keto acids form hemiacetals in methanol.[19] Consequently, the hemiacetal **17** may well form, but obviously plays no part in the fragmentation of the hydroperoxy keto acid **9**. This contrasts with autoxidation

Table II. Products Obtained from the Oxygenation of the Enolic Tautomer of **6** in Various Solvents and Basic Media

entry	conditions[a]	aromatic products[b] 8	10	12	oxalic acid[b]	gaseous products[b] CO	CO_2	oxalic acid % CO %
1	MB*, O_2, CH_3CN	82	11	7	28	40	72	0.95
2	MB*, O_2, CH_3OH	95		5	44[c]	25	40	1.76
3	BB, O_2, H_2O	100			70			∞
4	SH, O_2, H_2O	100			80		*d*	∞
5	SM, O_2, CH_3OH	100			80[e]		*d*	∞
6	PB, O_2, DMSO	100			35[f]	15	*d*	2.33

[a] All reactions were carried out on 5.5 mmol of **6** in 50 mL of various solvents. MB* = methylene blue (10^{-3} M) irradiated with visible light (ref 31). BB = 0.2 M sodium borate buffer, pH 7.4. SH = sodium hydroxide (55 mmol). SM = sodium methoxide (55 mmol). PB = potassium *tert*-butoxide (55 mmol). [b] As for Table I. [c] No monomethyl oxalate. [d] CO_2 dissolves, cannot be measured. [e] Entirely monomethyl oxalate. [f] No *tert*-butyl oxalate.

in water at pH 7.4 (entry 3) where oxalic acid formation presumably results from cleavage of the hydrate **18.** This apparent discrepancy springs from the conditions which are different. Owing to the strength of the α-keto acid (pK_a = 2.4), oxygenation in methanol (entry 2) proceeds under high acidity, whereas borate buffer (entry 3) ensures alkalinity. In a general way, three processes ought to be favored by acid (eq 5, 7, and 8). Under basic conditions two processes are feasible (eq 4 and 9).



(7)

(8)

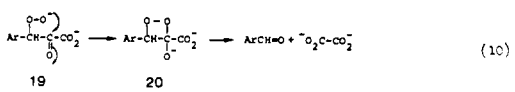
(9)

In pure methanol, eq 5 dominates over eq 7 (R = CH_3) as water is removed by the anhydrous medium, thereby displacing the equilibrium. The acyl shift (eq 8), which would be revealed by trapping with methanol, does not operate as the potential migrating group is electron poor. In water at pH 7.4, fragmentation would be expected (eq 4), but, as already mentioned, this is slow. Although hydration (eq 7, R = H) is not favored, it still persists;[21] consequently base cleaves the hydrate **18** (eq 9, R = H) giving aldehyde **8.**

In the presence of bases, autoxidation of **6** occurs readily in the absence of light. In aqueous sodium hydroxide (entry 4), only oxalic acid was obtained.[22] Although evolution of carbon dioxide would not be expected from basic solution, carbon monoxide should be, but nevertheless was not, detected.[22]

In methanolic sodium methoxide (entry 5) monomethyl oxalate was obtained instead of free oxalic acid and, moreover, no carbon monoxide was evolved. This suggests that in both these cases decomposition proceeds by attack of hydroxide or methoxide ion on the carbonyl group followed by cleavage (eq 9).

Potassium *tert*-butoxide catalyzed autoxidation of **6** in dimethyl sulfoxide is reported to be weakly chemiluminescent.[7] We found that under these conditions both oxalic acid and carbon monoxide were formed. No trace of mono-*tert*-butyl oxalate was detected. Most probably, *tert*-butoxide ion is too bulky to be able to attack the carbonyl group of **9.** Instead it simply removes a proton from the hydroperoxy group, whereupon closure to the dioxetane occurs (**19** → **20,** eq 10),



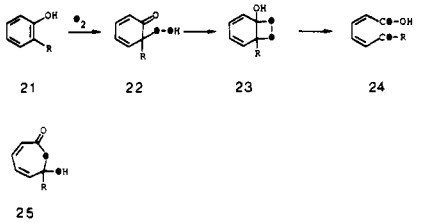
(10)

which is ultimately responsible for chemiluminescence and oxalic acid. Nonetheless, as the conditions are strongly basic, fragmentation (eq 4) giving carbon oxides vies with cleavage.

Conclusions

Our results demonstrate that the ketone function in the hydroperoxy keto acid **9,** although sufficiently susceptible to nucleophilic attack, does not undergo uncatalyzed cyclization to a dioxetane to any detectable degree. In methanol and acetonitrile, fragmentation to the oxides of carbon takes place. In aqueous solution or in the presence of nucleophilic bases, attack at the carbonyl group gives a tetrahedral intermediate which subsequently cleaves to oxalic acid and aldehyde. Bulky bases, which cannot approach and bond to the carbonyl group, promote base-catalyzed cyclization to a dioxetane which spontaneously cleaves with chemiluminescence.

The inability of the β-hydroperoxy group in **9** to attack the adjacent carbonyl group despite its high reactivity toward nucleophiles may be relevant to those biological processes for which dioxetane intermediates have been frequently proposed. For example, the cyclization of hydroperoxy ketone intermediates **22** to transitory dioxetanes **23** has been proposed[23] to account for the pattern of labeled oxygen in the acid product **24** deriving from the dioxygenase-catalyzed cleavage of certain phenolic substrates **21** (eq 11). Hamilton,[24] however, has

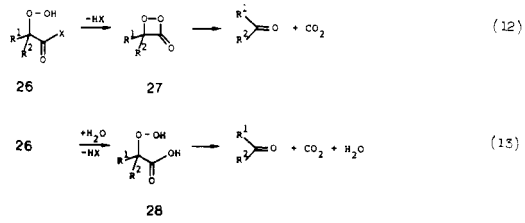


(11)

pointed out that highly strained dioxetanes are not obligatory intermediates as rearrangement of **22** to **25** would also give the same labeling pattern. Complexation of **22** with the ferric cofactor has recently been suggested to enhance this rearrangement.[25]

Our results must be taken as support for Hamilton's proposal. As the carbonyl function of **22** is less activated than that of **9,** cyclization to **23** would not be expected to occur without considerable help from the enzyme.

Dioxetane intermediates have also been proposed to explain the bioluminescent decarboxylation of the peroxidized luciferins of fireflies, coelenterates, and the crustacean, *Cypridina.*[2,26] The key question of whether the leaving group X of the luciferyl hydroperoxide **26** is displaced by the adjacent hydroperoxy group to give the α-peroxylactone **27** (eq 12) or by water to the α-hydroperoxycarboxylic acid **28** (eq 13) *should* have been resolved by labeling studies. Unfortunately, these have so far been contradictory.[2,26] Our findings clearly favor the latter mode of fragmentation. Although the carboxylic acid function of **9** cannot act as a leaving group, it should activate



(12)

26 27

(13)

26 28

the α-carbonyl group as much as the X groups do in the peroxidized luciferins. The preference shown by **9** to add water rather than cyclize suggests that the same may be true in the biological system.

Experimental Section

Materials. 4-Hydroxyphenylpyruvic acid (**6**),[27] 4-methoxyphenylpyruvic acid (**16**) (mp 185 °C, lit.[28] 185–187 °C), and 4-methoxymandelic acid[29] were prepared by standard procedures. Monomethyl oxalate was obtained by hydrolysis of Merck methyloxalyl chloride. Trimethylsilyl derivatives were prepared according to House et al.[30] Reactions carried out in basic media were acidified with dry hydrogen chloride and evaporated to total dryness before treatment with bis-(trimethylsilyl)acetamide. This last reagent, phenylpyruvic acid, DL-mandelic acid, 4-hydroxymandelic acid, azobis(isobutyronitrile), 2,6-di-*tert*-butyl-4-methylcresol, and all the dyes were purchased from Fluka AG (Buchs, CH-9230) and were used without purification.

Analytical Methods. Carbon dioxide was determined by passing effluent gases through a sequence of traps containing aqueous barium hydroxide. The weight of precipitated barium carbonate was calibrated with carbon dioxide liberated from a known weight of sodium carbonate. All figures quoted have been adjusted accordingly. Carbon monoxide was determined by the oxidation of decarbonated effluent gases using a solution of iodine pentoxide in sulfuric acid. Carbon dioxide so produced was then determined in the previously described manner. Analysis of the precipitated barium carbonate revealed no sulfate.

NMR spectra were recorded on a Varian T-60 spectrometer. Gas chromatograms of trimethylsilyl derivatives were performed on a Carlo Erba Model FTV/2100 instrument equipped with a flame ionization detector. For analysis, a 90-cm 15% SE-30 column was used. A program in which the temperature rose at 3.5 °C increments min^{-1} from 80 to 200 °C after an initial 3-min pause was adopted with carrier gas flowing at 100 mL min^{-1}. The reaction products were isolated on a 1.5-m 20% SE-30 preparative column. Approximate analytical column retention times in minutes (with relative molar response ratios) for the trimethylsilyl derivatives of the following compounds are: monomethyl oxalate, 7.1 (0.45); oxalic acid, 8 (0.50); 4-hydroxybenzaldehyde, 14.2 (0.52); 4-hydroxybenzoic acid, 17.5 (0.67); 4-hydroxyphenylacetic acid, 18 (0.85); 4-hydroxymandelic acid, 21 (0.81); 4-hydroxyphenylpyruvic acid, 25.3 (1.00); benzoic acid, 15 (0.36); mandelic acid, 18.5 (0.65); phenylacetic acid, 15 (0.60); phenylpyruvic acid, 22.6 (0.76); 4-methoxybenzoic acid, 20 (0.45); 4-methoxyphenylacetic acid, 20.5 (0.65); 4-methoxymandelic acid, 23 (0.70); and 4-methoxyphenylpyruvic acid, 25.0 (0.85). Benzaldehyde, 10.2 (0.30), and 4-methoxybenzaldehyde, 16.8 (0.37), do not form trimethylsilyl derivatives.

High-pressure liquid chromatographic (LC) analyses were performed using a Waters 6000A chromatograph. Untreated reaction mixtures were analyzed using a μ-Bondapak 30 cm by 4 mm column eluted with a 60:40 mixture of water and methanol at a flow rate of 2 mL min^{-1} at 3000 psi. The eluent was monitored for UV absorption at 254 nm. This technique was used to verify qualitatively the results obtained by GLC.

Oxygenation in Aqueous Borate Solution. A 0.25×10^{-3} M solution of 4-hydroxyphenylpyruvic acid in 0.2 M boric acid adjusted to pH 7.4 by addition of sodium hydroxide was oxygenated with a stream of oxygen at 0–2 °C. Reaction progress was monitored according to the procedure of Nishinaga et al.[5] using UV spectrophotometry. Only partial reaction was indicated after 7 days. Concentration in vacuo at 10 °C permitted NMR examination (in H_2O) which showed that the starting material (indicated by vinyl proton at 6.5 ppm), 3-hydroperoxy-3-(4-hydroxyphenyl)-2-oxopropionic acid (**9**) (C–H at 6.1 ppm), and 4-hydroxybenzaldehyde were the only species evident. Acidification to pH 3.5 and extraction of this solution with ethyl acetate gave a mixture of unreacted starting material (50% by NMR), 4-hydroxybenzaldehyde (ca. 30%), and 4-hydroxymandelic acid (ca. 20%). The original unconcentrated solution from 7 days oxygenation was also treated with excess (10×) of 30% hydrogen peroxide. After 24 h the reaction mixture was acidified and extracted with ethyl acetate. NMR spectroscopy indicated a 50:50 mixture of 4-hydroxyphenylacetic acid and hydroquinone. The presence of these products was verified by TI C.

Acknowledgment. We are indebted to the Swiss National Science Foundation for the support of this research (Grant 2.430-0.75).

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