Tetrahedron Letters,Vol.25,No.5,pp 581-584,1984
Printed in Great Britain

0040-4039/84 $3.00 + .00

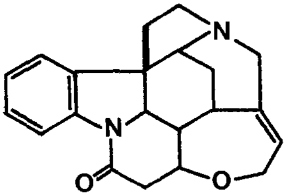
STRYCHNINE : A FAST PHYSICAL QUENCHER OF SINGLET OXYGEN ($^1\Delta_g$)

A. A. Gorman*, I. Hamblett, K. Smith and M. C. Standen

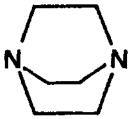
Chemistry Department, University of Manchester, Manchester M13 9PL

Pulsed laser excitation of 2-acetonaphthone in aerated benzene, toluene, acetone, acetonitrile or ethanol results in formation of $O_2(^1\Delta_g)$*, the infrared luminescence of which has been monitored by time-resolved emission spectroscopy. The rate constants for the quenching of this emission by the indole alkaloid strychnine in all five solvents have been determined and compared with the corresponding values for the well-known* O_2 $(^1\Delta_g)$ *quencher DABCO. Strychnine (1) is the fastest known tertiary amine quencher of this species via a process which is at least 99% physical in character.*

The quenching of singlet oxygen, O_2 $(^1\Delta_g)$, by amines in both gas[1] and liquid[3] phases is well documented. Correlations of quenching rate constants with amine ionisation potentials,[1,3c,3e] together with Hammett plots[3c,3d] indicate that some degree of electron transfer from quencher to O_2 $(^1\Delta_g)$ contributes to the overall process. Thus, efficiencies are highest for tertiary amines and may correspond to either physical or chemical processes. The latter appear to require the formation of an immonium system and are thus dependent on (a) the presence of hydrogen on a carbon adjacent to nitrogen and (b) the ability of the σ-framework to accommodate a double bond at nitrogen.[4] To date the fastest reported aliphatic/alicyclic tertiary amine quencher of O_2 $(^1\Delta_g)$ has been 1,4-diazabicyclo-octane (DABCO, 2) which for obvious steric reasons is exclusively a physical quencher of this species and is routinely used in diagnostic tests for its involvement



(1)



(2)

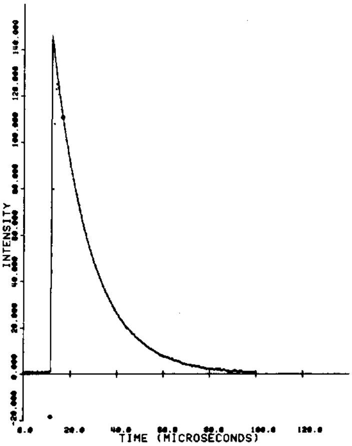


Figure 1 Time dependence of $O_2(^1\Delta g)$ emission at 1270 nm after absorption of a 10 ns laser pulse by 2-acetonaphthone (6.4×10^{-3} mol L^{-1}) in aerated benzene containing strychnine (2.7×10^{-5} mol L^{-1}). Solid line is the first-order fit.

in chemical and biochemical oxidative processes. In this paper we report that the tertiary amine function in the indole alkaloid strychnine (1) is the fastest known O_2 ($^1\Delta_g$) quencher of its type, that this quenching appears exclusively physical in nature and that slow chemical destruction of the molecule occurs, probably *via* attack by O_2 ($^1\Delta_g$) at the trisubstituted double bond.

We have determined rate constants for quenching of O_2 ($^1\Delta_g$) by both strychnine and DABCO in five solvents using the time-resolved detection of the infrared luminescence of this species at 1270 nm.[5] Typically aerated solutions of 2-acetonaphthone (2-A; 3-7 x 10^{-3} mol L^{-1}) as sensitizer containing varying concentrations of amine (0-15 x 10^{-5} mol L^{-1}) were subjected to the 10 ns pulse of the third harmonic (355 nm) of a Q-switched Nd:YAG laser. Singlet oxygen is produced exclusively *via* channel 1 in this situation.[6] The combination of processes 2 and 3 resulted in strictly exponential decay of its luminescence (Fig. 1) and a plot of the first-order

$$^3\text{2-A}^* + O_2\ (^3\Sigma_g^-) \longrightarrow \text{2-A} + O_2\ (^1\Delta_g) \qquad (1)$$

$$O_2\ (^1\Delta_g) \xrightarrow{k_d} O_2\ (^3\Sigma_g^-) \qquad (2)$$

$$O_2\ (^1\Delta_g) + \text{amine} \xrightarrow{k_q} \text{loss of } O_2\ (^1\Delta_g) \qquad (3)$$

constants for decay, k', against amine concentrations according to eq. 4 gave the overall quenching rate constants, k_q, and O_2 ($^1\Delta_g$) lifetimes ($\tau_\Delta = k_d^{-1}$). These are listed in Table 1.

$$k' = k_d + k_q\ [\text{amine}] \qquad (4)$$

It is to be noted that strychnine is, depending on medium, 2-20 times more efficient as an O_2 ($^1\Delta_g$) quencher than is DABCO. Indeed, in non-hydrogen bonding media it is one of the fastest known organic quenchers of this species, excluding electronic energy transfer quenchers such as β-carotene. The strychnine molecule contains three potential sites for reaction with O_2 ($^1\Delta_g$), although the aromatic chromophore ($\sim 10^5$ L $mol^{-1}s^{-1}$)[10] and trisubstituted double bond

Table 1 Lifetimes ($\tau_\Delta/\mu s$) and Rate Constants (k_q/L mol^{-1}s^{-1}) for Quenching of O_2 ($^1\Delta_g$) by Strychnine and DABCO

Solvent (τ_Δ)[a]	Strychnine	DABCO
benzene (31)	1.0×10^9	2.6×10^8 [b]
toluene (25)	9.3×10^8	2.1×10^8
acetone (50)	9.4×10^8	3.8×10^8
acetonitrile (56)	6.4×10^8	4.0×10^8
ethanol (13)	1.1×10^8	5.0×10^6

[a] Reference 7. [b] Reference 9.

(10^5-10^6 L mol^{-1}s^{-1})[8] cannot contribute significantly to a rate constant of the order of 10^9 L mol^{-1}s^{-1}. However, the double bond is probably responsible for the oxidation of strychnine witnessed on steady-state irradiation, which gives an as yet unidentified product. A limit has been placed on the rate constant for this chemical quenching in benzene by comparison with tetramethylethylene (TME), a substrate known to quench exclusively by chemical reaction. Irradiation of a series of reaction tubes containing 2-acetonaphthone (4.0×10^{-3} mol L^{-1}) and either strychnine or TME (3.4×10^{-2} mol L^{-1})[11] in aerated benzene on a carousel showed, after nmr analysis, that strychnine is *at least* an order of magnitude *less* reactive chemically with O_2 ($^1\Delta_g$) than is TME ($k_q = 4.0 \times 10^7$ L mol^{-1}s^{-1}). This means that deactivation of this species by strychnine is more than 99% physical in character, at least in benzene.

The ionisation potential of strychnine is unknown, but available evidence would indicate a higher value than for DABCO.[12] This fact together with the lack of systematic solvent effects (Table 1) indicates that factors other than charge-transfer may also be playing a significant role in the quenching process. In a related piece of work[13] we have shown that the quenchings of O_2 ($^1\Delta_g$) by both DABCO and triethylamine are entropy controlled, i.e. exhibit $\Delta H^\ddagger$ values of zero. This behaviour is also typical of a number of *chemical* quenchers of O_2 ($^1\Delta_g$), indoles,[14] furans,[14] olefins[15] and enol ethers,[16] and the similarities with photochemical processes involving rapid reversible exciplex formation have been emphasised.[16] It appears possible that the 'fast' physical quenching of O_2 ($^1\Delta_g$) by strychnine could at least in part, reflect particularly favourable entropy factors associated with exciplex formation.

Excluding mechanistic aspects, the fact that strychnine is an efficient, predominantly physical, quencher of O_2 ($^1\Delta_g$) raises interesting questions concerning a possible biological role for alkaloids in general. Do they protect plant tissue from O_2 ($^1\Delta_g$) induced damage ? Further work on such systems is in progress.

Acknowledgements

Singlet oxygen luminescence measurements were performed at the Center for Fast Kinetics Research at the Univesity of Texas at Austin. The CFKR is supported jointly by NIH Grant RR00886 from the Biotechnology Branch of the Division of Research Resources and by the University of Texas at Austin. The research was sponsored by the Science and Engineering Research Council.

References

1. (a) K. Furukawa and E. A. Ogryzlo, *J. Photochem.*, 1972, *1*, 63; (b) E. A. Ogryzlo, Reference 2, p. 17.
2. "Singlet Oxygen-Reactions with Organic Compounds and Polymers", B. Ranby and J. F. Rabek, eds., Wiley, New York, 1978.
3. (a) C. Ouannes and T. Wilson, *J. Amer. Chem. Soc.*, 1968, *90*, 6528; (b) R. H. Young and R. L. Martin, *ibid.*, 1972, *94*, 5183; (c) R. H. Young, R. L. Martin, D. Feriozi, D. Brewer and R. Kayser, *Photochem. Photobiol.*, 1973, *17*, 233; (d) R. H. Young, D. Brewer, R. Kayser, R. Martin, D. Feriozi and R. A. Keller, *Can. J. Chem.*, 1974, *52*, 2889; (e) B. Monroe, *J. Phys. Chem.*, 1977, *81*, 1861; (f) R. H. Young and D. R. Brewer, Reference 2, p. 36.
4. D. Bellus, Reference 2, p. 61.
5. (a) J. R. Hurst, J. D. McDonald and G. B. Schuster, *J. Amer. Chem. Soc.*, 1982, *104*, 2065; (b) J. G. Parker and W. D. Stanbro, *ibid.*, 1982, *104*, 2067; (c) P. R. Ogilby and C. S. Foote, *ibid.*, 1982, *104*, 2069; (d) M. A. J. Rodgers and P. J. Snowdon, *ibid*, 1982, *104*, 5541.
6. A. A. Gorman, I. Hamblett and M. A. J. Rodgers, submitted for publication.
7. Lifetimes are in excellent agreement with published values.[5a,b,c; 8]
8. J. G. Brummer and F. Wilkinson, *J. Phys. Chem. Ref. Data*, 1981, *10*, 809.
9. This is higher than published values.[8] Repetition of this experiment using different benzene and DABCO preparations and the O_2 $(^1\Delta_g)$ time-resolved luminescence facility at the Christie Hospital and Holt Radium Institute, Manchester, gave a value of 2.5×10^8 L $mol^{-1}s^{-1}$.
10. Estimated from the time-resolved quenching of O_2 $(^1\Delta_g)$ luminescence by N-methylacetanilide.
11. Laser experiments have shown that these substrate concentrations do not significantly compete with oxygen for ^{3}2-A*.
12. P. Bischoff, J. A. Hashmall and E. Heilbronner, *Tet. Letters*, 1969, 4025; S. F. Nelson and J. M. Buschek, *J. Amer. Chem. Soc.*, 1974, *96*, 7930.
13. I. R. Gould, Ph.D. Thesis, University of Manchester, 1980.
14. A. A. Gorman, G. Lovering and M. A. J. Rodgers, *J. Amer. Chem. Soc.*, 1979, *101*, 3050.
15. J. R. Hurst and G. B. Schuster, *J. Amer. Chem. Soc.*, 1982, *104*, 6854.
16. A. A. Gorman, I. R. Gould and I. Hamblett, *J. Amer. Chem. Soc.*, 1982, *104*, 7098.

(Received in UK 21 November 1983)