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PHOTOSENSITIZED OXYGENATION OF THE ENOL FORMS OF 1,2-CYCLOHEXANEDIONES

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Abstract: The enols of 1,2-cyclohexanediones have been found to undergo a photosensitized oxygenation in methanol to afford 5-oxoalkanoic acids and methyl 5-carboxy-2-hydroxypentanoates with liberation of carbon monoxide with a remarkable temperature dependency of the product distribution, which is best accounted for in terms of trapping of a five-membered endoperoxide intermediate by methanol.

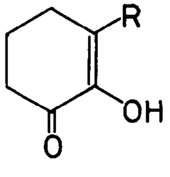
The ene reaction is considered to be common for enols in the photosensitized oxygenation.[1] However, no work has been reported about the enols 1a,b of 1,2-cyclohexanediones.[2] Since the enol function of 1 is conjugated with an electron-withdrawing carbonyl group, the mode of reaction with electrophilic singlet oxygen is hardly predicted. However, Matsuura and co-workers disclosed as an enzymatic model for quercetinase dioxygenation that 3-hydroxyflavones which have the conjugated enol function undergo the photosensitized oxygenation through the ene reaction.[3] We have also found that diosphenol is dioxygenated by base catalysis, in a pathway possibly similar to that for the photosensitized oxygenation of 3-hydroxyflavones.[4]

We report herein that the enol forms 1a,b of 1,2-cyclohexanediones[5] undergo a facile photosensitized oxygenation in methanol to give 5-oxoalkanoic acids 2a,b and methyl 5-carboxy-2-hydroxypentanoates 3a,b, respectively, with a remarkable temperature dependency of the product distribution, which suggests the existence of endoperoxides 5a,b as unstable intermediates.

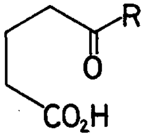
Typically, a solution of 1a (2 mmol) and rose bengal (3 mg) in 10 ml of methanol was irradiated with 100-w tungsten-halogen lamp (no filter) under oxygen atmosphere. During irradiation the solution was stirred magnetically. The absorption of oxygen and the evolutions of carbon monoxide and dioxide were followed both by manometry and by gas chromatography. The results for 1a,b are shown in Table I.

The transformations of 1a,b to products 2a,b, 3a,b, 8, and 9 are best accounted for by the reaction pathways shown in Schemes I and II. α-Ketohydroperoxide 4 formed from 1a in an ene fashion can be a common intermediate to both the five-membered 5a and the dioxetane 6 as proposed for 3-hydroxyflavones.[3] 5-Oxopentanoic acid 2a is formed mainly from 5a by decarbonylation and to a lesser extent from 6 through 7 by photosensitized decarboxylation.[6] The aldehydic acid 2a is partly converted to acetal 8 and glutaric acid 9[7] under the reaction conditions.

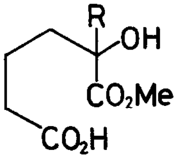
On the other hand, 5-oxohexanoic acid **2b** is formed from **5b** as the sole intermediate by decarboxylation as evidenced by the fact that no carbon dioxide has been released. In addition, the photooxygenation rate for **1b** is enhanced by a factor of about three[8] as compared to that for **1a**. Thus, the introduction of an electron-donating methyl group into the enol function increases the reactivity toward singlet oxygen but inhibits the dioxetane formation.



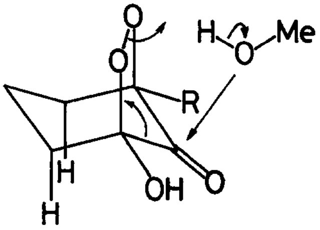
1a,b



2a,b



3a,b

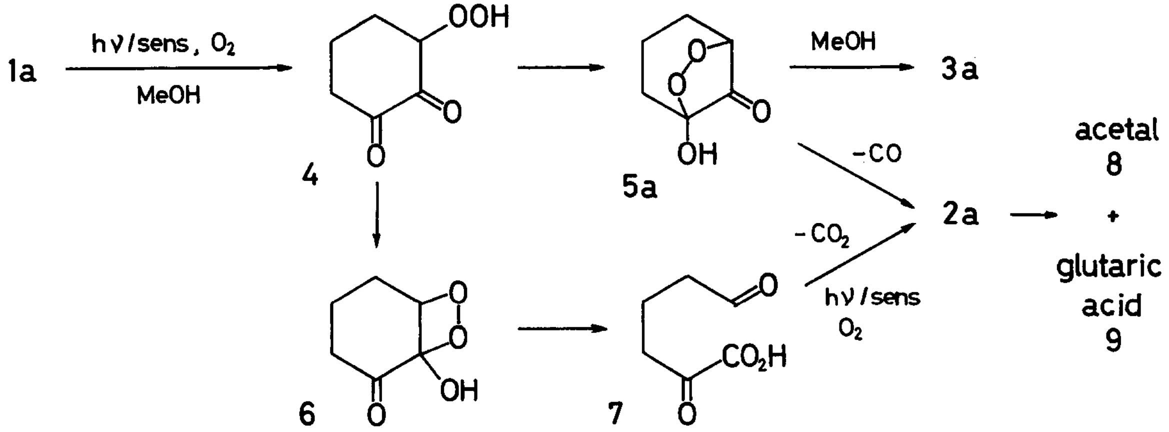


5a,b

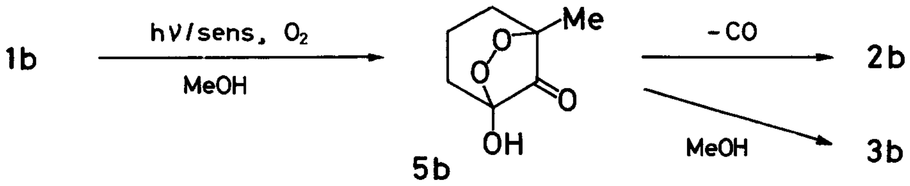
a: R = H

b: R = Me

Scheme I



Scheme II



The remarkable temperature dependency of product distributions as indicated in Table I is best accounted for in terms of trapping of the endoperoxide intermediates 5a,b by methanol to give 3a,b. The mechanism of trapping is tentatively given schematically. At higher temperatures, the lifetimes of the endoperoxides 5a,b will be shorter, permitting the trapping reaction only to a lesser extent. On the other hand, the trapping seems to be suppressed either by the decreased reactivity of methanol at -70 $^{\circ}$C for 5a or by the steric hindrance due to a methyl group attached to the α carbon for 5b.[9]

Table I. Photosensitized Oxygenation of the Enol Forms 1a,b of 1,2-Cyclohexanediones in Methanol[a]

substrate	sens	temp	time	product yield, %[b]					gas analysis, %[c]		
		$^{\circ}$C	h	2a	8	9	3a[d]	1a recovered	O_2 absorbed	CO evolved	CO_2
1a	rose bengal	40	13	62	10	0	1	0	137	62	4
		30	8	42	8	3	2	14			
		0	13	28	3	2	28	7	76	22	4
		-70	24	15	1	3	21	25			
				2b			3b	1b			
1b	rose bengal	40	4	91			0	0	95	86	0
		0	5	91			2	0	96	87	0
		-65	9	91			3	0	82	77	0
1b	methylene blue	40	4	92			2	0	89	84	0
		0	5	90			2	0	99	93	0
		-65	7	87			5	0	87	81	0

[a] A solution of 1a or 1b (2 mmol) and a sensitizer (3 mg) in 10 ml of methanol was irradiated with a 100-w tungsten-halogen lamp (no filter) under oxygen.

[b] Distilled as methyl ester and checked by GLC. Satisfactory ^1H and ^{13}C NMR and IR spectra were obtained for all the products.

[c] Calculated as (mmol of a gas)/(2 mmol) x 100.

[d] Satisfactory CI-MS spectra were obtained for the methyl ester.

One might attribute the very low yields of trapping product 3b to the very low stability of 5b. However, 5b appears moderately stable in comparison with 5a, as suggested by the following experiments: 1b was photoxygenated at -100 °C in ethanol without evolution of carbon monoxide, then the ethanolic solution was warmed slowly to -70 °C with vigorous evolution of carbon monoxide,[10] giving 2b as a major product.

Interestingly, the trapping product corresponding to 3b was not detected in the above experiments. This fact can reasonably be explained by inhibition of the trapping due to the increased steric requirement of nucleophilic ethanol.

The scope of the present reaction and the application to organic syntheses are being investigated.

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References and Notes

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8. Estimated from the reaction times in Table I. The factor of about 3 is considerably small in comparison with that for cyclohexenes (about 20). See Gollnick, K.; Kuhn, H. J. "Singlet Oxygen"; Wasserman, H. H.; Murray, R. W. Ed.; Academic Press: New York, 1979; pp 297–301.
9. The electron-donating nature of the methyl group will not affect the trapping since the α carbon bearing the methyl group remains untouched during the reaction.
10. 5a also releases carbon monoxide at -70 °C (Table I).

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