Tetrahedron Letters, Vol.22, No.40, pp 3949 - 3952, 1981
Printed in Great Britain

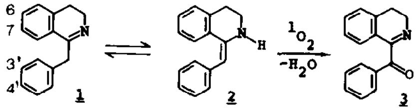
0040-4039/81/403949-04$02.00/0

EVIDENCE FOR A CHARGE-TRANSFER MECHANISM IN THE PHOTO-OXYGENATION OF AN ENAMINE

Ned H. Martin & Charles W. Jefford,*
Department of Organic Chemistry, University of Geneva
1211 Geneva 4, Switzerland

Summary. Evidence for a charge-transfer mechanism in the photo-oxygenation of the enamine form of 1-benzyl-3,4-dihydroisoquinolines is presented. Substituent effects, normalized to constant enamine concentration, fit best a mechanism involving the formation of a rate-determining charge-transfer complex.

Although charge-transfer mechanisms have been proposed for the photo-oxygenation of enamines[1] and enol ethers,[2] evidence has only been presented thus far for the special case of cyanoaromatic-sensitized photo-oxygenations.[2,3] We now report on the photo-oxygenation of 1-benzyl-3,4-dihydroisoquinolines (1), which are in equilibrium with their enamines (2). Analysis of the effects of substituents on the rate of photo-oxygenation enables the mechanistic possibilities to be limited to a charge-transfer mechanism.



Competitive methylene blue-sensitized photo-oxygenation of equimolar mixtures of substituted and unsubstituted 1-benzyl-3,4-dihydroisoquinolines in chloroform gave the relative rates.[4] A single oxidation product, the corresponding 1-benzoyl-3,4-dihydroisoquinoline (3), was obtained from each substrate.[5] The reactions obeyed pseudo-first order kinetics and the involvement of singlet oxygen was confirmed by the usual tests.[6] Plots of the logarithms of the relative rates against the Hammett σ constants[7] gave straight lines, the slopes of which were found to be ρ = +0.29 for the 3'- and 4'-substituted compounds, and +0.89 for the 6- and 7-substituted compounds (Fig. 1). The positive values of ρ appear to be inconsistent with the electrophilicity of singlet oxygen, but are due to the enhanced concentration of the enamine tautomer of compounds bearing electron-withdrawing substituents.[9]

The ultaviolet-visible spectrum of these compounds enables the equilibrium amount of enamine (2) to be determined since 2 has a chromophore absorbing at 345-455 nm characteristic of the α-aminostilbene grouping. Moreover, the molar extinction coefficient (ε) is essentially independent of substituents,[10] thus its value is proportional to the enamine concentration. The logarithms of ε correlate well with the Hammett σ values for both the 3'- and 4'- and the 6- and 7-substituted series (Fig. 2). This shows that the enamine concentration is a linear free energy function of the substituents.

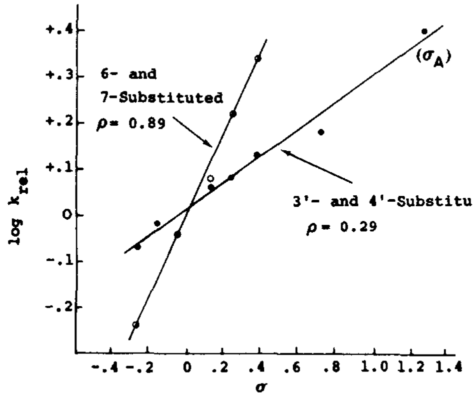


Fig. 1 Logarithm of relative photo-oxygenation rates of some 1-benzyl-3,4-dihydroisoquinolines *vs* Hammett σ constants

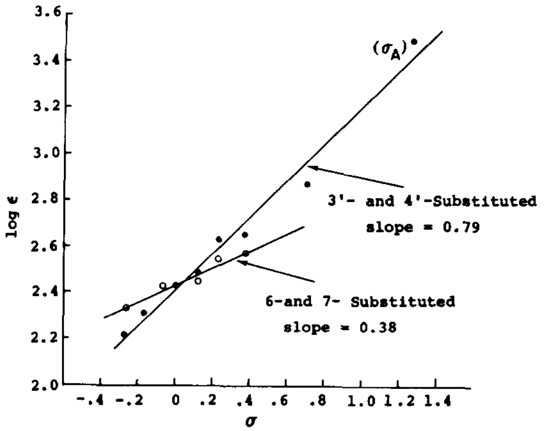


Fig. 2 Logarithm of molar extinction coefficients (ε) of some 1-benzyl-3,4-dihydroisoquinolines *vs* Hammett σ constants

In order to correctly determine the effect of substituents on the rate of singlet oxygen reaction, logarithms of the ratio of relative oxidation rates to ε for the various compounds were plotted against Hammett σ constants[7] (Fig. 3). It is seen that the slope for the 3'- and 4'-substituted compounds is negative (ρ' = -0.50), whereas the 6- and 7-substituted compounds give a positive value (ρ' = + 0.53). How can this result be reconciled with the possible mechanisms ? Five processes can be envisaged (Scheme). Firstly, singlet oxygen could react with the electron-rich double bond to generate a perepoxide (4) which could then abstract a proton to give the hydroperoxide 5 which by prototropy and dehydration gives the iminoketone 3.

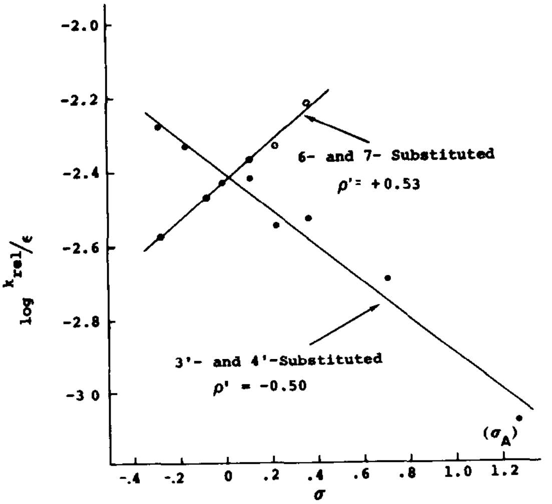
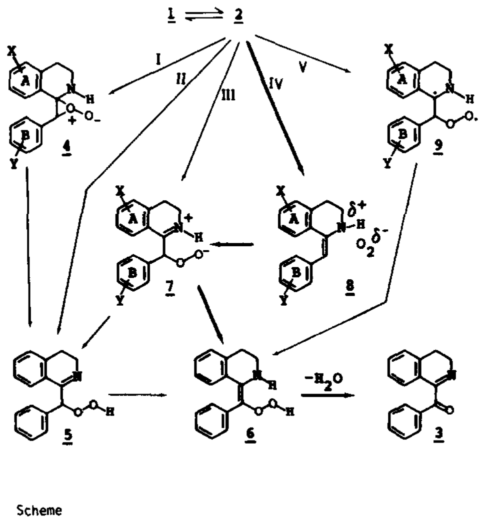


Fig. 3 Logarithm of the ratio of relative photo-oxygenation rates to ε *vs* Hammett σ constants



Scheme

Secondly, a concerted ene mechanism could occur to give the hydroperoxide 5 directly and then 3 by dehydration. Thirdly, a zwitterionic peroxide (7) could form, which again leads to 3 *via* the hydroperoxides 5 or 6. A fourth possibility involves transfer of charge from the enamine to singlet oxygen. The resulting complex (8) could collapse to 7 which would evolve to iminoketone 3. Lastly, a diradical mechanism could generate the peroxy diradical 9 to give successively 6 and 3.

We now examine these possibilities to see what effects substituents would have. (I) When substituents X and Y are electron-donating, they should equally stabilize the perepoxide 4 and exhibit negative ρ values. (II) The effect of electron-donating substituents X and Y would be to lower the energy of the transition state for the ene type mechanism, as the energy of the enamine HOMO should be raised. Negative ρ values would be predicted. (III) When X is an electron-donating substituent, the zwitterionic intermediate 7 should be stabilized. The nature of the Y substituent should have little effect on the stability of the intermediate as ring B is essentially insulated from the positive and negative centres. A negative ρ value is therefore expected for the X substituent and a zero value for substituent Y. (IV) An electron-attracting substituent X should stabilize the charge-transfer complex 8 in the same way as it stabilizes the enamine 2, although the effect may be moderated due to positive charge on the nitrogen atom. Moreover, when Y is an electron-donating substituent, the cationic centre on nitrogen should be stabilized. Opposing this effect is the destabilizing influence of electron-donating substituents on the enamine. A small positive ρ value is predicted for substituent X while a small negative value is expected for substituent Y. (V) The diradical intermediate 9 would be stabilized by an electron-donating substituent X, but the nature of Y would have little effect since both radical sites are insulated. A negative ρ value is expected for X and a negligible value is expected for the Y substituent.

In summary, it is seen that of the various mechanisms which are possible for the photooxygenation of 1 in its enamine form 2 the charge-transfer process is the one which best fits the substituent effects (Table).

Table

Mechanism		Signs of ρ' predicted for substituents	
		X	Y
I	Perepoxide	-	-
II	Concerted (ene)	-	-
III	Zwitterionic peroxide	-	0
IV	Charge transfer	+	-
V	Diradical	-	0
	Observed:	+	-

Acknowledgments. We wish to thank the Swiss National Science Foundation for the support of this work (grant No 2.418-0.79). N.H.M. is on leave from the University of North Carolina at Wilmington, Wilmington, North Carolina 28403, USA.

REFERENCES AND NOTES

1. (a) C.S. Foote & J.W.-P. Lin, Tetrahedron Letters 3267 (1968); (b) C.S. Foote, A.A. Dzakpasu & J.W.-P. Lin, *ibid.* 1247 (1975); (c) C.S. Foote, "Singlet Oxygen - Reactions with Organic Compounds and Polymers", B. Ränby & J.F. Rabek, Eds, Wiley, New York, 1978, p. 135.
2. A.P. Schaap, K.A. Zaklika, B. Kaskar & L.W.-M. Fung, J. Am. Chem. Soc. 102, 389 (1980).
3. L.T. Spada & C.S. Foote, J. Am. Chem. Soc. 102, 391 (1980).
4. The photo-oxidations were carried out as described in ref. 5b.
5. (a) N.H. Martin, P.B. Belt & S.L. Champion, Tetrahedron Letters 2613 (1980); (b) N.H. Martin & C.W. Jefford, Helv. Chim. Acta (submitted).
6. The rate of photo-oxygenation was unaffected by the addition of 2,6-di-*t*-butyl-*p*-cresol, but was diminished considerably by DABCO; reaction ceased in the absence of light. Identical products and relative rates were obtained using 1,4-dimethylnaphthalene-1,4-endoperoxide in the dark as source of singlet oxygen. See ref. 5b.
7. The constant σ_A, designed for anilinium ion acidity,[8a] but also used for β-aryl enamines (vinylogous aniline),[8b] provided the best fit with the experimental data for the 4'-nitro compound.
8. (a) H.H. Jaffé, Chem. Rev. 53, 191 (1953); (b) H. Ahlbrecht, H. Hanisch, W. Funk & R.D. Kalas, Tetrahedron 28, 5481 (1972).
9. (a) H. Ahlbrecht & S. Fischer, Tetrahedron 26, 2837 (1970); (b) H. Ahlbrecht, J. Blecher, H. Hanisch, G. Papke & M. Th. Reiner, *ibid.* 29, 3079 (1973); (c) H. Ahlbrecht, *ibid.* 26, 4783 (1970).
10. Only when a strong mesomeric electron-attracting group is conjugated with the nitrogen atom, as in the 4'-nitro compound, is the ε value significantly affected by substituents in α-aminostilbenes.[8b,9c] Adjustment of the k_{rel}/ε ratio to compensate for the enhanced ε of the 4'-nitro compound gives a ρ' of -0.35 (r = 0.977).

(Received in Germany 9 June 1981)