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Intermediates in the Dye-Sensitized Photooxygenation of Nitrones and Hydrazones

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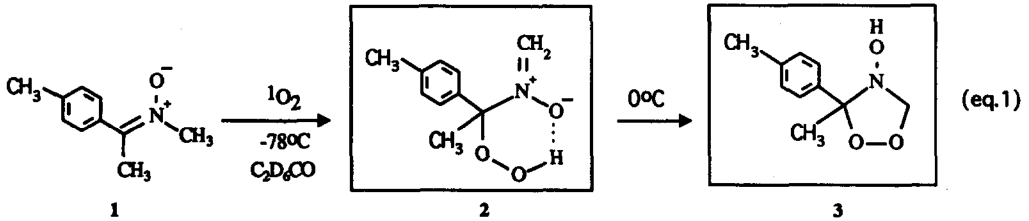
Abstract: In the dye-sensitized photooxygenation of C-Aryl nitrones and hydrazones, short-lived peroxidic intermediates are observed. Their characterization, mechanisms leading to them, as well their decomposition pathways are discussed.

Recently we reported a survey of the reactions of singlet oxygen with several types of C=N-containing compounds.[2] The results indicate that strong electron donors attached to nitrogen greatly facilitate reaction. Product spectra in most of these reactions indicate that the mechanisms involved are more complex than those governing the singlet oxygenations of the C=C analogs. The postulated mechanism for the nitrone photooxygenations was mainly inferred from the product structures as well as the low intensity NMR signals due to a transient intermediate which we had tentatively assigned to a cyclic peroxide. We now report results of more definitive experiments designed to test the intermediacy of this compound. We also report an extension of this study to the low temperature photooxygenations of N,N-dimethyl-C-aryl hydrazones.

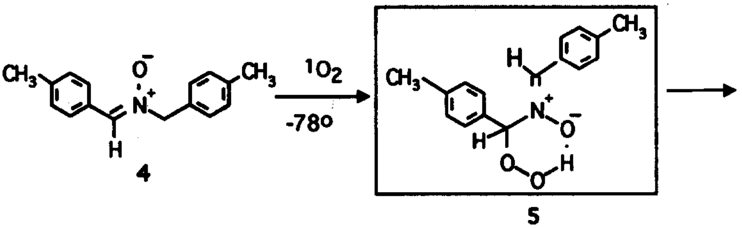
C-Arylnitrones. A solution of nitrone 1 in acetone-d_6 was photooxygenated at -78° C and an ^{1}H NMR spectrum of the photolysate was recorded at -60° C. The spectrum indicated the presence of a single compound the structure of which was assigned to that of hydroperoxide 2 (eq.1). The N=CH_2 group gives rise to an AB quartet centered at 7.05 ppm (^2J=6.9 Hz); the singlets at δ 2.12 and 2.33 ppm are ascribed to the C-methyl and Ar-methyl groups.



The aromatic hydrogens exhibit an AB quartet, centered at δ 7.3 (^3J= 8.1 Hz). The most characteristic signal is the broad singlet at 12.9 ppm, assigned to the hydroperoxy hydrogen. The signal is unusually low for a OO-H group which ordinarily absorbs at ca. 8-9 ppm. The observed shift in the present case is attributable to intramolecular H-bonding to the N-O group. Compound 2 can be considered an "ene"-type product, and there is precedent for a similar hydroperoxide obtained from a cyclic nitrone by Foote and Ching.[3] Upon warming to 0°C, the signals due to hydroperoxide 2 are completely displaced by those of another compound; this compound has a strong peroxidic odor, and reacts strongly to common peroxide tests. It was identified as the cyclic peroxide 3 we had previously observed[2] in low concentrations during the photooxygenation of 1 at 0°C. The lack of the signals due to the ultimate decomposition products in the present case permitted a complete structural assignment: the N-OH group absorbs at δ 9.26; the aromatic hydrogens display AB doublets at δ 7.4 and 7.1 (^3J= 8 Hz). The singlets due to the

C-methyl and Ar-methyl are at δ 1.6 and 2.3, respectively. The protons on the CH_2 group exhibit AB doublets at 4.8 and 4.3 ppm (^2J= 6 Hz), in accord with the cyclic peroxide structure in **3**. Upon warming to room temperature, **3** gradually and quantitatively decomposes to the previously observed products. In addition to the spectroscopic evidence, the identity of **3** was further confirmed by a chemical test: treatment of a solution of **3** at -60° with dimethylsulfide (DMS) resulted in deoxygenation, as verified by the formation of dimethyl sulfoxide and a 3:2 mixture of *p*-methylacetophenone and the corresponding oxime, respectively. The formation of both compounds indicates that attack by DMS on either oxygen of the peroxidic bond in **3** is taking place.

We have also prepared several N-benzyl-C-aryl nitrones of the type **4**. Upon photooxygenation at -78° C, nitrone **4** gave quantitatively the hydroperoxide **5** (eq.2), as confirmed by its ^{1}H NMR spectrum at -60°.[4] Upon warming, a mixture of aldehyde **6**, oxime **7**, and minor amounts of *p*-toluic acid **8** and the hydroxamic acid **9** were formed. In this case, however, the cyclic peroxide intermediate was not observed, suggesting that either it is not formed, or is too unstable to be detected. In order to address this latter question two unsymmetrically substituted benzylnitrones, **10** and **12**, were reacted with $^1O_2$ under the same conditions. Low-temperature ^{1}H NMR spectra of the photolysates obtained from both reactions revealed two different hydroperoxides **11** and **13**,[5] with no traces of the alternative isomer in each case (eq.3). Upon warming to room temperature, very similar product mixtures were formed from both.[6] These results strongly imply that hydroperoxides **11** and **13** decompose through a common intermediate.



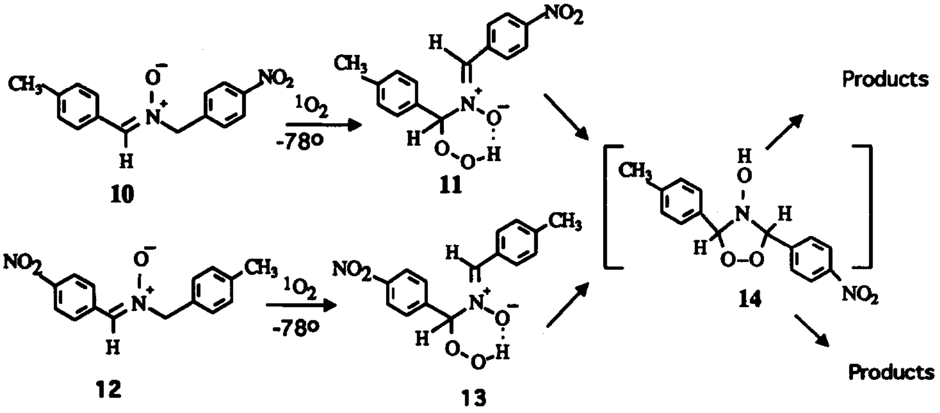
6 p-Tolyl-CH=O (8.5)

7 p-Tolyl-CH=NOH (6.5)

8 p-Tolyl-CO_2H (1.5)

9 $p\text{-Tolyl-}\underset{\underset{\text{O}}{\|}}{\text{C}}\text{NHOH}$ (1)

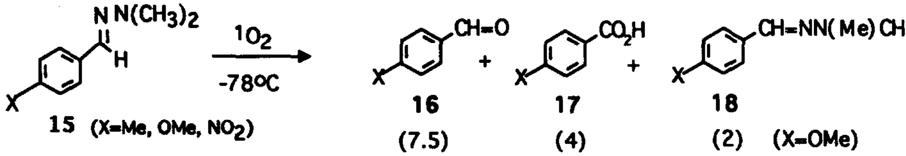
(eq.2)



(eq.3)

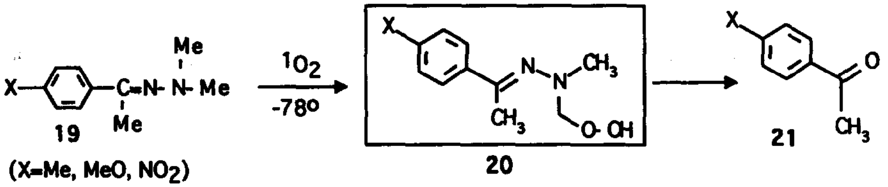
We suggest that this common intermediate is the cylic peroxide **14**, similar to **3** obtained from the N-methylnitrone **1**. Our results are consistent with the mechanism postulated in our initial report for the singlet oxygenations of C-arylnitrones: the reaction with $^1O_2$ commences with an ene reaction. Cyclization to the azaozonide **14** ensues which then decomposes to give the observed products. The slightly different product mixtures obtained from the two nitrones suggests that a small part of the products may arise directly from **11** or **13**, bypassing **14**.

N,N-Dimethylhydrazones. The singlet oxygenation of N,N-dimethylhydrazones of aliphatic aldehydes and ketones has been reported by Enders[7] to result in the oxidative cleavage of the C=N bond after deoxygenation of the photolysate with PPh_3 and subsequent aqueous workup. An "ene" mechanism leading to N-alkenyl-N-hydroperoxy-N,N'-dimethyl hydrazines has been implicated in these reactions. By contrast, as our studies indicate, $^1O_2$ combines with N,N-dimethylhyrazones derived from aryl aldehydes and ketones by an entirely different mechanism. Aromatic aldohydrazones give, without a detectable intermediate, a mixture of the corresponding aldehydes and carboxylic acids as major and N-formyl-N-methylhydrazones, **18**, as minor products (eq.4).[8]



(eq.4)

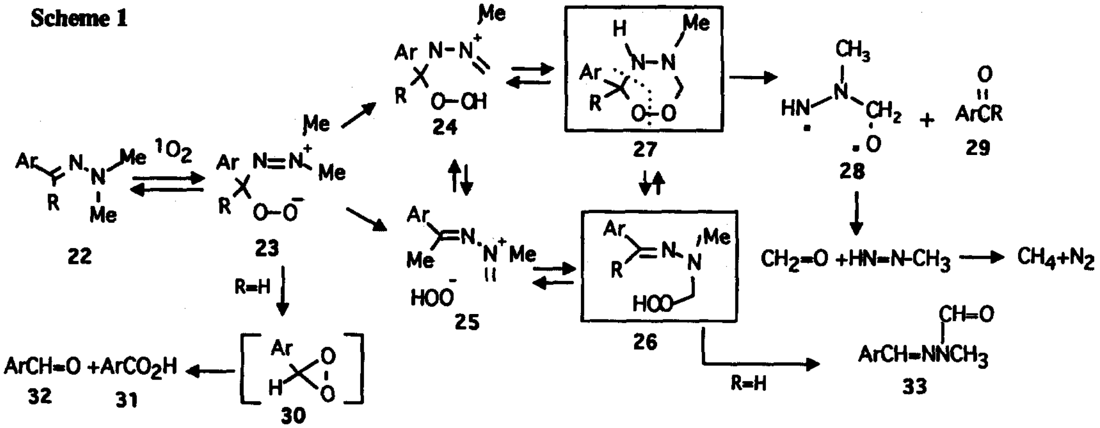
Arylketohydrazones cleanly give rise to the corresponding ketones. In these latter cases, ^1H NMR spectra taken of the photolysate at -60°C showed the presence of a single compound in each instance, to which the structures of hydroperoxides of the type **20** were assigned (eq.5). Typically, the hydroperoxides exhibit singlets at δ 2.65 (N-Me), 2.3 (C-Me) and 4.85 ($N-CH_2$) ppm, whereas the OO-H group absorbs at δ 8.8 as a broad singlet. Upon warming to room temperature the hydroperoxide intermediates cleanly decompose to the respective acetophenone derivatives.



(eq.5)

Based on these observations we postulate that the combination of C-arylhydrazones with $^1O_2$ is perfectly analogous to that of other C=N compounds (Scheme 1). Oxygen attaches itself to the carbon of the C=N bond to give the zwitterion **23** which leads to the observed hydroperoxide intermediate **26** by two alternative pathways. The decomposition mechanism of **26** to the observed products is conveniently rationalized, as in the case of nitrones, by cyclization to an endoperoxide of the type **27**. Subsequent fragmentation of **27** would lead to the carbonyl componds. Vigorous gas evolution during the decomposition of the photolysate upon warming is consistent with this pathway. In one case (X= OMe), upon warming the photolysate from -60° to -40° the signals due to the hydroperoxide intermediate partially disappeared and new sets of peaks became visible in the NMR spectrum. Two sets of AB doublets at δ 5.27 and 4.75 (J_{AB}= 10.5 Hz) and 4.70 and 4.50 (J_{AB}= 13.1 Hz), respectively, could be ascribed to the protons on the CH_2-group in the cyclic intermediate **27**. The two sets of signals for the CH_2 group might stem from two different conformers of **27**, the interconversion of which would be slow enough on the NMR time scale at -40° C to permit the observation of both. Moreover, the singlets at δ1.4 and 1.8 for the C-Me and N-Me groups are in accord with the structure. Within minutes at -40°, the hydroperoxide quantitatively gives way to the cyclic intermediate which decomposes exclusively to *p*-methoxyacetophenone.[9]

Scheme 1



In this study direct (spectroscopic) as well as indirect (as inferred from product analysis) evidence has been presented for the intervention of peroxidic intermediates in the photooxygenations of nitrones and hydrazones. Further work in this area will emphasize the substitutent effects on the photooxygenation rates of these compounds.

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References and Notes

1.Presented at the 2nd Pan American Chemical Congress in San Juan, Puerto Rico on September 25, 1991.

2.Castro,C., Dixon, M., Erden, I., Ergonenc, P., Keeffe, J.R., and Sukhovitsky, A. *J. Org. Chem.* 1989, 54, 3732.

3.Ching,T.-Y., Foote, C. S. *Tetrahedron Lett.* 1975, 3771.

4.Characteristic ^{1}H NMR absorptions (300 MHz, d_6-acetone): δ 8.4 (s, 1H, N=CH), 6.3 (s, 1H, CH-OO), 12.6 (br.s, 1H, OOH).

5.Characteristic ^{1}H NMR signals (300 MHz, d_6-acetone): **11**: δ 8.4 (s, 1H, N=CH), 6.3 (s, 1H, CH-OO), 12.6 (br.s, 1H, OOH); **13**: δ 8.2 (s, 1H, N=CH), 6.5 (s, 1H, CH-OO), 12.7 (br.s, 1H, OOH).

6.Products from thermal decomposition of **11** (**13**) : *p*-tolyl-CH=O [42%(37%)]; *p*-$NO_2C_6H_4$-CH=O [15%(19%)]; *p*-tolyl-CH=NOH [trace(5%)]; *p*-$NO_2C_6H_4CH$=NOH [33%(18%)]; *p*-tolyl-C(O)NHOH [8%(12%)]; *p*-$NO_2C_6H_4$-C(O)NHOH [2%(9%)].

7.Friedrich, E., Lutz, W., Eichenauer, H., Enders, D. *Synthesis*, 1977, 893.

8.Minute amounts of the corresponding methyl ester and traces of N-nitroso-N,N-dimethylamine were also formed in each case.

9.In this case (X=OMe), small amounts of 1-methyl-1-formylhydrazine ($NH_2N(CH_3)$-CH=O) were also formed, presumably by base-catalyzed decomposition of the cyclic peroxide **27**. Additionally, small peaks at δ 3.4 and δ 0.23 were seen in the photooxygenation of **19** (X=OMe). The former disappeared and the latter increased over time. These observations are consistent with the formation of methylazine and its decomposition to methane.

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