

EXCITED STATE PROPERTIES OF 2-PHENYLBENZTHIAZOLE AND 3-PHENYL-1,2-BENZISOTHIAZOLE

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(Received February 3, 1987)

Summary

The excited state behavior of 2-phenylbenzthiazole and 3-phenyl-1,2-benzisothiazole was examined by laser flash photolysis techniques in order to determine which reaction intermediates preceded their subsequent photochemistry. Both compounds, together with related derivatives, form long-lived readily detectable triplet states. Quenching constants with representative olefins have been determined and the energy transfer equilibrium between 3-phenyl-1,2-benzisothiazole and 1-methylnaphthalene has been examined. The results suggest that olefins and alkynes react with excited states of 2-phenylbenzthiazole and 3-phenyl-1,2-benzisothiazole by 1,2 addition, and no evidence for prior ring opening was obtained.

1. Introduction

Photochemical rearrangements of fused 6,5 heterocyclic compounds containing two or more heteroatoms in the five-membered ring have been studied extensively since Schmid and coworkers [1] reported the formation of benzimidazole from benzoimidazole:

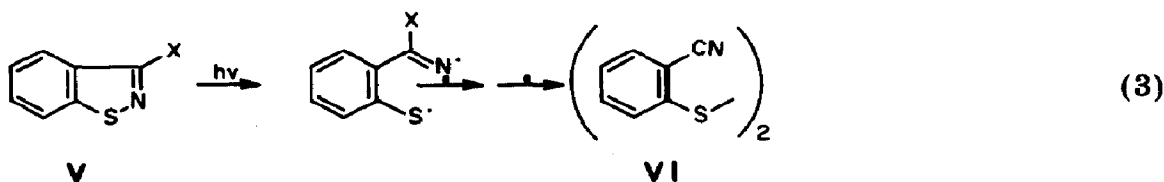


The rearrangement of benzosoxazoles to benzoxazoles has also received considerable attention [2 - 6]:

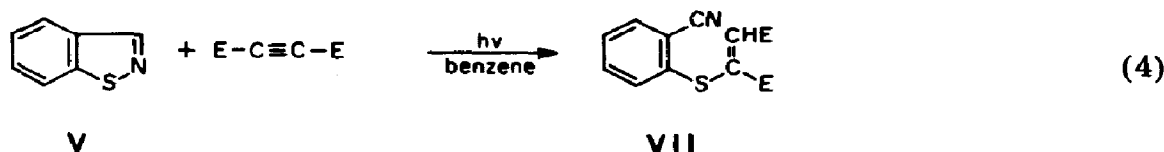


On the basis of the evidence it can be concluded that a general mechanism involving a heteroatom bond cleavage is likely in these photorearrangements. The nature of the ring-opened species formed immediately after light absorption, either a biradical or zwitterion [3 - 5], has not been established.

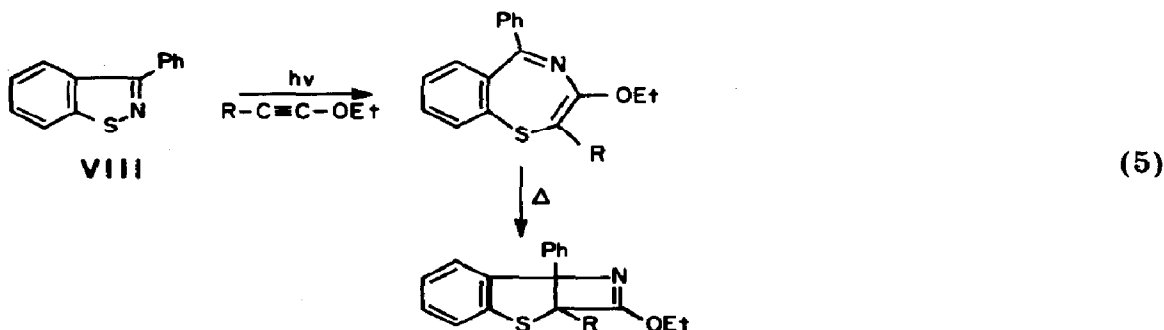
The photochemistry of the corresponding benzthiazoles and benzisothiazoles is similarly rich and also suggests the possibility of primary sulfur-nitrogen homolysis. Ring-opened products, similar to those obtained from benzisoxazole [7], were obtained from benzisothiazole V and may result from an initially formed biradical intermediate [7, 8]:



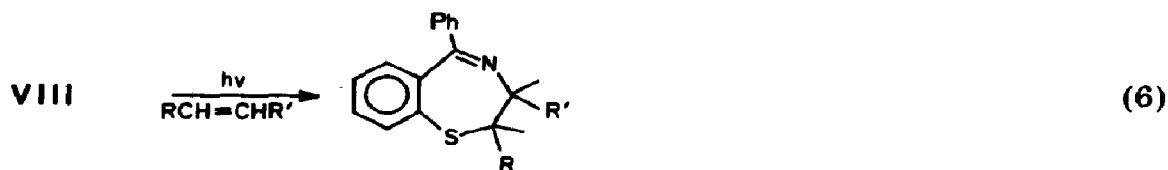
This postulate is supported by the reaction of benzisothiazole with electron-poor alkynes which produce ring-opened products (albeit in low yields) [8] ($E \equiv -COOCH_3$):



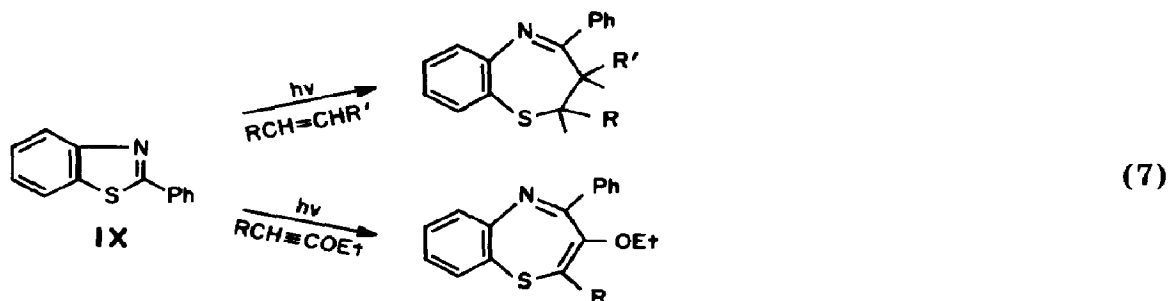
The intermediate involved in the photochemical reaction of substituted benzthiazoles and benzisothiazoles is less certain. 3-Phenyl-1,2-benzisothiazole VIII reacts with electron-rich alkynes to afford principally 3,4-benzo-2,6-thiabicyclo[3.2.0]hepta-3,6-dienes, presumably by way of a rapid thermal ring closure from an initially formed 1,4-benzthiazipine [9]



while in the presence of alkenes the photolysis of VIII yields 2,3-dihydro-1,4-benzthiazepines [9]:



Substituted benzthiazoles also give ring-expanded products when reacted with alkenes and alkynes [10, 11]:



Since the unsubstituted compounds lead to ring-opened products, it may be assumed that the ring expansion products of reactions (6) and (7) are the result of alkene (or alkyne) trapping of a ring-opened intermediate.

The study of photoprocesses such as those in reactions (3) - (7) has frequently been motivated by attempts to develop photochemical synthetic routes leading to unusual heterocyclic compounds, some of which may provide a direct entry to the pharmacologically active benzodiazepines and analogs in the benzoxazepine and benzthiazepine series [8, 9, 12].

This study was undertaken in order to gain some insight into the behavior of the intermediates involved in the photochemistry of 3-phenyl-1,2-benzisothiazole and of benzthiazole and some of its aryl-substituted derivatives. Our studies, using predominantly laser flash photolysis techniques, have allowed us to characterize the triplet states of these molecules and examine their quenching by various substrates, in particular, olefins. Biradicals, which are potential intermediates in these reactions, could not be characterized; unfortunately the results do not reveal whether these species are too short lived, produced in low yields or not at all.

2. Experimental details

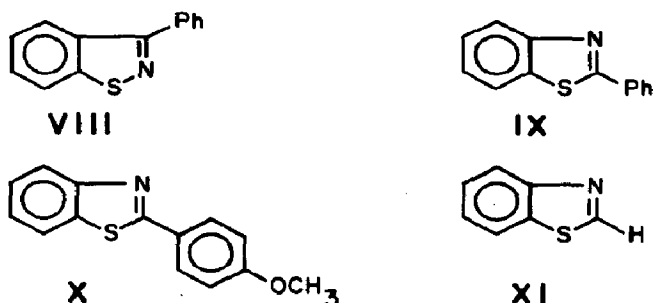
Benzthiazoles were prepared according to the method of von Hofmann [13]. 3-Phenyl-1,2-benzisothiazole was prepared and purified as previously described [14, 15].

UV-visible spectra were recorded in a Hewlett-Packard 8451 diode array spectrometer. Luminescence spectra were obtained using a Perkin-Elmer LS-5 spectrofluorometer operated via a PE-3600 data station.

Laser flash photolysis experiments were carried out using for excitation either 337.1 nm pulses from a Moletron UV-24 nitrogen laser (about 8 ns, 6 mJ pulse⁻¹ or less) or 308 nm pulses (about 5 ns, 50 mJ pulse⁻¹ or less) from a Lumonics TE-860-2 excimer laser operated with Xe-HCl-He mixtures. The detection system consists of a monochromator and photomultiplier (RCA-4840) combination, which leads to signals that are recorded by a Tektronix R-7912 transient digitizer. These signals are then transferred to a PDP11/23 computer that also provides processing, storage and hardcopy capabilities. Further details have been reported elsewhere [16, 17].

3. Results

Substrates VIII - XI



were examined in this work. Unless otherwise indicated all experiments were carried out in deaerated solutions at room temperature (about 22 °C).

3.1. Phosphorescence

Substrates VIII - XI show readily detectable phosphorescence in polar glasses at 77 K. Figure 1 illustrates the phosphorescence spectrum of IX in ethanol monitored during a 1.0 ms time window starting 1 ms after excitation. Table 1 summarizes the corresponding 0,0 band positions and triplet energies. The spectra were typically obtained at substrate concentrations in the $(2 - 7) \times 10^{-3}$ M range. In order to check for possible concentration effects the phosphorescence spectrum of IX was monitored in the range from 5×10^{-5} to 7×10^{-3} M. The fine structure and band positions remained unchanged and only changes in overall intensity were noted.

Although there appears to be no report in the literature of the phosphorescence of VIII - XI, the phosphorescence of benzoxazole, the oxygen analog of XI, has been reported [3, 6]. The two spectra are similar in terms of band structure, but the triplet from benzoxazole is 9 kcal mol⁻¹ higher in energy than that of XI.

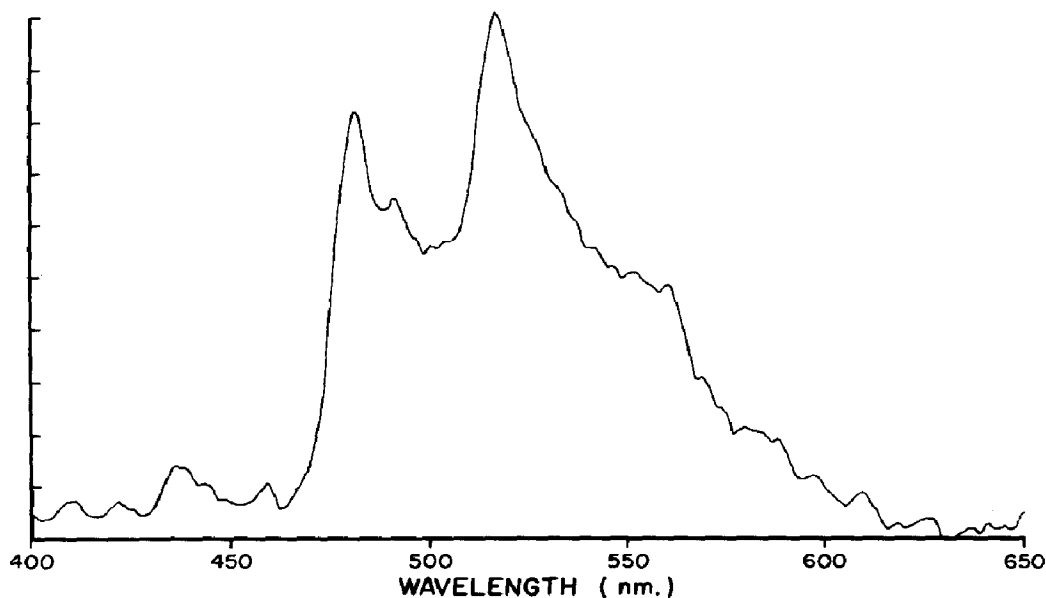


Fig. 1. Phosphorescence from IX in an ethanol glass at 77 K ($\lambda_{\text{ex}} = 250$ nm).

TABLE 1

Phosphorescence data^a

Substrate	λ_{T} (nm) ^b	E_{T} (kcal mol ⁻¹)
VIII	478.0	59.8
IX	480.5	59.5
X	483.5	59.2
XI	425.0	67.3

^aDeaerated ethanol glass at 77 K.

^b ± 0.5 nm.

3.2. Transient absorption spectra obtained by laser flash photolysis

In the cases of VIII, IX and X, laser photolysis at either 308 or 337 nm led to strong absorption signals that were characterized as being due to the corresponding triplet states. Figure 2 shows the triplet-triplet (T-T) absorption spectra for VIII - XI recorded in chlorobenzene. The decay traces observed for VIII - X were wavelength independent, suggesting that only one transient is responsible for each of these spectra in Fig. 2.

For all practical purposes XI is transparent at $\lambda > 320$ nm; thus, excitation of this substrate was carried out exclusively with the 308 nm laser pulses. The resulting T-T spectrum is also shown in Fig. 2. The decay traces obtained were not completely wavelength independent (see below). The spectrum of XI was less intense than those for substrates VIII - X.

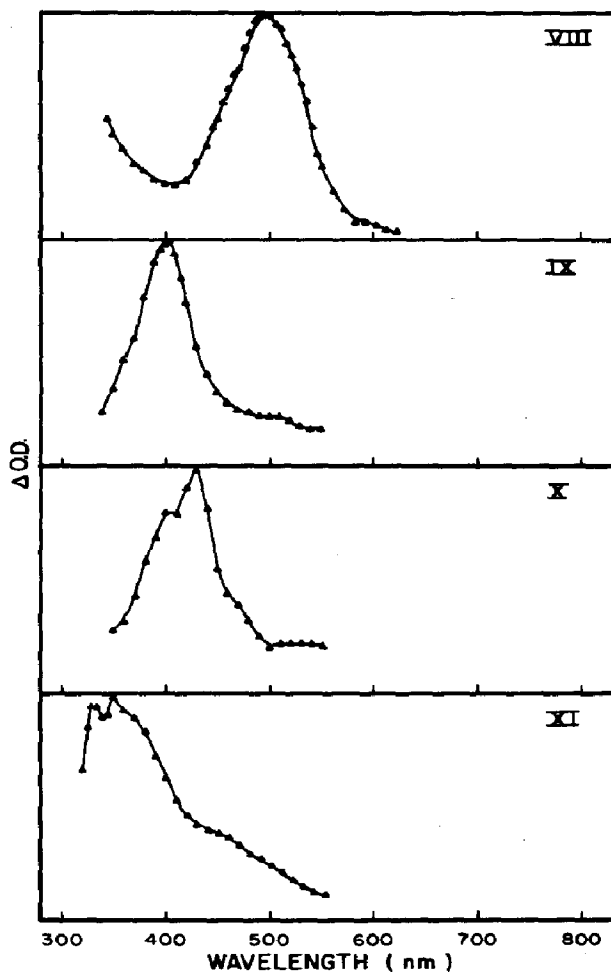


Fig. 2. T-T absorption spectra recorded in chlorobenzene at room temperature.

3.3. Decay kinetics

The decay of XI was essentially first order in the concentration range examined. However, the triplet states of VIII - X decayed by a combination of first- and second-order processes; the latter are attributed to T-T annihilation and are quite common processes under conditions of laser excitation. On a first approximation, the decays were fitted with a first-order kinetics expression k_{obs} , and the triplet lifetimes were obtained as the reciprocal of k_{obs} extrapolated to zero laser dose. The excitation beam was attenuated with a calibrated set of neutral density filters. Figure 3 shows representative plots illustrating the extrapolation to zero excitation dose. We use the transient optical density (TOD) before significant decay takes place in the horizontal axis, rather than the transmittance of the neutral density filter. Both parameters are a measure of the incident light dose, but TOD has the advantage of being calibration independent. Table 2 summarizes the corre-

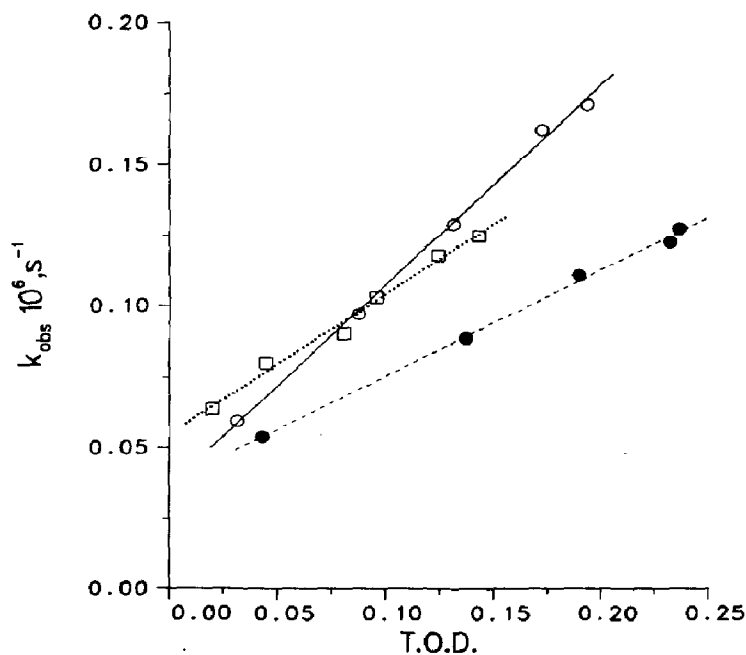


Fig. 3. Reciprocal lifetime k_{obs} as a function of the transient optical density (TOD) before significant triplet decay for VIII (○), IX (●) and X (□).

TABLE 2

Spectra and decay kinetics for the triplet states^a

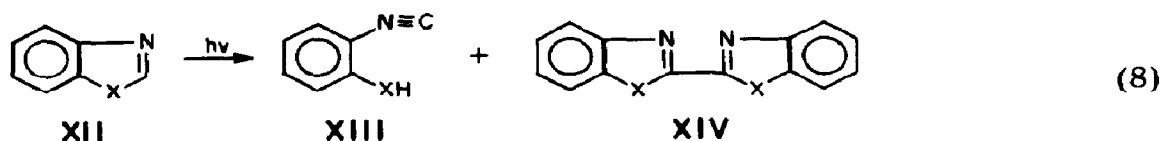
Substrate	λ_T (nm)	τ_T (μs) ^b	Highest substrate concentration (M)
VIII	495	27.8 ± 4.4	2.0×10^{-4}
IX	405	26.4 ± 2.8	1.0×10^{-4}
X	430	18.2 ± 1.8	3.2×10^{-4}
XI	350	6.9 ± 0.4	6.6×10^{-4}

^aIn chlorobenzene at 25 °C.

^bExtrapolated to zero laser dose (see text).

sponding triplet lifetimes τ_T . The values τ_T were found to be independent of the substrate concentration for concentrations below and up to those quoted in Table 2.

In the case of XI, we observe a long-lived transient, detected as a residual absorbance that does not decay significantly in the time scale of our experiments (about 12% residual absorbance at 450 nm). The spectrum for this residual absorption is not unlike that of the triplet state, suggesting the presence of a similar chromophore. In steady state studies of benzoxazole (XII; X ≡ O) Grellmann and Tauer [18] have shown that in deaerated inert solvents the following reaction occurs:



The precursor of products XIII and XIV may be a free radical, which in the case of the sulfur analog (XI) would correspond to species XV or XVI:



3.4. Quenching by energy transfer

The assignment of the transient signals of Fig. 2 and Table 2 to the corresponding triplet states was confirmed in a series of triplet quenching experiments. For example, conjugated dienes are excellent triplet quenchers with triplet energies around 58 - 59 kcal mol⁻¹ [19]. 1,3-Octadiene and 2,5-dimethyl-2,4-hexadiene were used as triplet quenchers. Under these conditions, the observable pseudo-first-order decay k_{obs} of the triplet is given by

$$k_{obs} = k_0 + k_q[Q] \quad (9)$$

where k_0 corresponds to the reciprocal lifetime in the absence of quencher and k_q is the bimolecular rate constant for quenching by quencher Q. Figure 4 shows representative plots according to eqn. (9), and Table 3 summarizes the kinetics data. It should be noted that, for VIII - X, these processes, while fast, are not diffusion controlled. For example, the rate constant for quenching for benzophenone triplets by 1,3-octadiene in chlorobenzene is $(4.7 \pm 0.6) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ at 293 K. The rate constant for XI approaches this value since energy transfer from this substrate is clearly exothermic (Table 1); the rates are much smaller for all the other substrates where energy transfer is approximately thermoneutral. In principle in these systems an energy transfer equilibrium could be established; however, the triplet lifetimes for acyclic dienes are too short and the substrate concentrations too low for such an equilibrium to be established. For all practical purposes, energy transfer to dienes is irreversible.

The situation is somewhat different in the case of 1-methyl-naphthalene (MeN). Its triplet energy is about 60 kcal mol⁻¹, but its triplet lifetime is usually quite long and the triplet energy transfer equilibrium can be readily established, with substrates VIII - X, for example, in the case of VIII. Figure 5 illustrates the evolution of the transient spectrum with time. At short times (25 ns or less after excitation) the spectrum is essentially that of triplet VIII, while after about 600 ns (for [MeN] = 0.003 M) the dominant species is triplet MeN. Thus, at wavelengths around 500 nm we observe the decay of triplet VIII, while at 420 nm the observable signal is a build-up leading to

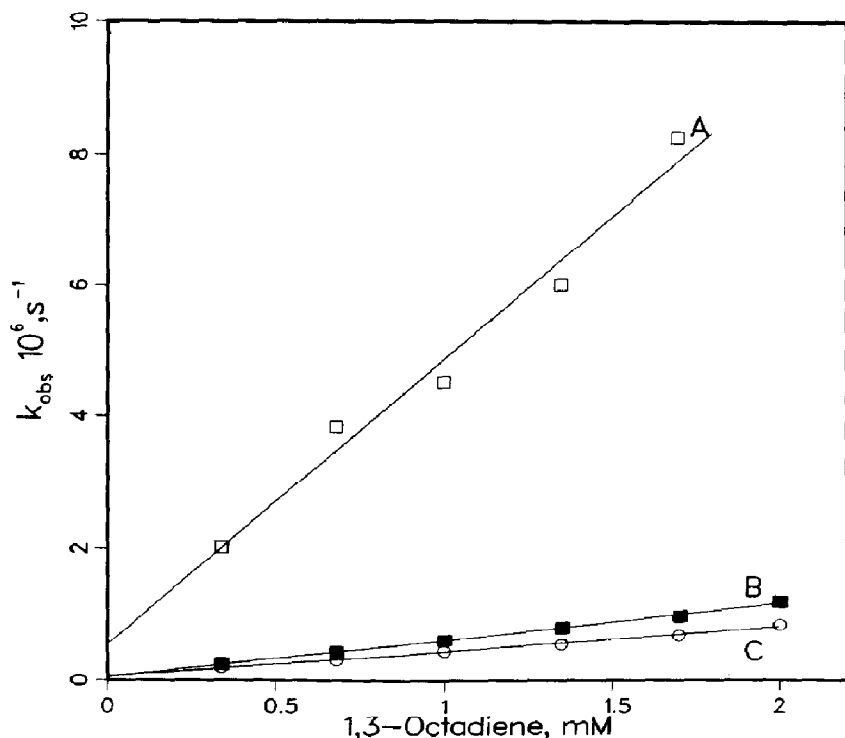


Fig. 4. Quenching of the triplet states of VIII (line C), IX (line B) and XI (line A) by 1,3-octadiene in chlorobenzene at room temperature.

TABLE 3

Triplet quenching rate constants^a

Compound	Triplet quenching rate constants k_q ($M^{-1} s^{-1}$) for the following quenchers			
	1,3-Octadiene	DMHD ^b	1,4-Cyclohexadiene	1-Octene
VIII	$(3.8 \pm 0.2) \times 10^8$	$(2.0 \pm 0.1) \times 10^9$	$(3.6 \pm 0.2) \times 10^5$	$(2.5 \pm 0.5) \times 10^4$
IX	$(5.6 \pm 0.1) \times 10^9$	$(2.25 \pm 0.04) \times 10^9$	$(3.9 \pm 0.2) \times 10^5$	$(1.84 \pm 0.73) \times 10^5$
X	$(3.7 \pm 0.1) \times 10^8$	$(2.0 \pm 0.1) \times 10^9$	$(3.5 \pm 0.4) \times 10^5$	$(1.74 \pm 0.38) \times 10^7$
XI	$(4.3 \pm 0.8) \times 10^9$	$(3.6 \pm 0.4) \times 10^9$	$(1.1 \pm 0.1) \times 10^6$	—

^aIn chlorobenzene.

^b2,5-Dimethyl-2,4-hexadiene.

the characteristic spectrum of the MeN triplet, *i.e.*



Thus, according to eqn. (10), the equilibrium constant will be given by

$$K_{\text{eq}} = \frac{[\text{VIII}][\text{MeN}^*]}{[\text{VIII}^*][\text{MeN}]} \quad (11)$$

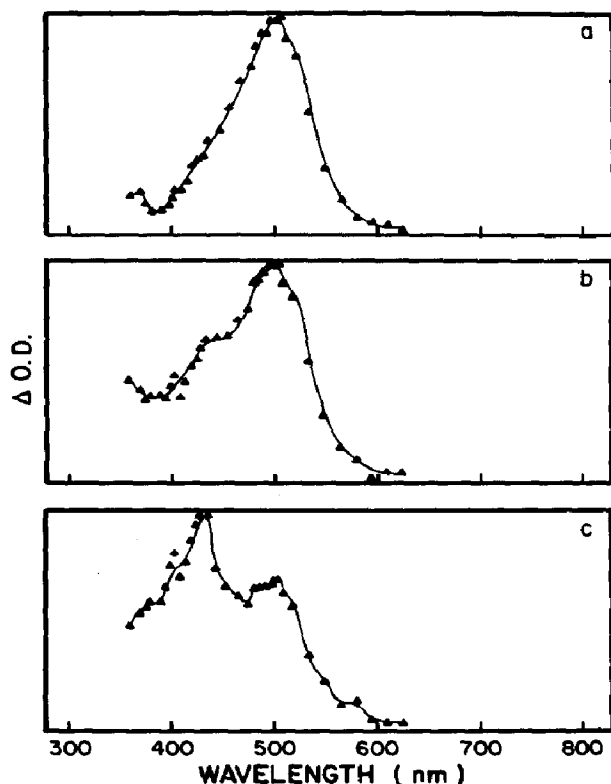


Fig. 5. Evolution of the transient spectrum with time for 2.5 mM VIII and 3.0 mM MeN in chlorobenzene. Spectra recorded (a) 50 ns, (b) 140 ns and (c) 600 ns after laser excitation.

In a first approximation $[\text{MeN}^*]$ will be given by

$$[\text{MeN}^*] = [\text{VIII}^*]^0 - [\text{VIII}^*] \quad (12)$$

where $[\text{VIII}^*]^0$ is the initial concentration of triplet VIII, before significant decay takes place. This analysis leads to $K_{e,q} = 1.5$ at 300 K in chlorobenzene, from which we can estimate the difference in free energy of excitation, *i.e.*

$$\Delta G_T(\text{MeN}) - \Delta G_T(\text{VIII}) = -0.24 \text{ kcal mol}^{-1} \quad (13)$$

Similar experiments with IX and X led to similar qualitative observations, but extensive spectral overlap between the corresponding triplets (see Fig. 2) and the MeN triplet prevented a quantitative analysis. In the case of XI, which is essentially transparent at 337.1 nm, similar experiments were not possible, and judging from its triplet energy (Table 1) energy transfer to MeN would be expected to be irreversible.

A few experiments using β -carotene as a triplet quencher led to the readily detectable formation of its triplet state via energy transfer [20]. The process was essentially diffusion controlled (typically $1 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$) but studies were rather difficult as a result of some absorption by β -carotene at the laser wavelength (308 nm).

3.5. Triplet quenching by other substrates

Triplet quenching by non-conjugated olefins is relatively slow. The data for 1-octene and 1,4-cyclohexadiene have been included in Table 3. In general XI was more reactive than the other substrates with lower triplet energies.

In addition to quenching the triplet lifetime, 1,4-cyclohexadiene also reduced the initial signal intensity (and thus initial concentration) of the observed triplet states. This suggests 1,4-cyclohexadiene also quenches the excited singlet state. The reciprocal of TOD was plotted against concentration in a Stern–Volmer plot:

$$\frac{[\text{TOD}]_0}{[\text{TOD}]} = 1 + k_q \tau_s [\text{Q}] \quad (14)$$

The resulting plot for X is shown in Fig. 6. In the case of XI there was no sign of quenching of the excited singlet. This is probably due to a short singlet lifetime τ_s and a low quenching rate constant. In the case of VIII - X, the $k_q \tau_s$ values obtained were $0.62 \pm 0.08 \text{ M}^{-1}$, $0.68 \pm 0.13 \text{ M}^{-1}$ and $0.68 \pm 0.12 \text{ M}^{-1}$ respectively. If we assume a k_q value of $1 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ it can be concluded that all three singlets are short lived, with τ_s of less than 1 ns.

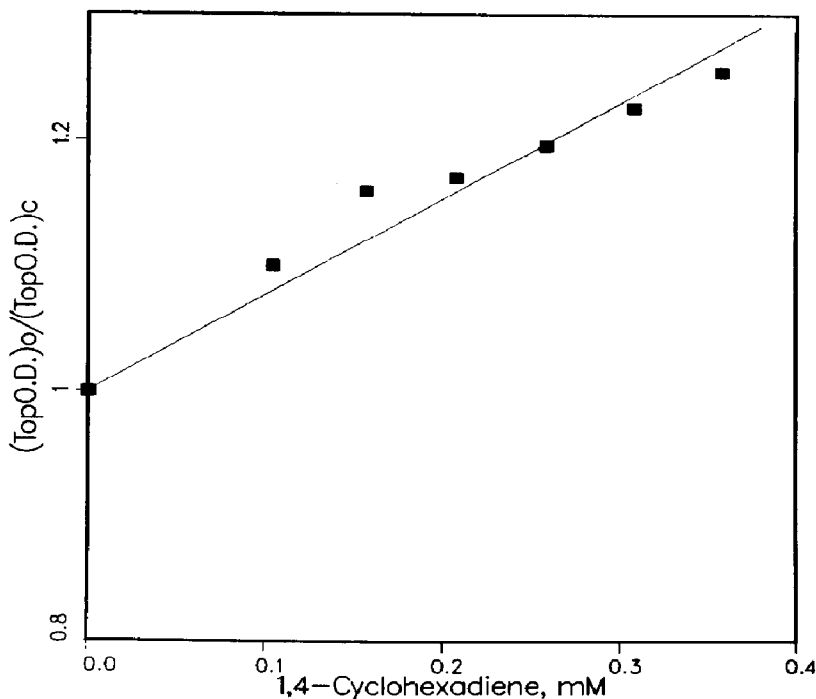


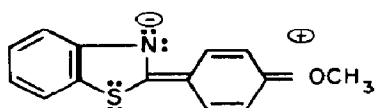
Fig. 6. Stern–Volmer plot for the quenching of triplet X (as measured by TOD) by 1,4-cyclohexadiene.

4. Discussion

On the nanosecond and microsecond time scale there appears to be no evidence of any intermediate other than the triplet states from VIII - X. The most likely reaction intermediates would be benzenethiyl type radicals or biradicals. Benzenethiyl radicals have been reported to have broad absorptions and modest extinction coefficients (e.g. $\epsilon_{450} \approx 340 \text{ M}^{-1} \text{ cm}^{-1}$ for $\text{C}_6\text{H}_5\text{S}\cdot$ [21]). These long-lived intermediates typically decay by second-order kinetics with self-reaction rate constants of $10^8 - 10^9 \text{ M}^{-1} \text{ s}^{-1}$ [21, 22]. These parameters are such that their detection under our experimental conditions would be straightforward; in spite of this, compounds VIII - X gave no indication of intermediates of this type, since they yield no residual absorption following triplet decay. At shorter times, the lack of wavelength dependence of the decay traces again indicates that the signals observed are dominated by the absorptions from a single transient, namely the triplet.

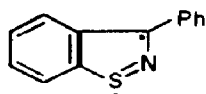
In the case of VIII no long-lived transients were observed. It is known that the oxygen analog, 3-phenylbenzisoxazole, isomerizes via ring opening in non-polar solvents to yield the substituted benzoxazole in high yields [5]. In this study no sign of a ring-opened intermediate or long-lived azene [5] was obtained. It would therefore appear that such intermediates are very short lived, or are produced in very low yields or not at all.

The triplet lifetimes, quenching rate constants and energies of the triplets derived from the structurally similar VIII - X compounds are almost identical, although there are substantial differences in the T-T absorption spectra. The T-T absorption spectrum of VIII, for example, is shifted to the red by 90 nm relative to that of structurally isomeric IX ($\lambda_{\text{max}} = 405 \text{ nm}$). *p*-Methoxy-IX (i.e. X) also shows a red shift relative to the parent compound and suggests contributions to the triplet not from ring-opened forms but from charge-separated derivatives [14]:



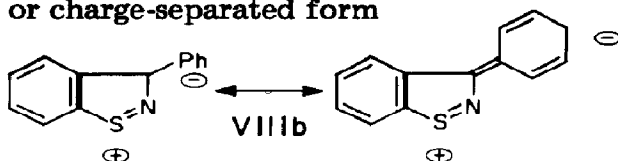
Xa

3-Phenyl-1,2-benzisothiazole (VIII) triplet belies conjugation much extended when compared with IX. A triplet biradical model



VIIIa

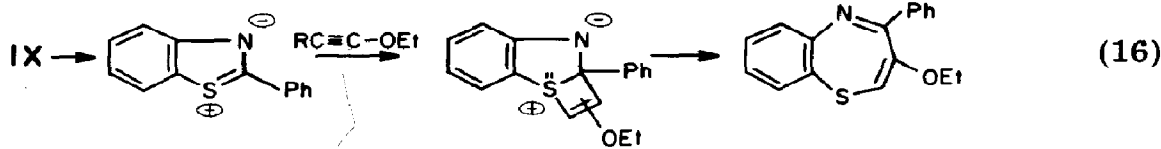
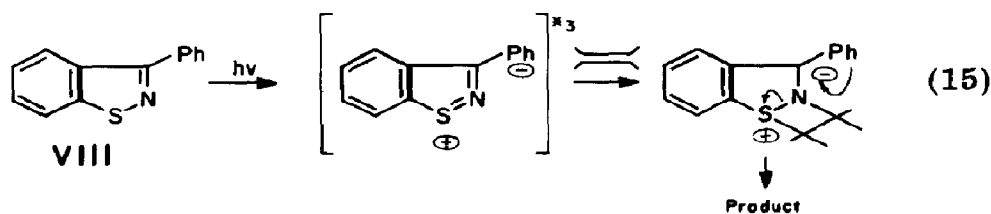
or charge-separated form



represents one possible valence bond model for the triplet. The quinomethine which derives from sulfur-nitrogen bond scission (the Heinzelmann nitrene) is also a possible model for the isothiazole triplet although the spectrum of the triplet is probably too red shifted for this to be its structure.

On the basis of He(I) and He(II) photoionization spectra, as well as calculations, Palmer and Kennedy [23] reported that for the parent compounds benzisothiazole is more stable than benzthiazole and that, in both instances, positive charge density localizes on the sulfur in both π and σ ionization states.

Given the failure to detect reaction intermediates other than the triplet state of VIII - X, it appears to be reasonable to give serious consideration to mechanistic alternatives. Taken together with the strong signal from a long-lived triplet state which belies differential charge separation in IX and in X relative to the parent XI, it seems to be unlikely that the photoproducts formed from 3-phenyl-1,2-benzisothiazole and similarly 2-phenylbenzthiazole derive from an initially formed ring-opened biradical or zwitterion, but are instead the result of reaction of the charge-separated triplet with olefin or alkyne in both cases VIII and XI at the positively charged sulfur. The formed intermediate undergoes subsequent reaction leading to the products. Thus we suggest the following 1,2-cycloaddition mechanisms on the basis of triplet state quenching. 1,2-Cycloaddition has been suggested previously by Dopfer and Neckers [24] to explain unusual rearrangement products deriving from cycloadditions of alkynes to benzo[*b*]thiophene. Since it seems to be similarly applicable this time we suggest the following scheme for the photochemical additions of olefins and alkynes to benzothiazoles and benzisothiazoles. The following mechanisms are proposed in the cases of VIII and IX:



In the case of the unsubstituted compound, XI, the initial photoprocesses may lead to the ultimate homolysis of the 2-H bond. Grellmann and Tauer [18] have shown that in some solvents (usually air saturated) no yield of the dimer, 2,2'-dibenzthiazole, could be observed. Furthermore, in the benzoxazole system a reduction in temperature to -40°C prevented entirely the formation of 2,2'-dibenzoxazole (90% yield in ethanol) and only the ring-opened product, 2-isocyanophenol, was observed. It is thus possible that for

benzthiazole the radical XV is not stable and that rapid ring opening occurs. This ring-opened radical XVI may be responsible for the weak transient observed in our experiments.

Acknowledgments

This work was partially supported by the National Institutes of Health (Grant RO1 NS 14883). We are grateful for their support. Thanks are due to Mr. S. E. Sugamori for technical assistance.

This work is issued as NRCC 26849 from the Natural Research Council of Canada.

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