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TEMPERATURE- AND SUBSTITUENT-DEPENDENCE IN THE PHOTOSENSITIZED OXYGENATION OF N,N-DISUBSTITUTED HYDRAZONES[1].

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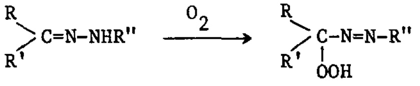
Summary: Methylene blue-sensitized photooxidation of N,N-disubstituted hydrazones 1a-f gave various products 2-9, depending on the reaction temperature and N-substituents. The major reaction modes from the photooxidation of N,N-diphenylhydrazones were α-oxidation at room temperature and C=N cleavage at -78 °C in contrast to C=N cleavage as an only reaction mode for the photooxidation of N,N-dimethylhydrazones at either room temperature or -78 °C.

Despite that extensive studies have been focused on the chemistry of 1,2-dioxetanes in the last decade in connection with chemiluminescence and bioluminescence,[2] only little attention has been drawn to the chemistry of 1,2,3-dioxazetidines.[3] In order to explore this field, we have been studying oxidation of imine derivatives with oxygen species, e.g.,oxidation of oxime ethers with singlet oxygen and ozone.[4] The oxidation of N-substituted hydrazones having a general formula I with molecular oxygen (triplet or singlet) proceeds rapidly at room temperature to produce the azo-hydroperoxides II.[5] Although N,N-disubstituted hydrazones are not reactive with



I II

triplet oxygen, it was recently found that N,N-dimethylhydrazones of aliphatic ketones regenerated the parent ketones by the reaction with singlet oxygen.[6] This report prompted us to report that the reaciton of N,N-disubstituted hydrazones 1 with singlet oxygen shows a unique dependence on substituents at the nitrogen atom and on the reaction temperature as well as on the solvent.

Table I. Products from the Photosensitized Oxygenation of N,N-Disubstituted Hydrazones 1a-f.

	Hydrazone 1					Solvent	Temperature °C	Products (%)	
	R^1	R^2	R^3	R^4	R^5			C=N cleavage	α-oxidation
a)	Me	Ph	Ph	Ph	Ph	CH_2Cl_2	RT	-	4a(59), 5a(18), 6a(9), 7a(15), 8a(trace)
						CH_2Cl_2	-78	2a(~100), 3a(72)	6a(trace), 7a(trace)
b)	Ph	H	Pr	Ph	Ph	CH_2Cl_2	RT	-	9b(36)
						CH_2Cl_2	-78	2b(10), 3a(5)	9b(30)
						CCl_4	RT	-	9b(65)
						CH_3OH	RT	2b(44)	9b(17)
						CH_3CN	RT	2b(27)	9b(27)
c)	Ph	H	Pr	Me	Ph	CH_2Cl_2	RT	-	9c(40)
d)	Ph	H	Pr	Me	Me	CH_2Cl_2	RT	2b(~100)	-
						CH_2Cl_2	-78	2b(~100)	-
e)	Ph	H	Ph	Ph	Ph	CH_2Cl_2	RT	2e(trace)	9e(32)
						CH_2Cl_2	-78[a]	-	-
f)	Ph	Me	Me	Ph	Ph	CH_2Cl_2	RT	-	4f(trace), 6f(15), 8f(66)
						CH_2Cl_2	-78	2f(70), 3a(56)	-

[a] The reaction was very slow at -78 °C.

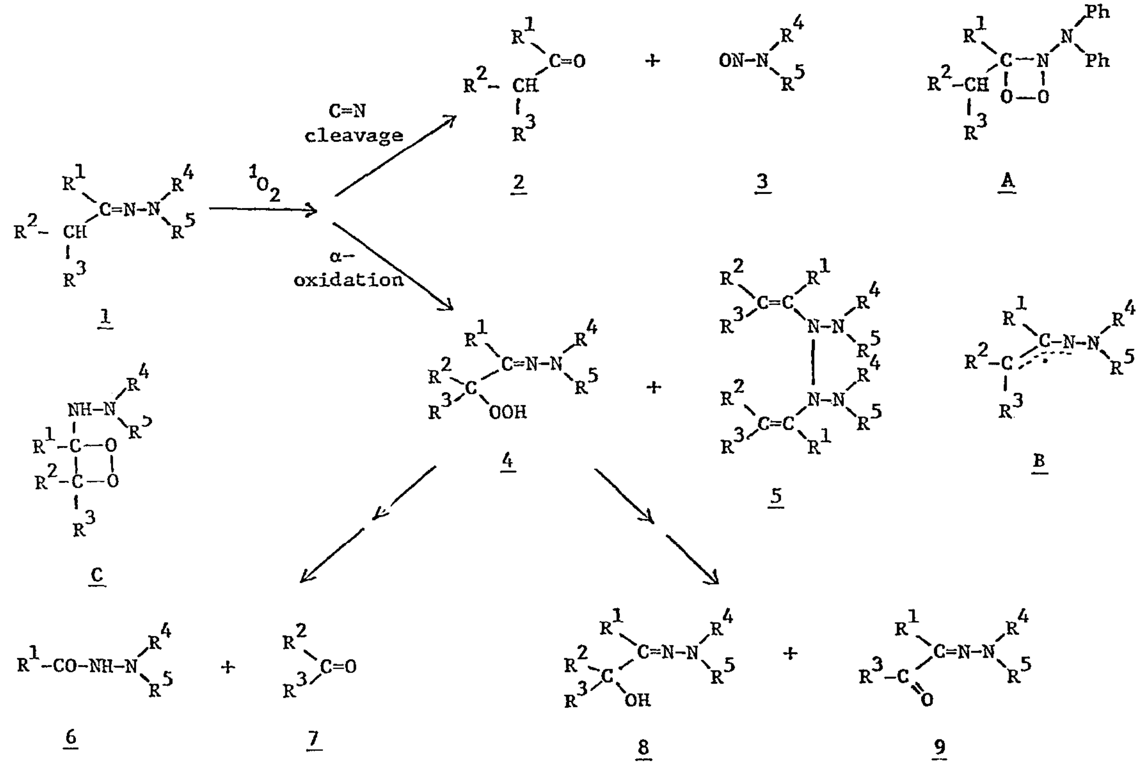
Methylene blue-sensitized photooxidation of the hydrazones 1a-f in CH_2Cl_2 solution at either room temperature (RT) or low temperature (-78 °C) yielded various products 2-9 (Table I).[7] The effect of solvent (CCl_4, CH_3OH and CH_3CN) on the photooxidation of 1b was also studied. As was found previously,[6] the N,N-dimethylhydrazone of valerophenone 1d gave the parent ketone, valerophenone 2b, quantitatively in CH_2Cl_2 solution.[8] In sharp contrast, N-phenyl-substituted hydrazones were photooxidized in CH_2Cl_2 solution at room temperature to afford α-oxidation products (1a → 4a-8a, 1b → 9b, 1c → 9c, 1e → 9e, and 1f → 4f + 6f + 8f)[9] instead of the parent ketones 2. However, at -78 °C these hydrazones underwent carbon-nitrogen double-bond cleavage to afford the corresponding parent ketones 2 and N-nitrosodiphenylamine 3a (1a → 2a + 3a, 1b → 2b + 3a, and 1f → 2f + 3a). It should be noted that the course of photooxidation of N,N-diphenylhydrazones of 1,1-diphenylacetone (1a) and isobutyrophenone (1f) was completely altered by this temperature change. Photooxidation of 1b in polar solvents (CH_3OH and CH_3CN) at room temperature gave substantial amounts of the parent ketone 2b in addition to the α-oxidation product 9b.

Since the parent ketone 2 and N-nitrosodiphenylamine 3a were formed in comparable yields in the photooxidation of the N,N-diphenylhydrazones at -78 °C (Table I) in contrast to the failure of detection of N-nitrosodimethylamine in the case of N,N-dimethylhydrazones,[6] a dioxazetidine

A seems to be the best candidate for the intermediate. The photooxidation mixture of 1a at -78 °C was chemiluminescent (λ_{max} 530 nm) during warming-up to RT. It also seems that 4 and 5 were formed via a common precursor, e.g., a radical B. We feel that an electron transfer from the hydrazones 1 to singlet oxygen is the primary step for the production of B like that for photooxidation of amines.[10] The hydroperoxide 4a was significantly chemiluminescent above 50 °C with an added fluorescer (DBA, perylene and rubrene), and the emission spectra agreed with the fluorescence spectra of the added fluorescers.[11] 4a decomposed slowly at 50-55 °C in $CDCl_3$ to give both 6a and 7a quantitatively. Possibly a dioxetane C is an intermediate for this transformation. A similar transformation has been reported with Schiff bases.[12]

The involvement of singlet oxygen in the photooxidation of these hydrazones was supported by the efficient quenching of the reaction with DABCO[13] (0.01 M) and by the fact that these hydrazones were oxidized in an analogous way with triphenyl phosphite ozonide[14] at -15 - 0 °C in CH_2Cl_2, e.g., 1a → 4a(80 %) + 5a(8 %) + 6a(5 %) + 7a(5 %) and 1d → 2b(96 %).

The exact nature of the temperature- and substituent-dependence in the present reaction is obscure at this stage. Interesting examples of temperature dependence of the reaction mode in



certain singlet-oxygen reactions have recently been reported.[15]

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7. Irradiations were carried out with a tungsten-bromine lamp through a filter solution of 5 % potassium dichromate (>520 nm). In some cases photooxidations were also done with tetraphenylporphine, but the results were not altered. The hydrazones were prepared by a standard procedure from the corresponding ketones and hydrazines. Products were isolated by chromatographic methods and their structures were determined by NMR (^{1}H and ^{13}C), IR and Mass spectra. All new compounds gave satisfactory elemental analyses except 4f and 8f. The hydroperoxide 4f and the alcohol 8f were unstable to work-up procedures and their isolation in pure states has been unsuccessful yet.
8. As previously reported,[6] we could not detect N-nitrosodimethylamine 3d in the reaction mixture (GLC and NMR analyses). We found that 3d was stable under our photooxidation conditions.
9. The hydroperoxide 4a decomposed into 6a and 7a on silica gel or by heating its solution above room temperature. It also decomposed slowly under the present photooxidation conditions to afford 5a(25 %), 6a(61 %), 7a(61 %) and 8a(9 %). On treatment with triphenylphosphine, 4a was quantitatively transformed into the alcohol 8a. The isolation of 4a was done by low-temperature column chromatography (-70 °C) on silica gel, mp. >110 °C (decomp).
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11. The decay of the chemiluminescence was first order with $k=3.4\times10^{-5}s^{-1}$ at 90 °C in xylene (4a, 2.4×10^{-4}M; perylene, 1×10^{-2}M) and the chemiluminescence quantum yield was approximately 5×10^{-5} Einsteins/mole under these conditions. Luminol was used as a standard of photon emission.
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