

REACTIVITY OF SYDNONES WITH SINGLET OXYGEN

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Summary

The rate constants k_r for the reaction of several sydnones with singlet oxygen ($^1\text{O}_2^*$) have been measured by the competition technique based on the 485 nm laser flash photolysis of a $^1\text{O}_2^*$ sensitizer and the kinetics of depletion of 1,3-diphenylisobenzofuran. The sydnone with a methyl substituent at the 4-position is particularly reactive ($k_r = (1 - 5) \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$ in various solvents). In contrast, the sydnones that are unsubstituted at the 4-position exhibit only poor reactivity towards $^1\text{O}_2^*$ ($k_r \leq 5 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$ in methanol and benzene). The solvent polarity has a small positive influence on k_r ; for example, on going from carbon tetrachloride to acetone or acetonitrile, the increase in k_r for 4-methyl-3-*p*-tolylsydnone is only twofold to threefold. This can be explained by a slight increase in dipole moment on achieving a transition state from a sydnone substrate that is already considerably polar.

1. Introduction

Singlet oxygen ($^1\text{O}_2^*$, $^1\Delta_g$) is known for its reactivity toward a variety of heterocyclic π systems [1, 2]. A common example is provided by furans which undergo facile 1,4-cycloaddition reactions with $^1\text{O}_2^*$ forming endoperoxides [1]. In an earlier study [3], based on steady state irradiation and product analysis, it has been shown that the sensitized photo-oxygenation of sydnones leads to α,β -diaroylhydrazines as the major isolable products. As shown in Fig. 1, with 3,4-diphenylsydnone 1a as the substrate, the various steps apparently comprise the loss of CO_2 from the 1,3-adduct of a sydnone with $^1\text{O}_2^*$ producing an *N*-nitroso derivative, which undergoes rearrangement and decomposition to benzoic acid. The latter becomes a trapping agent for *N,C*-diphenylnitrilimine, photogenerated from the sydnone, producing an imidoester which subsequently rearranges to give α,β -dibenzoylphenyl-

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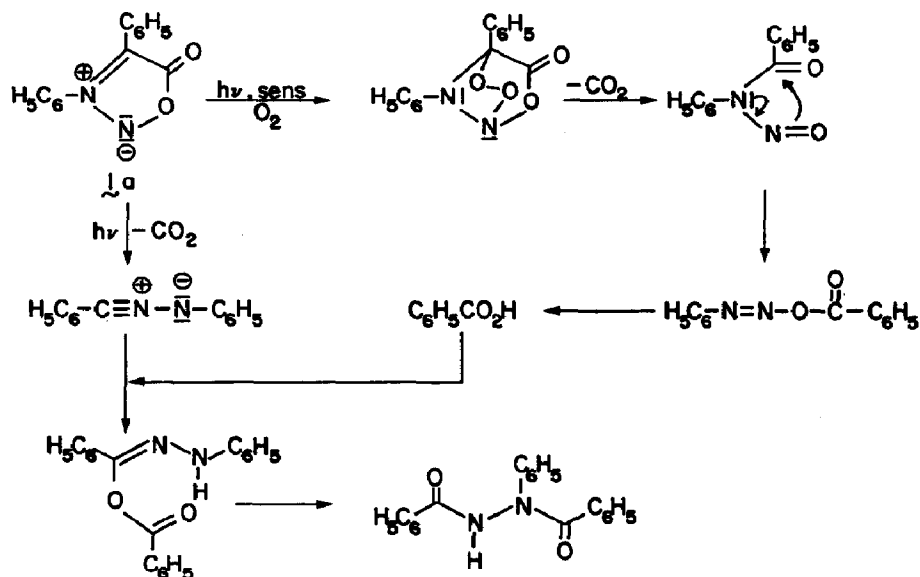
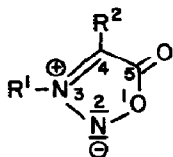


Fig. 1. Sensitized photo-oxygenation of 3,4-diphenylsydnone.

hydrazine. To the best of our knowledge, no data are available in the literature for the reactivity of sydnone with $^1\text{O}_2^*$.

In this paper we are reporting on the kinetics of the reaction of several sydnone 1 - 6



- 1) R¹ = R² = C₆H₅
- 2) R¹ = *p*-CH₃C₆H₄; R² = C₆H₅
- 3) R¹ = CH₃; R² = C₆H₅
- 4) R¹ = *p*-CH₃C₆H₄; R² = CH₃
- 5) R¹ = C₆H₅; R² = H
- 6) R¹ = *p*-CH₃C₆H₄; R² = H

with $^1\text{O}_2^*$, as investigated by laser flash photolysis. Apart from being a continuation of the earlier photo-oxygenation study [3], this work was motivated by the fact that sydnone is mesoionic [4 - 6] in the ground state and incorporates an azomethine imine moiety. Thus, the results are expected to throw light on the behavior of $^1\text{O}_2^*$ as a dipolarophile and to present a parallelism for $^1\text{O}_2^*$ reactivity towards carbonyl and azomethine ylides [7 - 9].

2. Experimental details

The preparation of the sydnones was carried out by literature methods referred to elsewhere [3 - 6]. Benzene (Aldrich), methanol (Aldrich), acetone (Fisher) and cyclohexane (Matheson, Coleman and Bell) were of spectral grade. Acetonitrile (Aldrich) and carbon tetrachloride (Fisher) were distilled under nitrogen. Camphorquinone (CQ) (Aldrich) and 1,3-diphenylisobenzofuran (DPBF) (Aldrich) were recrystallized from ethanol. *N*-Methylthioacridone (NMTA) was prepared from *N*-methylacridone (Aldrich) using reported procedures [10, 11].

The laser flash photolysis experiments were carried out exclusively with 485 nm pulses (1 - 8 mJ; about 6 ns). A methanolic solution of coumarin 480 (Exciton) was pumped in a Quanta-Ray PDL-1 dye laser unit using the output (third harmonic, 355 nm) from a Quanta-Ray Nd-YAG laser system. For all flash photolysis experiments, rectangular quartz cells (path lengths, 1 - 2 mm) with optically flat surfaces were used in a front-face configuration; the angle between the direction of laser pulses and the monitoring light was about 20°. Details regarding the kinetics spectrophotometer and computer-controlled data collection system are available in previous publications [12, 13] from the Radiation Laboratory.

All experiments involving $^1\text{O}_2^*$ measurements were performed in air-saturated solutions. To minimize the loss of DPBF ($^1\text{O}_2^*$ monitor) as a result of the absorption of the analyzing light by the sample before the arrival of the laser pulse, an interference filter (ORIEL 5429) was placed in the path of the light before the photolysis cell. This filter offered a sharp window (bandwidth, 9 nm) at 420 nm near the maximum of DPBF ground state absorption. In a given laser flash experiment, the net depletion of DPBF was kept at 12% or less of its total concentration used.

3. Results

The rate constants k_r for the reaction of $^1\text{O}_2^*$ with sydnones were determined by the competition technique in which the pseudo-first-order kinetics of the bleaching of DPBF at a given concentration (0.04 - 0.05 mM) were followed by the loss of absorption at 420 nm in the presence of various concentrations (0.5 - 20 mM) of the sydnones. NMTA and CQ were used as triplet photosensitizers. The advantages in using these two sensitizers were that they could be selectively excited at the 485 nm laser wavelength at which DPBF or the sydnones did not absorb and that they offered windows at 380 - 420 nm at which the depletion of DPBF could be monitored. Furthermore, at the concentrations used in the present experiments (0.02 - 0.05 mM for NMTA and 0.02 - 0.03 M for CQ), the rates of reaction of $^1\text{O}_2^*$ with the sensitizer ground states were negligible.

The various photoprocesses initiated by the 485 nm laser excitation of NMTA or CQ are as follows (Sens \equiv sensitizer; S \equiv sydnone; D \equiv DPBF):



In a companion study [14], we have shown that the sydnones are characterized by triplets with energies E_T at 41 - 47 kcal mol⁻¹ and lifetimes k_5^{-1} at 0.2 - 2 μ s. The triplets are quenched by oxygen predominantly by an energy transfer mechanism (eqn. (6a)). The quenching of ${}^3\text{CQ}^*$ ($E_T = 52$ kcal mol⁻¹ [15]) by sydnones is expected to be dominated by exothermic energy transfer (eqn. (4)). Since the rate constant for the quenching of ${}^3\text{CQ}^*$ by oxygen is rather small (2.2×10^8 M⁻¹ s⁻¹ in benzene), the origin of ${}^1\text{O}_2^*$ for reaction with sydnones in this case is primarily the oxygen quenching of sydnone triplets. In contrast, although the quenching of ${}^3\text{NMTA}^*$ ($E_T = 43$ kcal mol⁻¹ [16]) by sydnones occurs with relatively large rate constants ($k_{4a} + k_{4b} = (1 - 4) \times 10^9$ M⁻¹ s⁻¹ in benzene [14]), the efficiency of energy transfer (eqn. (4a)) in the course of this process can be less than quantitative [14], particularly with sydnones 3 - 6. However, since the rate constants for the quenching of ${}^3\text{NMTA}^*$ by oxygen are relatively large ($(5 - 12) \times 10^9$ M⁻¹ s⁻¹) in various solvents [11, 17] and the efficiencies of ${}^1\text{O}_2^*$ photosensitization by ${}^3\text{NMTA}^*$ are close to quantitative [11], ${}^1\text{O}_2^*$ available for reaction with sydnones at relatively low [S] is furnished in part by ${}^3\text{NMTA}^*$ quenching by oxygen (*i.e.* process (3a) competes favorably with processes (4a) and (4b)).

On the basis that processes (7) - (9) contribute to the decay or consumption of ${}^1\text{O}_2^*$, the observed pseudo-first-order rate constant $k_{\text{obsd}}^{\text{D}}$ for the depletion of DPBF is given by

$$k_{\text{obsd}}^{\text{D}} = k_7 + k_r[\text{S}] + k_9[\text{D}] \quad (I)$$

where

$$k_r = k_{8a} + k_{8b}$$

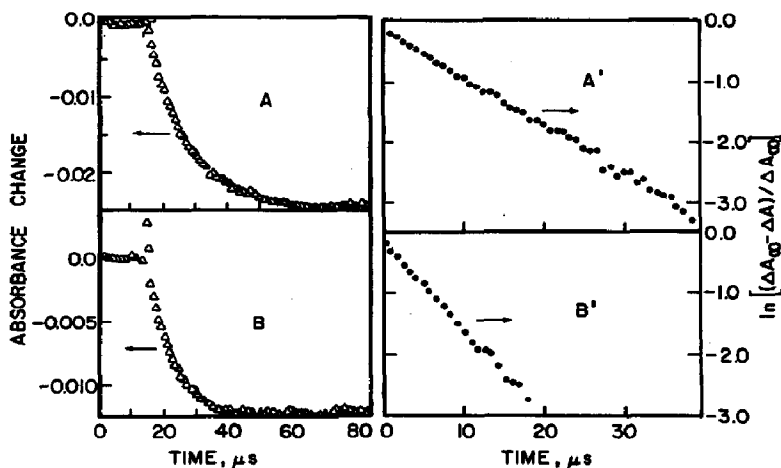


Fig. 2. Kinetics traces for DPBF bleaching at 420 nm in the absence of a sydnone (curve A) and in the presence of 13.6 mM **1** (curve B) both in air-saturated benzene containing 0.04 mM NMTA and 0.05 mM DPBF. The plots of the transient absorbance data according to the integrated equation $\ln\{(\Delta A_{\infty} - \Delta A)/\Delta A_{\infty}\} = k_{\text{obsd}}^D t$ are shown as curves A' and B' respectively.

Two representative traces for DPBF bleaching, illustrating the enhancement of its kinetics in the presence of sydnone **1**, are presented in Fig. 2. From eqn. (I) at a constant $[\text{DPBF}]$, the plot of k_{obsd}^D versus $[\text{S}]$ should be linear, with its slope equal to k_r . Several such plots are shown in Fig. 3. The data regarding k_r are compiled in Table 1.

It is noted that sydnone **4** exhibits the highest reactivity towards $^1\text{O}_2^*$. For this substrate, several solvents in addition to benzene and methanol were tried as media for measuring k_r . Unfortunately, the solubility of the sydnone in non-polar solvents (*e.g.* aliphatic hydrocarbons) is low; this, coupled with the fact that the k_r values are lower in non-polar solvents, puts a limitation on reliable measurements of the k_r values in these solvents.

To show that the interaction of $^1\text{O}_2^*$ with sydnones results in a chemical reaction (*e.g.* 1,3-endoperoxide formation (see Fig. 1)), it is worthwhile to look for the depletion of sydnone ground state absorption (280 - 370 nm). Unfortunately, except for **4**, the rate constants for the reaction of sydnones with $^1\text{O}_2^*$ are not large enough and do not allow experiments at sufficiently low $[\text{S}]$ (millimolar) so that the ground state depletion can be monitored. Figure 4 shows the absorbance changes that occur on 485 nm laser excitation of NMTA (0.05 mM) in the presence of about 1 mM of sydnone **4** in air-saturated benzene. It should be noted that, under the conditions of the experiment, $^1\text{O}_2^*$ is consumed to the extent of about 50% by interaction with the sydnone. As evident from Fig. 4 (including the inset), loss of sydnone does occur on a time scale commensurate with the decay of $^1\text{O}_2^*$ (enhanced by reaction with the substrate).

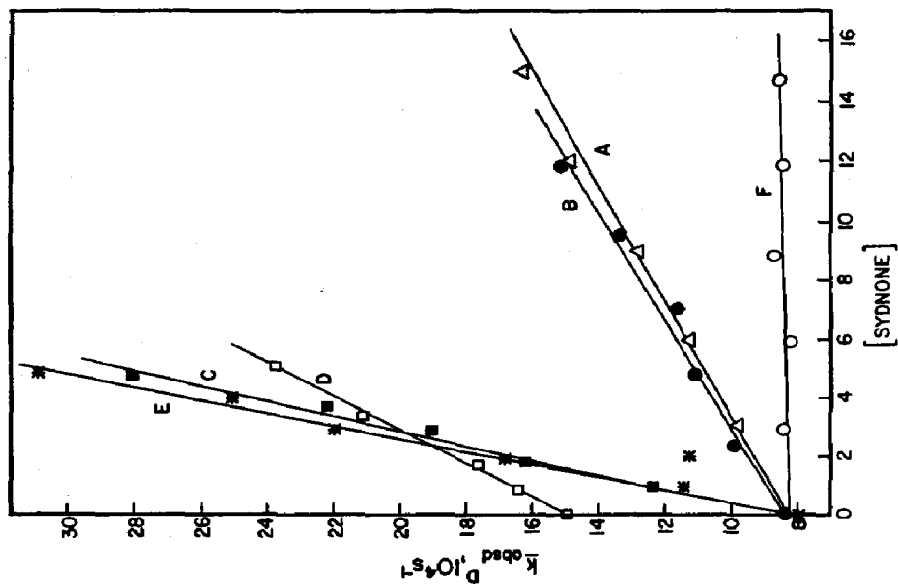


Fig. 3. Plots based on eqn. (10) ($[DPBF] = 0.05 \text{ mM}$): line A, 1 in benzene; line B, 2 in benzene; line C, 4 in benzene; line D, 4 in methanol; line E, 4 in acetone; line F, 5 in benzene.

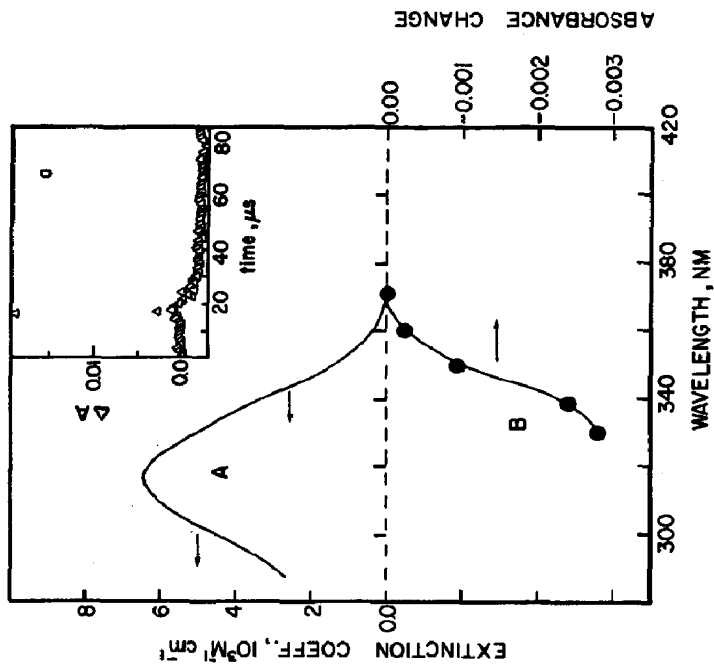


Fig. 4. Ground state absorption spectrum of sydnone 4 in benzene (curve A) and absorbance changes in the region of ground state absorption of 4 at $40 \mu\text{s}$ following 485 nm laser flash photolysis of 0.05 mM NMTA in air-saturated benzene containing 0.94 mM 4 (curve B). Inset is a kinetics trace showing the bleaching of 4 at 340 nm (the initial fast-decaying positive transient absorptions after the laser flash are due to NMTA and sydnone triplets).

TABLE 1

Rate constants k_r for the reaction of sydrones with singlet oxygen at 296 K

Sydnone	Solvent	Sensitizer	Maximum [S] (mM)	k_r^a ($\times 10^6$ M $^{-1}$ s $^{-1}$)
1	Benzene	NMTA	15.0	5.3
	Methanol	NMTA	7.4	2.8
2	Benzene	NMTA	11.9	5.4
	Methanol	NMTA	7.8	3.5
3	Benzene	NMTA	17.5	2.7
	Methanol	NMTA	9.1	2.2
4	Benzene	NMTA	4.7	40
	Methanol	NMTA	6.8	17
	Acetonitrile	CQ	5.7	49
	Acetone	NMTA	5.0	42
	Carbon tetrachloride	CQ	3.5	18
	Cyclohexane	CQ	2.0	≈ 10
5	Benzene	CQ	14.8	< 0.5
	Methanol	NMTA	9.0	< 0.5
6	Benzene	CQ	18.0	< 0.5
	Methanol	NMTA	8.8	< 0.5

^a $\pm 15\%$.

4. Discussion

It is evident from the rate constant data in Table 1 that, except for the two sydrones unsubstituted at the 4-position (*i.e.* 5 and 6), these dipolar heterocycles are moderately reactive toward $^1\text{O}_2^*$. The photo-oxygenation of four of the sydrones under study, namely 1 - 3 and 5, has been studied [3] under sensitization by Rose Bengal in oxygen-saturated methanol. Among these four substrates, 1 - 3 gave products, α,β -diaroylhydrazines and/or benzoic acid, that could be traced to the initial oxygenation of the sydrones forming endoperoxides (Fig. 1). In contrast, sydnone 5 failed to give such photo-oxygenation-derived products. In the light of the present kinetics data, one reason for this behavior may be that sydnone 5 is not reactive enough to trap $^1\text{O}_2^*$ in methanol. Given the concentration of 8.9 mM for 5 used in the photo-oxygenation study [3], the fraction of $^1\text{O}_2^*$ reacting with it would be less than 4% (on the basis of a lifetime of 10 μs for $^1\text{O}_2^*$ in methanol [18, 19]).

The substituent effect on k_r is interesting. The sydrones (1 - 4) substituted by a phenyl or methyl group at the 4-position are much more reactive toward $^1\text{O}_2^*$ than those (5 and 6) unsubstituted at this position. This can be explained in terms of more favorable frontier molecular orbital interactions in these cases [20 - 22]. Sydrones are substituted azomethine imines and

molecular orbital calculations [20, 21, 23 - 26] indicate a pronounced lowering of the lowest unoccupied (LU) orbital and a lesser lowering of the highest occupied (HO) orbital, compared with the unsubstituted azomethine imine. Also, the CO attachment ("electron-withdrawing end" of the carboxyl group) will lower the LU coefficient at the site of attachment, while the oxygen atom attachment ("electron-releasing end") will raise the LU coefficient at the site of attachment. $^1\text{O}_2^*$ containing a π molecular orbital between two heteroatoms will inevitably have low energy HO and LU orbitals, compared with ethylene, and the reaction of $^1\text{O}_2^*$ with sydnone would be expected to be "HO-dipole-controlled" reactions. Aryl and alkyl substituents at the C(4) position of sydnone would result in a large destabilization of HO and a smaller stabilization of LU and thereby accelerate the HO-dipole-controlled reaction with $^1\text{O}_2^*$, as observed in the present study. It may be mentioned, in passing, that a similar enhancement in the dipolarophilic reactivity of a sydnone resulting from an alkyl substituent at C(4) position has been reported earlier [27] in the reaction of 4-methyl-3-phenylsydnone with ethyl phenylpropionate, compared with that of 3-phenylsydnone.

As it appears from the data in Table 1, the solvent effect on k_r does not show a definitive trend. For 1 - 4, k_r drops by a factor of 1.2 - 2.4 on going from benzene to methanol. In contrast, for 4, k_r is two to three times larger in acetone and acetonitrile than in carbon tetrachloride. The latter increase in k_r with solvent polarity may be contrasted with the case of the dipolarophilic reactivity of 4-methyl-3-phenylsydnone with ethyl phenylpropionate at 140 °C, where the rate constant is found to decrease progressively with increase in solvent polarity [27] (e.g. there is an approximate sixfold decrease on going from paraffin oil to nitrobenzene). Considering the fact that sydnone is a zwitterionic substrate, characterized by large dipole moments (5 - 7 debyes) [4, 28], the small positive influence of solvent polarity on k_r in the case of 4 can be interpreted as an indication that the transition state is even slightly more polar [22, 29]. The lowering of k_r for 1 - 4 in methanol relative to benzene is probably a manifestation of hydrogen bonding at the N(2) position, providing an additional barrier for the interaction of sydnone with $^1\text{O}_2^*$.

Finally, it should be noted that, because of their aromaticity [4 - 6], sydnone is not truly representative of open-chain 1,3-dipolar systems (ylides). Semiempirical calculations [30 - 32] of the charge distribution in sydnone show that the exocyclic oxygen atom carries a substantially larger negative charge (about $0.45 e^-$) than either the N(2) or C(4) atoms forming the zwitterionic $-\bar{\text{N}}-\overset{+}{\text{N}}=\text{C}<$ moiety in the ring (about $0.1 - 0.2 e^-$). In the course of 1,3-addition of $^1\text{O}_2^*$ to sydnone their aromaticity is lost. The k_r values observed for these mesoionic heterocycles represent the lower limit of the reactivity expected in general for an open-chain azomethine imine with $^1\text{O}_2^*$. An instructive example in this regard is provided by the isoquinolinium imines with the azomethine imino group partially incorporated into an aromatic ring. The 1,3-dipolar reactivity of these compounds is much lower than that of the corresponding 3,4-dihydroisoquinoline *N*-imines [33, 34].

Acknowledgments

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