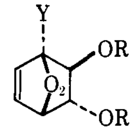
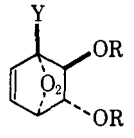
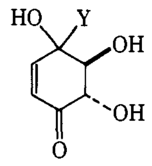
oxygen with cyclic 1,3-dienes[15] afford cis 1,3-diepoxides by rearrangement under both thermal[16] and photochemical[17] conditions, oxygenation of **10** or **11** appeared to offer an attractive route to crotepoxide and/or its isomer **3**. Diacetate **10** proved to be totally unreactive towards singlet oxygen under all conditions but **11**, upon irradiation (25 °C) in pyridine in the presence of oxygen with hematoporphyrin as sensitizer, gave a mixture of unstable epidioxides **21** and **22** (52%, 1:1; δ^{CDCl_3} 3.3 (2 H, broad, exchanged with D_2O), 3.56 and 3.74 (1 H, m), 3.79 (2 H, s), 3.94 and 4.00 (1 H, m), 4.58 (2 H, s), 4.63 (1 H, broad s), 7.35 (1 H, d, $J = 9$ Hz), 7.67 (1 H, t, $J = 9$ Hz), 7.30 (5 H, s)). Prolonged irradiation or heating in pyridine resulted in the conversion of **21** and **22** to the cyclohexenone **23**, characterized as its triacetate **24**. However, the reverse sequence, in which **21**/**22** was acetylated under mild conditions (Ac_2O, Na_2CO_3) and the mixture of endoperoxide diacetates **25** and **26** subjected to refluxing 1,2-dichloroethane in the presence of 2,6-di-*tert*-butyl-*p*-cresol, afforded **17** (24% based on **11**) with no indication of an epimeric diepoxide (**27**). Endoperoxide **26** appears to give mainly an aromatized product tentatively assigned structure **28** and attributed to a facile elimination resulting from the trans disposition of the C-3 proton and peroxide bridge. Endoperoxide rearrangement thus provides an alternate route to **1**.[18]



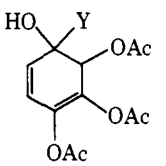
21, R = H
25, R = $COCH_3$



22, R = H
26, R = $COCH_3$



23



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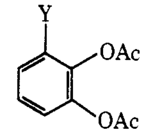

28

Y = $CH_2OCH_2C_6H_5$

Epoxidation or oxygenation of suitably functionalized 1,3-cyclohexadienes not only affords feasible pathways to crotepoxide (**1**) and its stereoisomers **2** and **3** but should also be applicable to other members of this important group of natural products, including the highly active antileukemic compound triptolide[4a,19] and the antibiotic LL-Z1220.[4c,20]

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(20) Financial support of this work by the National Science Foundation (MPS 74-01286 A01) is gratefully acknowledged.
(21) National Institutes of Health Postdoctoral Fellow, 1971–1972.

Martin R. Demuth, Patricia E. Garrett,[21] James D. White*
Department of Chemistry, Oregon State University
Corvallis, Oregon 97331

Received October 14, 1975

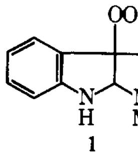
Photosensitized Oxygenation of N^b-Methoxycarbonyltryptophan Methyl Ester and N^b-Methoxycarbonyltryptamine. Isolation and Novel Transformations of a 3a-Hydroperoxypyrroloindole

Sir:

There has been considerable recent interest in the reaction of singlet oxygen with the enamine system.[1] In our recent studies,[2] we have shown that N^b-methyltryptamine reacts with singlet oxygen to give **1** as the primary intermediate[2b] which undergoes either intramolecular oxidation to give **3** or **2a** under the reaction conditions. The *o*-formylaminoacetophenone type compound which has been widely known as the normal product of photooxygenation of tryptophan[3] and indoles,[4] however, was not isolated. These results led to a study of the effect of N^b-acylation on the photooxygenation of tryptophan and tryptamine derivatives.

We wish to report here the direct isolation of 3a-hydroperoxypyrroloindole (**5a**) from the reaction of **4a** with singlet oxygen and the conversion of **5a** into the formylkynurenine derivative **7a**, the N^b-formylkynurenine derivative **8a**, as well as the 3a-hydroxypyrroloindole **6a**, and its acid catalyzed rearrangement to the 1,4-benzoxazine derivative **9**.

When a thoroughly O_2-saturated solution of **4a** (4.6 mmol) was irradiated in 5% pyridine in methanol with a 200-W halogen lamp for 3 h in the presence of rose bengal under ice-cooling followed by alumina and silica gel column chromatography, **6a**, mp 126–127 °C[5] (18%), **7a**, mp 97.5–99 °C (9%), and **8a** (18%) were isolated[6] (**6a:** λ_{max}^{EtOH} nm (ϵ) 242 (8750), 298 (2390); NMR ($CDCl_3$) δ 5.10 (1 H, s, NCHN). **8a:** λ_{max}^{EtOH} 228, 257, 364 nm; mass 250 (60) M^+; picrate, mp 99.5–100.5 °C). Alkaline hydrolysis of **6a** gave the parent compound, **2b:** mp 173.5–175 °C; λ_{max}^{EtOH} nm (ϵ) 243.5 (8275), 301.5 (2440), $\lambda_{max}^{EtOH-HCl}$ 236 (7840), 294 (2350); NMR (pyridine-d_5) 5.32 (1 H, s, NCHN). Both **7a** and **8a** were deformylated to give N^b-methoxycarbonylkynureamine, mp 98–99 °C, when refluxed with Al_2O_3 in methanol. Likewise, irradiation of **4b** in similar conditions gave **6b**, mp 124–125 °C (14%), **7b**, mp 128–129 °C (18%), and **8b**, mp 115–116 °C (8%).[7] The



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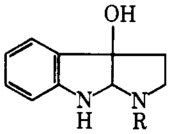
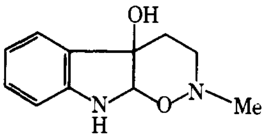


2a, R = Me
b, R = H



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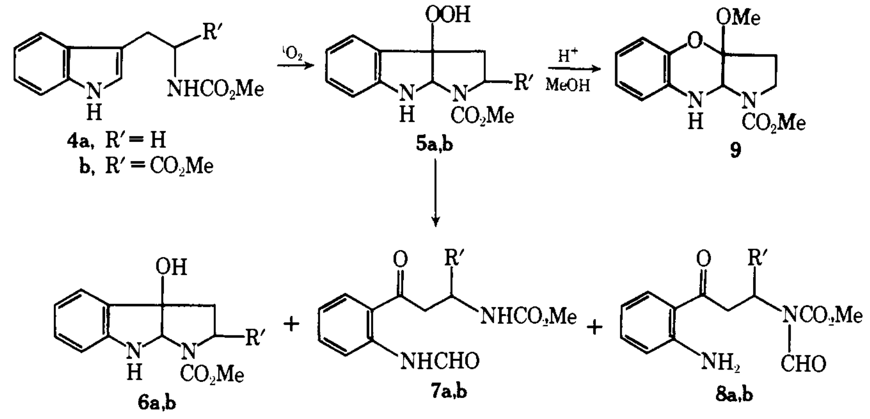

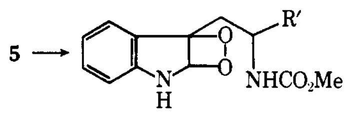

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unexpected product of transformylated **8a** along with **6a** and **7a** was obtained whether the solvent used was acetone, *tert*-butyl alcohol, methanol, or 5% pyridine in ethanol, demonstrating that the N^b-formyl group did not originate from the solvent. Neither irradiation of **7a** in 5% pyridine in methanol nor treatment of **7a** with silica gel in the same solvent yielded **8a**, eliminating the formation of **8** from **7**.

When, however, the reaction mixture was concentrated and filtered through an alumina column followed by preparative TLC (Al_2O_3), the 3a-hydroperoxide **5a** was isolated in 41% yield as an oil together with small amounts of **6a** and **7a** (**5a**: λ_{max}^{EtOH} 244, 305 nm; NMR ($CDCl_3$) δ 2.10–2.80 (2 H, m, CH_2), 3.00–3.40, 3.40–4.00 (2 H, m, CH_2N) 3.68 (3 H, s, Me), 4.80 (1 H, broad s, OOH or NH, exchangeable), 5.10 (1 H, broad s, OOH or NH, exchangeable), 5.62 (1 H, s, NCHN), 6.40–6.90, 7.00–7.40 (4 H, m, aromatic H); mass 250 (35) M^+, 234 (58) M − O, 232 (100) M − 18; positive KI-starch test). $NaBH_4$ reduction of **5a** provided **6a** quantitatively.

An important, characteristic reaction of **5a** is its transformation into **8a** (44%), **7a** (17%), and **6a** (18%) when treated with silica gel in CH_2Cl_2, although **5a** is stable in a solvent like benzene, CH_2Cl_2, or methanol at room temperature for 5 h.[8] The formation of **7** from **5** may occur via a dioxetane intermediate **10**. However, at the present time, we are unsure of the exact mechanism of formation of **8** from **5**.[9]

Another characteristic reaction of **5a** is its facile acid catalyzed rearrangement in methanol at room temperature to afford the 1,4-benzoxazine derivative **9** in 89% yield[10] (**9**: mp 202–203°; λ_{max}^{EtOH} nm (ϵ) 242 (9080), 292 (3890);[10b] NMR ($CDCl_3$) δ 1.90–2.20, 2.28–2.60 (2 H, m, CH_2), 3.30–3.90 (2 H, m, CH_2N), 3.42 (3 H, s, OMe), 3.68 (3 H, s, CO_2Me) 5.00 (1 H, d, J = 4 Hz, NCHN, collapses to a singlet on addition of D_2O), 5.21 (1 H, broad s, NH, exchangeable), 6.50–7.00 (4 H, m, aromatic H)). Due to the lack of a basic nitrogen, **5a** undergoes rearrangement to **7**, **8**, and **9** under mild conditions in contrast to **1** which undergoes rapid intramolecular oxidation to give the N^b-oxide followed by spontaneous rearrangement to **3**.[2]

The photosensitized oxygenation of tryptophan to kynurenine is believed to proceed via formylkynurenine derived from a dioxetane intermediate such as **10**. The evidence presented herein provides another possibility for formation of kynurenine and significant implications for biological oxidation of tryptophan[11] including its transformation to *o*-aminophenol.[12]

Acknowledgment. Financial support of the Ministry of Education and Foundation for the Promotion of Research on Medicinal Resources (Japan) is acknowledged.

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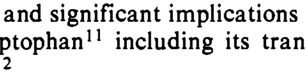
(5) In the absence of rose bengal or light, **6a**, **7a**, and **8a** were not formed.

(6) The new compounds given with reported melting point analyzed correctly for C, H, and N.

(7) Essentially the similar result was obtained when N^b-acetyltryptamine was irradiated.

(8) After 48 h in CH_2Cl_2 at room temperature, **5a** was converted to **6a**, **7a**, and **8a**, while **6a** (11%), **7a** (13%), and **8a** (26%) were obtained when refluxed in benzene for 18 h.

(9) It could be derived from an intermediate such as I.



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(12) Acid hydrolysis of 9 yielded o-aminophenol.

Masako Nakagawa,* Haruo Okajima, Tohru Hino
Faculty of Pharmaceutical Sciences, Chiba University
1-33, Yayoi, Chiba, Japan 280

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The Reduction of Molybdenum(II) Trifluoroacetate by Pulse Radiolysis in Methanol[1]

Sir:

Previous studies of the redox reactions of molybdenum(II) carboxylates have included the oxidation of $[Mo_2(O_2CC_3H_7)_4]$ to $[Mo_2(O_2CC_3H_7)_4]^+$ by cyclic voltammetry[2] and the conversion[3] of $[Mo_2(O_2CR)_4]$ species by halogens to such products as $[Mo_2(O_2CR)_4]I_3$. However, no reductions of these compounds appear to have been characterized. Preliminary studies have indicated that $[Mo_2(O_2CCF_3)_4]$ reacts with certain reductants; however, no molybdenum-containing products could be isolated in a pure state from the resultant mixtures. In view of these observations and the difficulties encountered by Cotton et al.[2,4-6] in isolating pure compounds subsequent to redox reactions of compounds containing multiple metal-metal bonds, an alternative approach to the reduction of $[Mo_2(O_2CCF_3)_4]$ was adopted. Pulse radiolysis techniques[7] were used since they allow the production of solvated electrons (e_s^-) in solution and have been shown[8] to be effective in the production of reduced metal ions such as Ni(I) and Zn(I). We have thus established that oxygen-free methanol solutions of $[Mo_2(O_2CCF_3)_4]$ do indeed react with e_s^-, by following the kinetics of the decy of the e_s^- absorption[9] at 550 nm in the presence and the absence of the compound.

$[Mo_2(O_2CCF_3)_4]$[10] was dissolved in freshly distilled, argon purged, methanol ("Analar", B.D.H.) and an atmosphere of argon was maintained above all solutions used, unless stated otherwise. The concentration of these solutions (typically $\geq 5 \times 10^{-3}$ mol l.$^{-1}$) was chosen such that, assuming a rate constant for the reaction of $[Mo_2(O_2CCF_3)_4]$ with the electron to be $\sim 10^{10}$ l. mol^{-1} s^{-1}, the electrons (available in solution in a molar ratio $[e_s^-]$: $[Mo_2]$ of typically ca. 1:100) should react with the compound in preference to the solvent. From such measurements, a rate constant for this reaction of 4.0 (±0.5) × 10^9 l. mol^{-1} s^{-1} was obtained.

The value of the rate constant for the reaction of $[Mo_2(O_2CCF_3)_4]$ with e_s^- is in the range expected[11] for a diffusion controlled process, suggesting that the species thus formed is the primary product (A) of this reaction and is presumably therefore $[Mo_2(O_2CCF_3)_4]^-$. (It has been established[12] that e_s^- reacts only very slowly with trifluoroacetate groups.) The absorption spectrum of this product was obtained by measurements of the post-pulse absorption (400-1000 nm) produced in $[Mo_2(O_2CCF_3)_4]$ solutions ($\geq 5 \times 10^{-3}$ mol l.$^{-1}$) where more than 90% of the e_s^- reacted with the compound. This spectrum[13] is shown in Figure 1 and its principal feature is an absorption at 780 (±20) nm (ϵ 2.6 (±0.3) × 10^3 l. mol^{-1} cm^{-1}).

A is very short lived, the 780-nm absorption decays very rapidly to ca. 20% of its maximum intensity and then more slowly to <1% of this value. Both of these decay processes follow second-order kinetics with respective rate constants[14] of 4.5 (±1.0) × 10^9 and 2.5 (±1.0) × 10^8 l. mol^{-1} s^{-1}. It seems possible that one of these decay processes is the electron exchange,

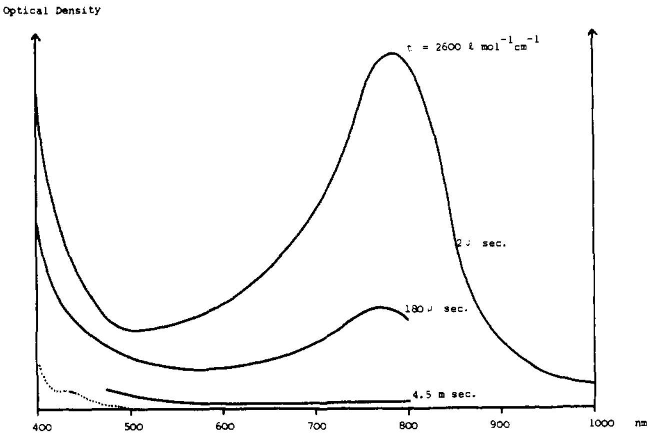

Figure 1. The electronic spectrum of the product of the reaction between $[Mo_2(O_2CCF_3)_4]$ and an electron in MeOH (recorded after the times shown; the spectrum of $[Mo_2(O_2CCF_3)_4]$ in MeOH shown for comparison (···)).

$$2[Mo_2(O_2CCF_3)_4]^- \rightarrow [Mo(O_2CCF_3)_4] + [Mo_2(O_2CCF_3)_4]^{2-}$$

In order to provide some confirmation of the above conclusions the following observations were carried out. (a) In radiolyzed methanol solution $\cdot CH_2OH$ radicals as well as e_s^- are transient products and possible reducing agents. To examine this latter possibility, solutions of $[Mo_2(O_2CCF_3)_4]$ in methanol were saturated with nitrous oxide which is known to react with e_s^- to produce O^-, the latter then forming $\cdot CH_2OH$ by reaction with methanol. The irradiation of such solutions produced a transient absorption at ca. 500 nm but none at ca. 780 nm. (b) To further support the formulation of A as a reduction product, the rate of decay of the 780-nm absorption was monitored in the presence of known amounts[15] of dioxygen. This rate of decay was found to be accelerated by the presence of dioxygen and the second-order rate constant for this process was determined as 5.9 (±0.3) × 10^9 l. mol^{-1} s^{-1}. The product of the reaction obtained under these conditions was not simply $[Mo_2(O_2CCF_3)_4]$ but a species with an absorption which extended through the visible region of the spectrum. (c) Glasses formed by dissolving $[Mo_2(O_2CCF_3)_4]$ (ca. 10^{-2} mol l.$^{-1}$) in methanol-1-propanol (100:3) and rapidly freezing to liquid nitrogen temperature, were subjected to γ-irradiation from a ^{60}Co source at ca. 1 krad min^{-1} over varying time intervals (15 min-2 h). The ESR spectra of these glasses maintained between 77 and 130 K contained, in addition to a strong signal characteristic of $\cdot CH_2OH$ radicals, a reasonably intense and broad (ca. 65 G in width) signal centered at $g = 1.91$, the profile of which suggested that the paramagnetic center involves some anisotropy. These observations strongly suggest that some of the electrons produced on γ-irradiation become trapped on the dimolybdenum center. The electronic structure of this reduced center would be anticipated to be $\ldots(\delta)^2\ (\delta^*)^1$, the magnetic properties of which, in view of the suggested electronic structure[16] for $Mo\equiv Mo$ units, might reasonably be expected to be similar to those of the corresponding oxidized species having the $\ldots.(\delta)^1$ configuration. The observed g value is in fact very similar to those reported[2,6] for $[Mo_2(O_2CC_3H_7)_4]^+$ and $[Mo_2(SO_4)_4]^{3-}$.

We conclude that these experiments have shown that it is possible to add an electron to $[Mo_2(O_2CCF_3)_4]$, the probable product being a molybdenum (1½) species which is very short-lived. Therefore the possibility of isolating this and related simple reduction products of the molybdenum(II) carboxylates appears to be considerably more remote than for