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CONCERNING THE INHIBITION OF SINGLET OXYGEN ATTACK ON COMPOUNDS CONTAINING URAZOLE RINGS‡

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The urazole ring is shown not to be an efficient quencher of singlet oxygen; however, electrophilic attack by $^1O_2$ on a double bond situated in a urazole-containing molecule may be entirely suppressed or retarded depending upon distance because of the powerful electron-withdrawing inductive effect of this heterocyclic unit.

Recently published work has examined the effect of relatively remote hydrazide lone pair electrons (as contained in a urazole ring, see **1** and **2**) on the stereochemistry and rate of singlet oxygen attack.[1] The observed reversal in stereospecificity for the allylic hydroperoxidation of **1** relative to the course of other electrophilic additions, coupled with marked kinetic retardation as compared to appropriate hydrocarbon models, led us to propose the possibility of frontier orbital control. In accordance with current HMO perturbation theory,[2,3] these phenomena were attributed to antisymmetric charge-transfer interaction between $HOMO_{NN}$ and $LUMO_{O_2}$ with resultant deactivation or quenching. The properties intrinsic to the urazole ring have now

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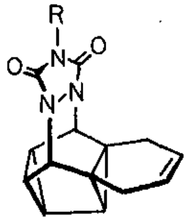
‡Dedicated to Professor Tetsuo Nozoe on the occasion of his 77th birthday.

been further assessed with the result that the interpretation advanced earlier can no longer be viewed as tenable.

Two methods were employed to assess the binary mixed quenching capabilities of **3**-**5** toward singlet oxygen. The first consisted of the β approximation method popularized by Foote[4] and made use of cyclohexene as standard.[5] Solutions in benzene-methanol (3:1) containing 5.28×10^{-4} *M* Rose Bengal were thermostated at 25 ± 1° and irradiated through Pyrex for 1 hr intervals while constantly purged with pure oxygen. Subsequent to hydroperoxide reduction with trimethyl phosphite and addition of a known quantity of internal standard (cyclohexanol), the extent of product formation was determined gas chromatographically (calibrated detector). Least squares analysis of the data for cyclohexene gave $\beta = 3.1$. Since $\beta = \underline{k}_d/\underline{k}_r$ and an estimate of $\underline{k}_d$ in this solvent mixture is available (6.25×10^4 sec^{-1}),[6] $\underline{k}_r$ (cyclohexene) = 2×10^4 ℓ mol^{-1} sec^{-1}. A competitive rate study by Kopecky and Reich had previously given $\underline{k}_r = 6.3 \times 10^3$ ℓ mol^{-1} sec^{-1}.[7] To calibrate our system, the inhibitory effectiveness of 0.0042 *M* diethylamine was determined and found to give a β_{app} value of 3.62. Application of the equation $\beta_{app} - \beta = \gamma[Q]$ where $\gamma = \underline{k}_q/\underline{k}_r$ shows $\underline{k}_q = 2.4 \times 10^6$ or 7.5×10^5 ℓ mol^{-1} sec^{-1} (compare with the data of



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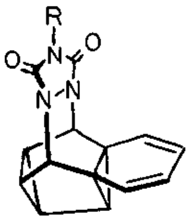

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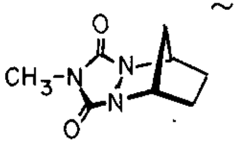

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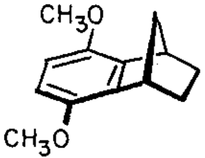

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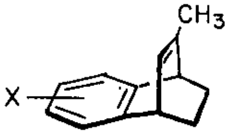
Matheson and Lee[8]).

The allylic hydroperoxidation of cyclohexene in the presence of urazole 3 (0.026 M) showed no measurable quenching. A tenfold concentration increase (to 0.24 M) actually led to a slight enhancement in the rate of cyclohexene consumption, perhaps because of solvent polarity changes at these excessive substrate levels. Our findings denote that the ability of 3 to quench $^1O_2$ is weak ($< 3 \times 10^5$ ℓ mol^{-1} sec^{-1}), if present at all. In contrast, 1,4-dimethoxybenzonorbornene (5) is an effective inhibitor of cyclohexene photooxidation at 0.026 M ($\beta_{app} = 10.5$, $k_q = 6 \times 10^6$ ℓ mol^{-1} sec^{-1}).

An independent set of quenching rate constants was obtained through the courtesy of Dr. M. A. J. Rodgers at the Center for Fast Kinetics Research, Austin, Texas. In their experiments a laser flash was used to generate anthracene triplets in aerated CH_2Cl_2 solutions containing diphenylisobenzofuran (DPIBF). The quenching of such triplets by O_2 ($^3\Sigma_g^-$) produced the $^1\Delta_g$ species, the reactivity of which was determined by time-resolved observation of DPIBF bleaching. Upon addition of 3, 4, and 5 to such reaction mixtures, the respective quenching rate constants (k_q) were determined to be $< 4 \times 10^4$, $< 3.9 \times 10^4$, and 1.3×10^7 ℓ mol^{-1} sec^{-1}, respectively. These results are in full agreement with those obtained by the β_{app} method.

Given that 3 does not affect the rate of cyclohexene oxidation, it remained of interest to determine what factor or factors were responsible for retarding the "ene" reactivity of 1 toward $^1O_2$. Since the stereoselectivity of singlet oxygen attack on methyl benzobicyclo[2.2.2]octa-2,5-dienes of type 6 [X = 1,4-$(OCH_3)_2$, H, F_4][9] varies significantly as a direct function of the electronic nature of the aryl substitution plan, the urazole 7 was prepared and subjected to photooxygenation. Contrary to 6, the urazole ring in 7 completely suppressed attack of $^1O_2$ at the trisubstituted bond. Importantly, 7 was found to be similarly unreactive toward other electrophilic reagents such as *m-chloroperbenzoic acid, etc.*

These observations suggest that the urazole ring constitutes a very powerful electron-withdrawing substituent capable of exerting inductive effects through the σ bond framework which are highly adverse to electrophilic attack. Untoward through-space reactivity of 1 denotes that such influences continue to persist, although understandably to an abated extent, at longer range.



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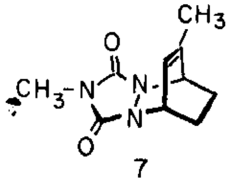

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The possible synthetic exploitation of the urazole ring system as a protective device for the stereoselective suppression of attack by electrophiles is presently receiving attention.

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9 *L. A. Paquette and F. Bellamy, unpublished observations.*

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