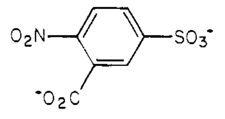
The formation of 3-carboxylato-4-nitrophenoxide ion (**4**) was monitored as a growing absorption peak at 425 nm in difference spectra during the course of the reaction (Figure 2A-D). The rate of formation of **4** was increased when oxygen was bubbled through the solution, but the final yield of **4** is essentially independent of whether or not oxygen has been deliberately provided.

In the first few minutes of the reaction, the difference spectrum also displayed an absorption maximum at ~315 nm (Figure 2A). When oxygen was not deliberately supplied by bubbling, this peak decayed very slowly as the product nitrophenoxide ion **4** was formed. When oxygen was bubbled through the solution for 3-min periods, the peak at ~315 nm was markedly diminished, and the nitrophenoxide peak at 425 nm was markedly enhanced (Figure 2B, C). With sufficient oxygen treatment, the peak at 315 nm was totally abolished, and the product spectrum became stable (Figure 2D).

These facts may be understood in terms of Scheme I, in which hydroxide ion very rapidly attacks the sulfenate ion **2** to form a Meisenheimer complex. The $pK_a'$ of the hydroxyl group of this complex would be less than the $H_-$ of the solvent (~18).[5] Thus, the complex would exist predominantly as its conjugate base (**5**). A two-electron oxidation involving $O_2$ would produce the Meisenheimer complex **6**, and the absorption maximum near 315 nm is due to **5** and/or **6**.[6] The oxygen sensitivity of this absorption is due to a further two-electron oxidation of **6** to the Meisenheimer complex **7** which undergoes rapid loss of sulfite ion[4] to give the product nitrophenoxide ion **4**.[7-9]

The species **7** is *formally* a deprotonated Meisenheimer complex of hydroxide ion with 3-carboxylato-4-nitrobenzenesulfonate ion (**8**). The decomposition of the sulfonate **8** in 15.3 M KOH is first order with a $k_{obsd}$ of 1.12 × $10^{-3}$ $s^{-1}$ at 25 °C.[10] The products are stable and consist of the nitrophenoxide ion **4** in 50% yield (presumably formed by way of **7**) and a new species[11] with $\lambda_{max}$ of 362 ± 2 nm ($\epsilon_{max}$ 15600 $M^{-1}$ $cm^{-1}$). No significant absorption in this region is produced during the decomposition of the disulfide **1** in 15.3 M KOH (Figures 1 and 2). *This establishes that the sulfonate **8** is not produced at any stage in the decomposition of the disulfide **1** in 15.3 M KOH.*



**8**

Although stable Meisenheimer complexes of trinitro[2a] and dinitro[2c] derivatives of benzene are well-known, Meisenheimer complexes of mononitro derivatives of benzene have heretofore been identified only as transient intermediates.[2a,b] The stability of **5** and/or **6** is presumably associated with lack of a good nucleofuge by virtue of loss of a proton in the highly basic medium.

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**Robert L. Blakeley,* Burt Zerner***
*Department of Biochemistry, University of Queensland*
*St. Lucia, Queensland, Australia 4067*

*Received April 28, 1980*

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[4] (a) The reaction mixture (13 mL) was diluted and acidified with $H_3PO_4$ (net concentration 2.2 M). Sulfur dioxide was distilled at gentle reflux in a stream of nitrogen into a tetrachloromercurate solution and then determined by the pararosaniline technique (Method B) of Scaringelli et al.[4b] Control experiments established a recovery of 65-70%. The corrected ratio $[SO_2]_\infty/[\text{3-carboxylato-4-nitrophenoxide}]_\infty$ was 0.8. (b) Scaringelli, F. P.; Saltzman, B. E.; Frey, S. A. *Anal. Chem.* **1967**, *39*, 1709-1719. Scaringelli, F. P.; Norris, D.; Hochheiser, S. *Ibid.* **1970**, *42*, 1818-1820.

[5] Yagil, G. *J. Phys. Chem.* **1967**, *71*, 1034-1044.

[6] The apparent value of $\epsilon_{315}$ is (1.3 ± 0.2) × $10^4$ $M^{-1}$ $cm^{-1}$. Similar values have been reported for 2,5-cyclohexadienones: Baird, R.; Winstein, S. *J. Am. Chem. Soc.* **1963**, *85*, 567-578.

[7] The final step (**7** → **4**) is analogous to the elimination of sulfite which occurs when 2,4,6-trinitrobenzenesulfonate reacts with amines to form the corresponding 2,4,6-trinitroaniline derivative (Fields, R. *Methods Enzymol.* **1972**, *25*, 464-468) and to the elimination of phosphate which occurs when 4-nitrophenyl phosphate reacts with dimethylamine (Kirby, A. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1965**, *87*, 3217-3224).

[8] Roughly 50% of the final [**4**] is produced in the first 3 min as oxygen initially present in the system is depleted. Subsequent conversion of **5** and/or **6** to **4** is much slower unless oxygen is supplied. The reproducibility and light insensitivity of these reactions render unlikely the possibility that aromatic radical mechanisms are involved.

[9] When the spectrum of **4** present at each stage (based on $A_{425}$) is subtracted from the difference spectra in Figure 2A-D, a new difference spectrum is obtained with $\lambda_{max}$ 475 ± 5 nm [$\epsilon_{475}$ (1.0 ± 0.1) × $10^4$ $M^{-1}$ $cm^{-1}$] (Figure 1D). This difference spectrum is essentially stable with respect to time and independent of oxygenation. It is postulated to be due to 3-carboxylato-5-sulfinato-2-nitrophenoxide ion or the corresponding sulfonate, produced by addition of hydroxide ion ortho to the nitro group of the sulfenate **2** [in parallel to para addition (Scheme I)] followed rapidly by the equivalent of hydride transfer to $O_2$ and oxidation of the sulfur. Loss of the hydrogen atom may involve transition-metal ion impurities which are present at ~0.1 mM in 15.3 M reagent grade KOH.

[10] (a) Species **8** was produced by performic acid oxidation[10b] of 5,5′-dithiobis(2-nitrobenzoic acid). The dried solid[10c] had a $\lambda_{max}$ of 263 nm at pH 7.0. Kinetics of decomposition in 15.3 M KOH were monitored at 263, 360, and 425 nm. (b) Moore, S. *J. Biol. Chem.* **1963**, *238*, 235-237. (c) Silverstein, R. M.; Hager, L. P. *Biochemistry* **1974**, *13*, 5069-5073.

[11] This species is tentatively identified as the 3-carboxylato-5-sulfonato-2-nitrosophenoxide ion, which would be expected to form on this time scale by addition of hydroxide ion ortho to the nitro group followed by proton abstraction.[2b]

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## Photochemistry of 4-Hydroxybenzothiazole: A Model for Pheomelanin Photodegradation

*Sir:*

The melanin pigments occurring in the hair and skin of most mammals are divided into two major classes, the brown-black eumelanins and the red-brown pheomelanins. Melanins are the major photoprotective pigments present in the epidermis.[1] However, compared to eumelanin, pheomelanin is exceptionally photolabile,[2] and it has been suggested that this photolysis contributes to the well-documented hypersensitivity to sunlight and susceptibility to chronic solar damage exhibited by fair-skinned individuals[3] whose epidermis contains pheomelanin. It is necessary to have further information on the mechanism(s) of pheomelanin photolysis to obtain a better understanding of these effects. Herein we report on the primary photochemical steps leading to photoionization of both pheomelanin (PM) and a model compound, 4-hydroxybenzothiazole (BTH).

Aerobic irradiation of red-brown pheomelanins has been shown to result in formation of the superoxide anion, $O_2^-\cdot$.[2b,c] Although the pigment consists of approximately 13% chromophore and 87% protein,[2b] photochemical production of $O_2^-\cdot$ has been shown to be a consequence of absorption of light by the chromophore and not the protein.[2c] The chromophore is believed to be a polymer incorporating the 4-hydroxybenzothiazole (BTH) moiety as the basic unit (structure **1**).[4] Problems with homogeneity and solubility have thus far frustrated attempts to investigate in detail the mechanism(s) of pheomelanin photolysis, and, thus, we have turned to BTH[5] as a model compound.

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[1] Pathak, M. A.; Fitzpatrick, T. B. In "Sunlight and Man"; Fitzpatrick, T. B., Ed.; University of Tokyo Press: Tokyo, 1974; pp 725-750.

[2] (a) Chedekel, M. R.; Post, P. W.; Deibel, R. M.; Kalus, M. *Photochem. Photobiol.* **1977**, *26*, 651-653. (b) Chedekel, M. R.; Smith, S. K.; Post, P. W.; Vessell, D. L. *Proc. Natl. Acad. Sci. U.S.A.* **1978**, *75*, 5395-5399. (c) Chedekel, M. R.; Agin, P. P.; Sayre, R. M. *Photochem. Photobiol.* **1980**, *31*, 553-555.

[3] Agin, P. P.; Sayre, R. M.; Chedekel, M. R. *Photochem. Photobiol.* **1980**, *31*, 359-362.

[4] Prota, G.; Thomson, R. H. *Endeavour* **1976**, *35*, 32-38.

[5] BTH was prepared as follows: 2-amino-4-methoxybenzothiazole, prepared by the method of Erlenmeyer and Uberwasser,[6] was first converted to 4-methoxy-benzothiazole[7] whereupon the methoxy group was removed.[6]

[6] Erlenmeyer, H.; Uberwasser, H. *Helv. Chim Acta* **1942**, *25*, 515-520.

[7] Chedekel, M. R.; Sharp, D. E.; Jeffery, G. A. *Synth. Commun.* **1980**, *10*, 167-173.

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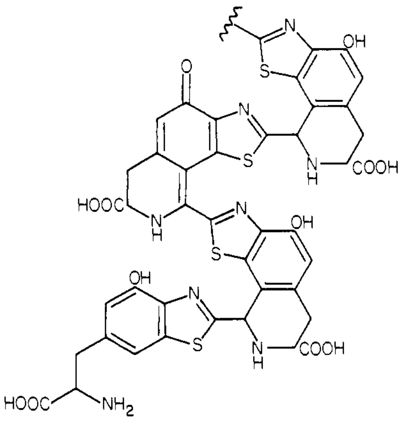
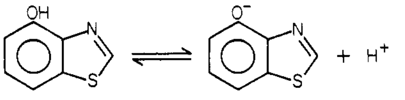
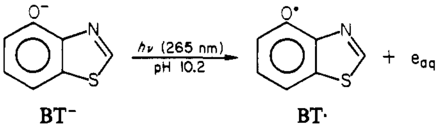


In both organic solvents and aqueous solutions at pH <8.0, the absorption spectrum of BTH contains a characteristic peak at 300 nm. At pH >9.9, this peak is red shifted to 325 nm. This spectral shift is presumably the result of ionization of the phenol function as shown in eq 1, and by monitoring the increase in absorption at 325 nm with pH we have obtained a corrected[8] p$K_a$ value of 8.9 at 20 °C.[9]

 (1)

BTH BT⁻

Laser flash photolysis[10] (265 nm) of 1 × $10^{-4}$ M BT⁻ in an argon-saturated aqueous solution, pH 10.2, yielded $e_{aq}^-$[11] with a quantum yield ($\Phi_I$) of 0.07 ± 0.02[12] and a long-lived ($t_{1/2}$ = 1 ms) transient. The absorption spectrum of this long-lived species (Figure 1), obtained in an $N_2O$-saturated solution immediately after the laser pulse, is most probably due to the 4-hydroxybenzothiazole neutral radical (BT·) as the predominant species. Thus, optical excitation of BT⁻ should yield equal concentrations of BT· and $e_{aq}^-$ (eq 2). At low BT⁻ concentrations where the decay of $e_{aq}^-$ is negligible during the flash, the extinction coefficient of BT· ($\epsilon_{BT\cdot}$) calculated by the relation in eq 3 is 4400 $M^{-1}$ $cm^{-1}$ at 450 nm.

 (2)

BT⁻ BT·

$$\epsilon_{BT\cdot} = OD_{BT\cdot}\frac{\epsilon_{e_{aq}}^{720\ nm}}{OD_{e_{aq}^-}^{720\ nm}} \qquad (3)$$

At pH 7.3 where BTH is not ionized in the ground state, 265-nm laser flash photolysis again causes photoionization and the formation of the same long-lived transient discussed above. The transient behavior is complicated by a strong, short-lived absorption superimposed on the long-lived species. Although this short-lived species was unaffected by $N_2O$ and $O_2$, addition of HCl dramatically increased its lifetime from 0.8 μs to 2 ms. Figure 2 shows the absorption spectrum obtained at pH 7.3 immediately and 4 μs after the laser pulse. Clearly, there is a strong, short-lived absorption, peaking at 330 nm, which is not obtained on laser flash photolysis of solutions at pH >9.0. This complex behavior suggests that BTH is photoionized to the cation radical $BTH^{+}\cdot$ which subsequently ionizes to BT· and $H^+$ as shown in eq 4 and 5.

$$BTH \xrightarrow[pH\ 7.3]{h\nu\ (265\ nm)} BTH^{+}\cdot + e_{aq}^{+} \qquad (4)$$

$$BTH^{+}\cdot \rightleftharpoons BT\cdot + H^+ \qquad (5)$$

Laser flash photolysis (265, 347, or 530 nm) of argon-saturated aqueous pheomelanin solutions, either in phosphate buffer, pH 7.4, or in 0.1 M NaOH, gave rise to $e_{aq}^-$ plus two additional transients. The optical density of the hydrated electron in both neutral and alkaline solution increased linearly with 530- and 347-nm laser intensity, indicating that production of $e_{aq}^-$ was a monophotonic process. While the latter two transients were probably oxidized species, at this time further characterization is difficult. Nevertheless, these experiments indicate that irradiation of aqueous solutions of pheomelanin both with ultraviolet and visible light leads to monophotonic produciton of $e_{aq}^-$, and they are consistent with the two-step mechanism shown in eq 6 and 7 for the production of $O_2^-\cdot$ from pheomelanin.

$$PM \xrightarrow[UV/vis]{h\nu} PM^{+}\cdot + e_{aq}^- \qquad (6)$$

$$e_{aq}^- + O_2 \rightarrow O_2^-\cdot \qquad (7)$$

Pulse radiolysis[17,18] of BTH in 0.1 M NaOH containing 1 × $10^{-2}$ M KCNS leads to radical formation via the sequence of reactions outlined in eq 8 and 9, $O^-\cdot$ being formed readily on pulse radiolysis of alkali solutions (pH>12) by rapid deprotonation of HO·. $(SCN)_2^-\cdot$ is quenched by BT⁻ ($k$ = 3.5 × $10^9$ $M^{-1}$ $s^{-1}$), producing two transients, one with an absorption spectrum and first-order decay kinetics ($k$ = 6.9 × $10^3$ $s^{-1}$) identical with the long-lived species produced in the flash photolysis experiment (vide supra). This species has been tentatively assigned as BT·.

$$O^-\cdot + 2SCN^- \rightarrow (SCN)_2^-\cdot + O^{2-} \qquad (8)$$

$$BT^- + (SCN)_2^-\cdot \rightarrow BT\cdot + 2SCN^- \qquad (9)$$

Pulse radiolysis of $N_2$-saturated methanol solutions of BTH and PM, where the main reactant is $e_{MeOH}^-$, yielded quenching constants ($k_q$) of 3.4 × $10^9$ $M^{-1}$ $s^{-1}$ and 4.9 × $10^9$ $M^{-1}$ $s^{-1}$ for reactions 10 and 11, respectively. No absorption spectra for $BTH^-\cdot$ or $PM^-\cdot$ were detected in the 320–750-nm region.

$$BTH + e_{MeOH}^- \rightarrow BTH^-\cdot \qquad (10)$$

$$PM + e_{MeOH}^- \rightarrow PM^-\cdot \qquad (11)$$

Attempts were made to generate the triplet state of BTH and PM by pulse radiolysis. However, no triplet absorption or quenching of donor triplets was observed when either biphenyl (in benzene) or benzene (in cyclohexane) was used as a triplet sensitizer. Although this does not completely rule out formation of singlet oxygen via the singlet excited state of PM or BTH,[19] the inability of PM and BTH to form triplet states with lifetimes ≥1 μs from high triplet energy donors such as benzene and biphenyl indicate that singlet oxygen, which forms normally by

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[8] Erlenmeyer, H.; Uberwasser, H. *Helv. Chim. Acta* **1938**, *21*, 1695–1698.

[9] In all subsequent experiments, the pH was adjusted to ensure the overwhelming predominance of one of these forms.

[10] McVie, J.; Sinclair, R. S.; Truscott, T. G. *J. Chem. Soc., Faraday Trans. 2* **1978**, *74*, 1870–1879.

[11] $\lambda_{max}$ = 720 nm, $t_{1/2}$ = 1 μs, efficiently quenched by both $N_2O$ and $O_2$.

[12] Determined by a comparative technique[13] in which the concentration of $e_{aq}^-$ was monitored at 720 nm ($\epsilon$ 18 600 $M^{-1}$ $cm^{-1}$[14]). This was compared to the concentration of triplet produced by a naphthalene actinometer in cyclohexane ($\Phi_T^N$ = 0.74; $\epsilon_T^N$ = 24 500 $M^{-1}$ $cm^{-1}$ at 414 nm[15]). Under conditions where BT⁻ absorbs the same number of excitation photons and at low (less than 10%) depletion of the ground state,[16]

$$\Phi_1 = \Phi_T^N \frac{OD(e_{aq}^-)}{\epsilon(e_{aq}^-)} \frac{\epsilon_T^N}{OD_T^N}$$

[13] Amand, B.; Bensasson, R. *Chem. Phys. Lett.* **1975**, *34*, 44–48.

[14] Fieldon, E. M.; Hart, E. J. *Trans. Faraday Soc.* **1967**, *63*, 2975–2982.

[15] Bensasson, R.; Land, E. J. *Trans. Faraday Soc.* **1971**, *67*, 1904–1915.

[16] Bensasson, R.; Goldschmidt, C. R.; Land, E. J.; Truscott, T. G. *Photochem. Photobiol.* **1978**, *28*, 277–281.

[17] Pulse radiolysis experiments were carried out with a Vickers 9–12-MeV linear accelerator, with quartz cells of optical path length 2.5 cm, as previously described.[18]

[18] Keene, J. P. *J. Sci. Instrum.* **1964**, *41*, 493–496.

[19] Stevens, B.; Small, R. D. *J. Photochem.* **1978**, *9*, 233–235.

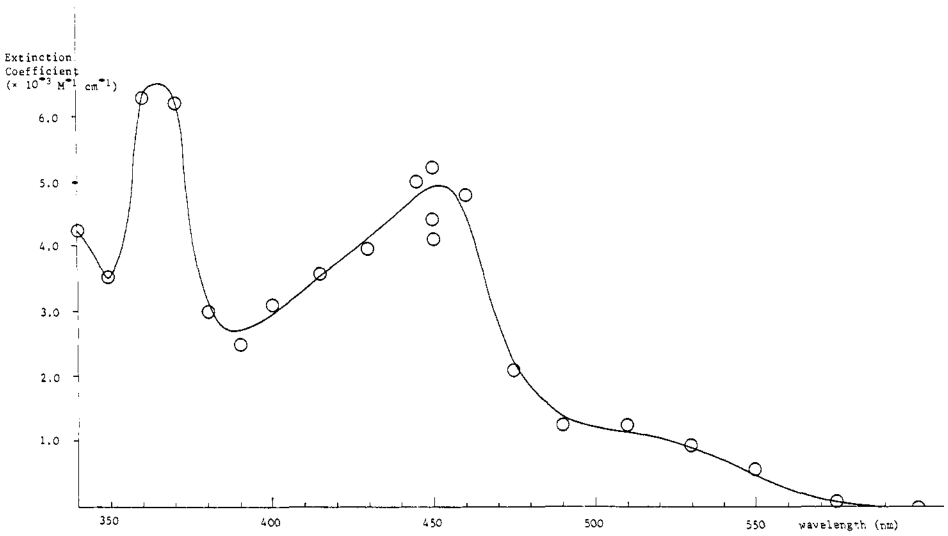

**Figure 1.** Spectrum obtained after 265-nm laser flash photolysis of $2 \times 10^{-4}$ M $BT^-$, pH 10.0, in an $N_2O$-saturated solution.

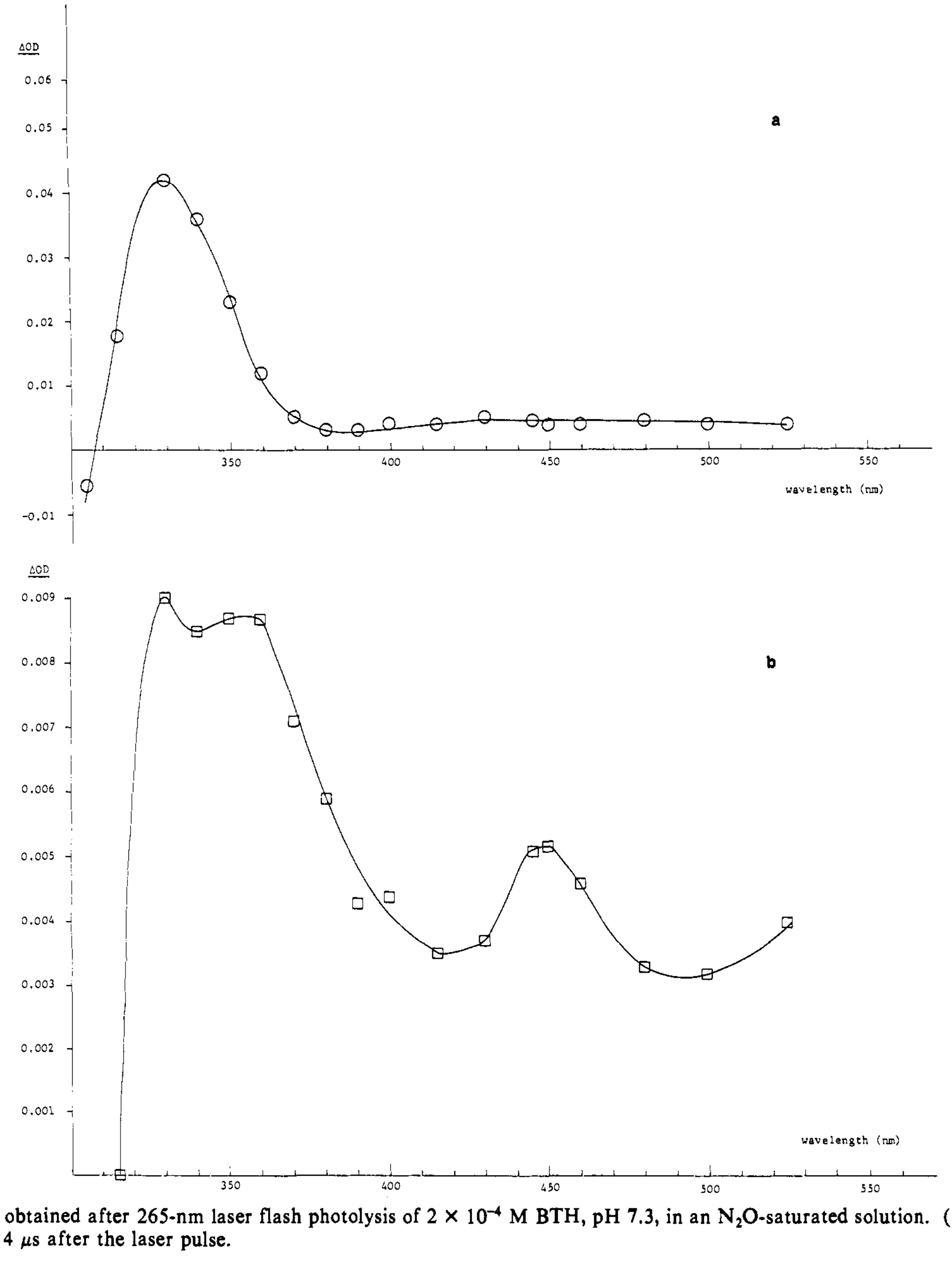

**Figure 2.** Spectrum obtained after 265-nm laser flash photolysis of $2 \times 10^{-4}$ M BTH, pH 7.3, in an $N_2O$-saturated solution. (a) Immediately after the laser pulse. (b) 4 μs after the laser pulse.

energy transfer to $O_2$ from a donor triplet, is unlikely to be involved in photosensitivity associated with pheomelanin.

As previously discussed, subsequent reactions of $O_2^{-}\cdot$ may lead to severe skin damage. Furthermore, pulse radiolysis showed that PM and BTH react at the diffusion-controlled rate with the solvated electron, a conclusion confirmed by the laser flash photolysis experiments where the apparent yield of $e_{aq}^{-}$ increased with decreasing PM and BTH concentrations. Although we were unable to detect them, degradation products resulting from such reactions may also play a role in photosensitivity.

In conclusion, our results indicate that BTH is a good model compound for PM in that both compounds photoionize and do not readily form triplets. Nevertheles, more complete photophysical data on PM could be obtained by working with the protein-free chromophore. Further work is also required to characterize the PM and BT radicals produced after photoionization.

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**Miles R. Chedekel***
*The Johns Hopkins University*
*School of Hygiene and Public Health*
*Department of Environmental Health Sciences*
*Division of Environmental Chemistry*
*c/o U.S.P.H.S. Hospital, Baltimore, Maryland 21211*

**Edward J. Land**
*Paterson Laboratories, Christie Hospital & Holt Radium*
*Manchester, M20 9BX, England*

**Roy S. Sinclair, David Tait, T. George Truscott**
*Department of Chemistry, Paisley College of Technology*
*Paisley, PA1 2BE, Scotland*

*Received May 19, 1980*

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## Preequilibrium Carbon Protonation in the Acid-Catalyzed Hydrolysis of a Phenylketene Dithioacetal

*Sir:*

Carbon protonation is usually a slow, rate-determining step in the acid-catalyzed hydrolysis of vinyl ethers,[1] vinyl sulfides,[2] and ketene acetals.[3] However, the protonation step could well be a rapid equilibrium, depending on the electronic structure of unsaturated substrates. To our knowledge, such cases have never been encountered[4-6] except for one unusual case.[7]

This communication presents direct evidence that in the acid-catalyzed hydrolysis of 1,1-bis(methylthio)-2-phenylethene (**1**)[8] the initial carbon protonation is rather a rapid reversible process which precedes a rate-determining collapsing of the carbonium

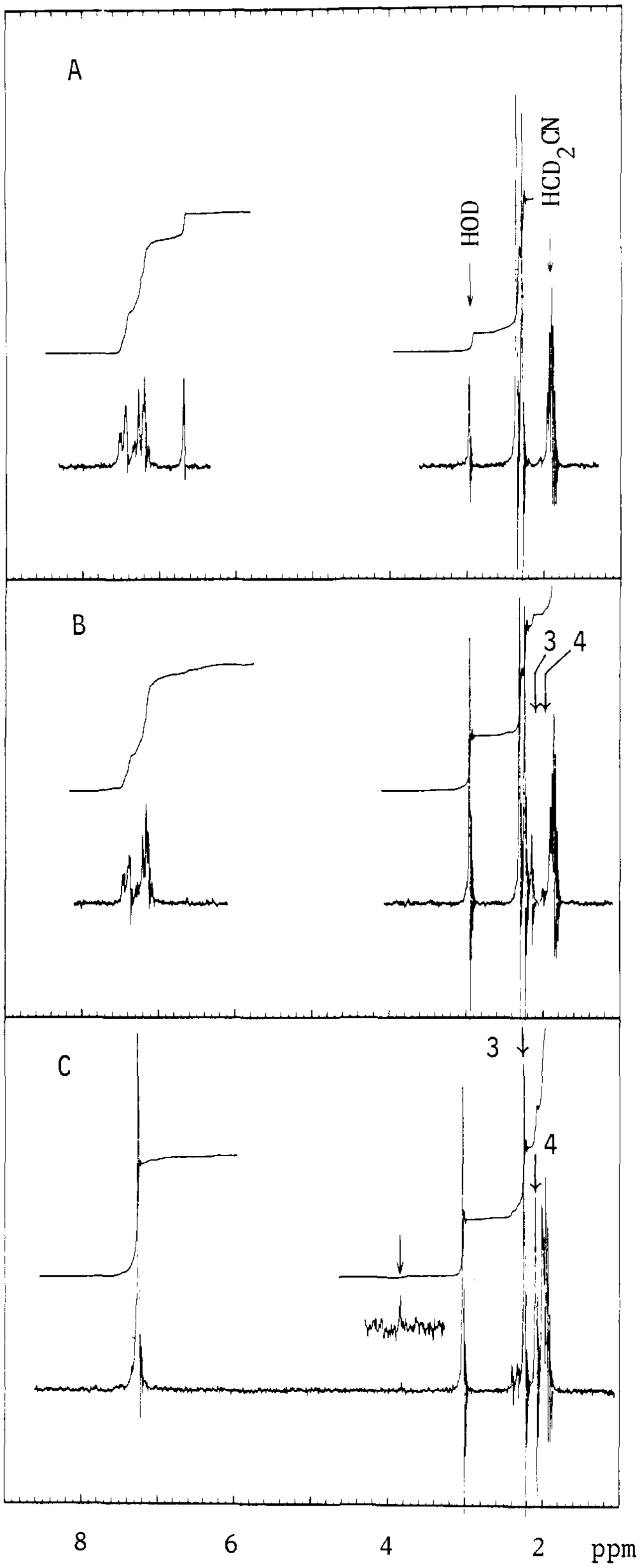

**Figure 1.** $^1$H NMR spectra for the hydrolysis of **1** in 90% $CD_3CN/D_2O$ at 35 °C. [DCl] $\simeq$ 0.002 M. $[\mathbf{1}]_0 \simeq 0.1$ M. Reaction times are 0, 100 min, and 20 h for spectra A, B, and C, respectively. Signals at ca. 3.0 and 1.9 ppm correspond to those of solvent HOD and $HCD_2CN$, respectively.

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(1) Salomaa, P.; Kankaanperä, A.; Lajunen, M. *Acta Chem. Scand.* **1966**, *20*, 1790–1801. Kresge, A. J.; Chiang, Y. *J. Chem. Soc. B* **1967**, 53–61. Okuyama, T.; Fueno, T.; Nakatsuji, H.; Furukawa, J. *J. Am. Chem. Soc.* **1967**, *89*, 5826–5831.

(2) Okuyama, T.; Nakada, M.; Fueno, T. *Tetrahedron* **1976**, *32*, 2249–2252. Okuyama, T.; Masago, M.; Nakada, M.; Fueno, T. *Ibid.* **1977**, *33*, 2379–2381.

(3) Gold, V.; Waterman, D. C. A. *J. Chem. Soc. B* **1968**, 839–855. Kankaanperä, A.; Tuominen, H. *Suom. Kemistil. B* **1967**, *40*, 271–276. Kankaanparä, A.; Aaltonen, R. *Ibid.* **1970**, *43*, 183–188. Hershfield, R.; Schmir, G. L. *J. Am. Chem. Soc.* **1972**, *94*, 1263–1270. Hershfield, R.; Yeager, M. J.; Schmir, G. L. *J. Org. Chem.* **1975**, *40*, 2940–2946.

(4) Kresge, A. J.; Chen, H. J. *J. Am. Chem. Soc.* **1972**, *94*, 2818–2822.

(5) Loudon, G. M.; Berke, C. *J. Am. Chem. Soc.* **1974**, *96*, 4508–4517.

(6) Kresge, A. J.; Chwang, W. K. *J. Am. Chem. Soc.* **1978**, *100*, 1249–1253.

(7) Cooper, J. D.; Vitullo, V. P.; Whalen, D. L. *J. Am. Chem. Soc.* **1971**, *93*, 6294–6296.

(8) Prepared from an ortho thioester by the method of Arens;[9] bp 144–145 °C (5 mmHg).

(9) Rinzema, L. C.; Stoffelsma, J.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1959**, *78*, 354–363.

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