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ZWITTERIONIC INTERMEDIATES IN ENAMINE-SINGLET OXYGEN REACTIONS.
CONFIGURATION-INTERACTION STUDIES ON THE INDOLE-SINGLET OXYGEN REACTIONS

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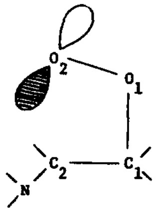
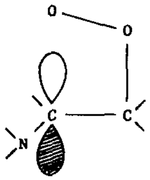
The theoretical calculations using INDO-RHF CI method have demonstrated that the reaction of singlet oxygen with 1,2,3-trimethylindoles proceeds via a zwitterionic peroxide intermediate. The calculations provide important predictions for the mechanism of enamine-singlet oxygen reactions.

There is much current controversy on the intermediacy of short-lived intermediates in the reaction of singlet oxygen with electron-rich alkenes such as enamines or enol ethers. It has been proposed theoretically or experimentally that a two-step 1,2-cycloaddition may occur via perepoxides,[1] zwitterions,[2] or 1,4-diradicals.[3] We previously reported that the singlet-oxygen reaction of enamines is regarded as a symmetry-forbidden nonradical reaction proceeding via a zwitterionic intermediate.[2b] The MINDO/3 calculations by Dewar and Thiel have also indicated the zwitterionic mechanism for the enamine-singlet oxygen reactions.[2a] Harding and Goddard, however, have recently proposed by GVB-CI calculations a mechanism involving a 1,4-diradical intermediate stabilized by an anomeric effect for the hydroperoxidation of methoxy-substituted olefins.[3] Recent trapping experiments using methanol have indicated that singlet-oxygen reactions of several electron-rich olefins proceed via polar peroxidic intermediates.[4] More recently, we have demonstrated that singlet-oxygen reaction of 1,3-dimethyl- or 1,2,3-trimethylindole proceeds via a zwitterionic intermediate and proposed a mechanism in which 1,4-zwitterion with its gauche-like conformation is equilibrated with a cisoid conformer.[5] In order to verify the zwitterionic mechanism we have carried out the theoretical calculations using INDO-RHF CI method[6] on the reaction of N-methylindoles with singlet oxygen.

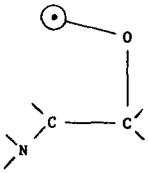
We first examined the $[2_s + 2_s]$ type reaction of singlet oxygen ($^1\Delta_g$) with 1,2,3-trimethylindole (model I of Fig. 1). The HOMO and LUMO obtained for this approach model are highly



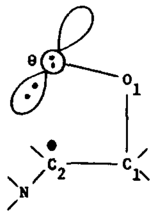
HOMO (σ_0)



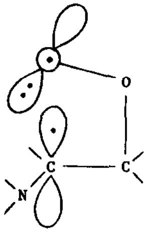
LUMO (σ_c)



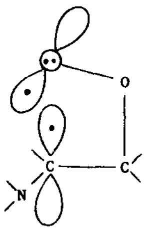
π_0



1, cis ZW $(\sigma_0)^2(\pi_0)^2$



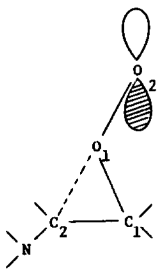
2, DR (σ,π) $(\sigma_0)^2(\pi_0)^1(\sigma_c)^1$



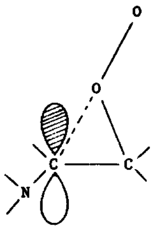
3, DR (σ,σ) $(\pi_0)^2(\sigma_0)^1(\sigma_c)^1$

localized on the O_2- and C_2-atoms, respectively. The π-type lone pair (π_0) of the terminal O_2-atom is the next HOMO. Therefore, three different electronic configurations with lower energies are illustrated as shown. Since electrons should enter into the lone pair MO's (σ_0 and π_0) in pairs in the ground state configurations, i.e., $(\sigma_0)^2(\pi_0)^2$, the ground state (S_0) may correspond to the zwitterion **1** (cis ZW). On the other hand, mono-excitations of the π_0- and σ_0-lone pair electrons to the LUMO (σ_c) give the σ,π- (**2**) and σ,σ-diradicals (**3**), respectively. The configuration mixing (CI) calculations[6] by use of these and other higher excited states configurations[7] have indicated that the ground state (S_0), first (S_1)- and second (S_2)-excited states should correspond to cis ZW (**1**), DR (σ,π) (**2**) and DR (σ,σ) (**3**), respectively. Thus the ground state intermediate for the approach model I is regarded as a zwitterion, not a diradical such as **2** or **3** (Fig. 1). Table I summarizes the total energies, net charges and bond indices calculated for the S_0-, S_1- and S_2-states at R = 1.5 Å and θ = 15° by the CI method. The net charges on the C_2- and O_2-atoms in the S_0-state are 0.33 and -0.37, respectively, showing a 1,4-zwitterionic property, whereas the corresponding values in the S_1-state are only -0.08 and -0.04 in accordance with a 1,4-diradical species.

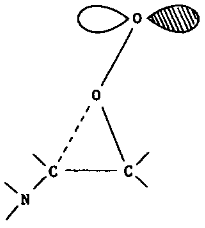
We next examined the reaction course leading to a three membered ring (perepoxide)(model II of Fig. 1). In this case also the three MO's are more or less localized on the terminal atom (O_2- or C_2 atom) as shown. Similarly, the ground state (S_0), first (S_1)- and second (S_2)-mono-excited states correspond to zwitterion **4** (gauche ZW), DR (σ,π) (**5**), and DR (σ,σ) (**6**), respectively. The net charges on the C_2- and O_2-atoms in the S_0-state by the CI calculations[6,7] are 0.28 and -0.51, respectively, for the intermediate at R = 1.5 Å and θ = 0° (Table I). The net charge on O_1-atom is only -0.02. In a perepoxide structure positive charge should be localized on the O_1-atom. Thus the reaction intermediate (4) may be regarded as a 1,4-zwitterion in the gauche conformation rather than a perepoxide. As shown in Table I, the calculations indicate that the cis ZW (1) is slightly stable than the gauche ZW (4) at least in the gas phase.[8] Essentially the same results have been obtained for the reaction of 1,3-dimethylindole with singlet oxygen.



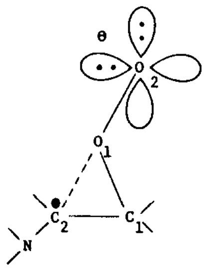
HOMO (σ'_0)



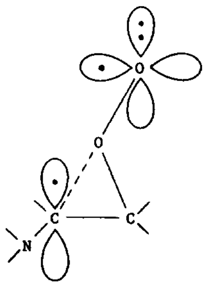
LUMO (σ'_c)



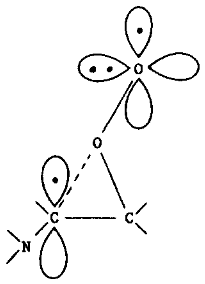
π'_0



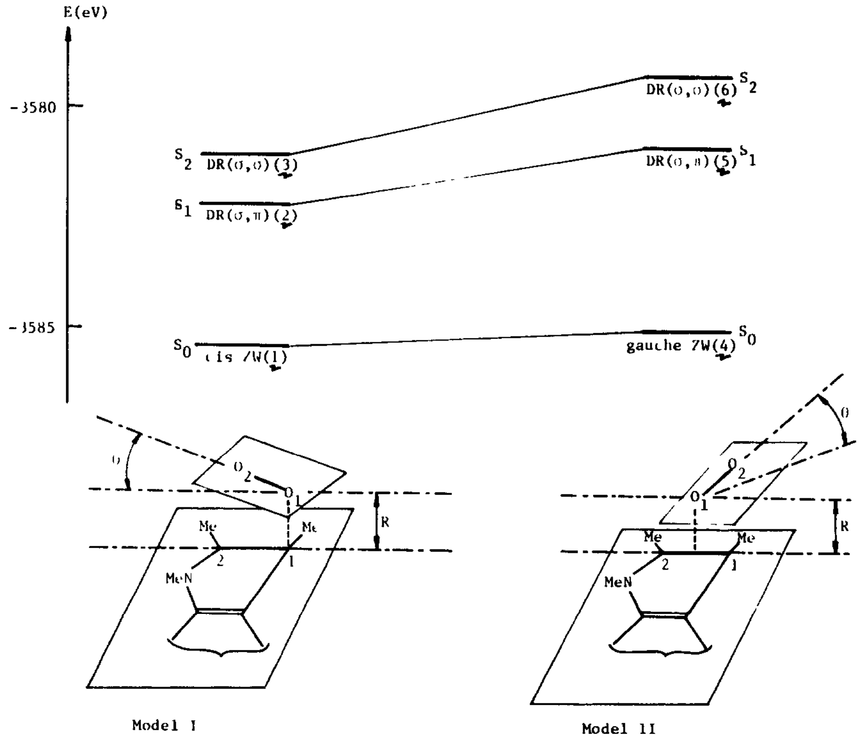
4, gauche ZW $(\sigma'_0)^2(\pi'_0)^2$



5, DR (σ,π) $(\sigma'_0)^2(\pi'_0)^1(\sigma'_c)^1$



6, DR (σ,σ) $(\pi'_0)^2(\sigma'_0)^1(\sigma'_c)^1$



Model I

Model II

Fig. 1 Calculated energy levels for the 1,2,3-trimethylindole-$^1O_2$ system

The present calculations are consistent with the experimental results observed in singlet-oxygen reactions of N-methylindoles.[4a,5] They also provide important predictions for the reaction courses of general enamine-singlet oxygen reactions; (1) since there is a weak covalent bonding between C_2- and O_2-atoms, the *cis* ZW (**1**) may well be a precursor of the dioxetane; (2) the gauche ZW (**4**) is capable of undergoing "ene" reaction directly, not by way of a perepoxide, because of the considerable negative charge on the O_2-atom and of a weak C_2-O_1 bonding;[5] (3) methanol should attack the C_2-carbons of both *cis*- and gauche ZW's from "outside", giving a trapping product with the same stereochemistry, while the *trans* ZW will give a mixture of diastereomeric trapping products.[9]

Table I. Net Charges and Bond Indices Calculated for the 1,2,3-Trimethylindole- $^1O_2$ system

Model	State	Total energy (eV)	Net charges				Bond indices				
			ΔP_{O_2}	ΔP_{O_1}	ΔP_{C_1}	ΔP_{C_2}	$W_{O_1O_2}$	$W_{C_1O_1}$	$W_{C_1C_2}$	$W_{C_2O_2}$	$W_{C_2O_1}$
I[a]	S_0	-3585.380	-0.365	-0.150	0.087	0.333	0.965	0.830	1.036	0.514	—
	S_1	-3582.111	-0.036	0.013	0.068	-0.076	1.140	0.704	1.113	0.174	—
	S_2	-3581.298	-0.150	-0.074	0.111	-0.009	1.127	0.531	1.196	0.058	—
II[b]	S_0	-3584.964	-0.512	-0.024	0.147	0.280	0.952	0.536	1.170	—	0.505
	S_1	-3580.861	0.179	-0.466	0.007	0.186	0.963	0.239	1.312	—	0.263
	S_2	-3579.256	0.196	-0.438	0.065	0.206	0.918	0.262	1.171	—	0.309

[a] R = 1.5 Å, θ = 15°. [b] R = 1.5 Å, θ = 0°.

References and Notes

1. (a) D. R. Kearns, *Chem. Rev.*, **71**, 395 (1971); (b) S. Inagaki, S. Yamabe, H. Fujimoto, and K. Fukui, *Bull. Chem. Soc. Jap.*, **45**, 3510 (1972); (c) P. D. Bartlett, *Chem. Soc. Rev.*, **5**, 149 (1976).
2. (a) M. J. S. Dewar and W. Thiel, *J. Am. Chem. Soc.*, **97**, 3978 (1975); (b) K. Yamaguchi, T. Fueno, and H. Hukutome, *Chem. Phys. Lett.*, **22**, 466 (1973).
3. L. B. Harding and W. A. Goddard, III, *J. Am. Chem. Soc.*, **99**, 4520 (1977); Tetrahedron Lett., 747 (1978).
4. (a) I. Saito, M. Imuta, Y. Takahashi, S. Matsugo, and T. Matsuura, *J. Am. Chem. Soc.*, **99**, 2005 (1977); (b) C. W. Jefford and C. G. Rimbault, *J. Am. Chem. Soc.*, **100**, 6437, 6515 (1978); (c) H. Takeshita and T. Hatsui, *J. Org. Chem.*, **43**, 3080 (1978).
5. I. Saito, S. Matsugo, and T. Matsuura, submitted to *J. Am. Chem. Soc.*.
6. (a) K. Yamaguchi, K. Ohta, Y. Yabushita, and T. Fueno, *Chem. Phys. Lett.*, **49**, 555 (1977); (b) K. Yamaguchi, *ibid.*, **33**, 230, 330 (1975).
7. The single and double-excitations from the RHF-zero-order configuration are considered for the present CI calculations. The lower five unoccupied and higher five occupied MO's are employed to constract these configurations. See, ref. 6a.
8. Relative stabilities among the *cis*- and gauche ZW's in solutions seem to be highly dependent on the polarity and/or hydrogen-bonding ability of solvents.[5]
9. The stereochemistry of the trapping products has not been fully understood. However, photooxygenation of indene in methanol gave a mixture of *trans*- and *cis*-2-hydroperoxy-1-methoxyindan,[4c] whereas a single trapping product has been obtained in the case of N-methylindoles[4a,5] and 2-methoxynorborn-2-ene.[4b]

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