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Research Note

A Novel Singlet Oxygen Reaction

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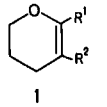
ABSTRACT

1-Aryl-2-methyl-4,5-dihydropyrrol-3-carboxylic acid ethyl ester (a cyclic enamine) was observed to dehydrogenate to give 1-aryl-2-methyl-pyrrol-3-carboxylic acid ethyl ester upon irradiation in the presence of oxygen and in the presence or absence of *meso*-tetraphenylporphine (TPP). *N*-Aryl cyclic amines were shown to be singlet oxygen sensitizers.

INTRODUCTION

Reaction of singlet oxygen ($^1\Delta_g$) with alkenes, enol ethers and enamines has been a subject of much interest (1–5). Generally, acyclic enol ethers and enamines give "dioxetane" cleavage products (6,7) whereas cyclic enol ethers and enamines were reported to give both "dioxetane" products and ene products (8–11). Recently, we have reported our results on the photooxygenation of cyclic enol ethers (5,6-disubstituted-3,4-dihydro-2H-pyrans [**1**]) (12–17). Two hydroperoxides (ene products) were isolated as primary products and Hock cleavage of one of them was observed to occur *via* the intermediacy of a dioxetane.

In this paper, we report our latest findings on the reaction of cyclic enamines—1-aryl-2-methyl-4,5-dihydropyrrol-3-carboxylic acid ethyl esters (**2**) with singlet oxygen. The double bond of interest has a similar substitution except the substrate (**2**) this time is a five-membered cyclic enamine rather than a six-membered cyclic enol ether (**1**).



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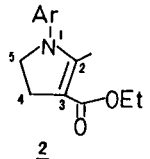
R¹= Me , Et , i-Pr , Ph
R²= COOEt , $COCH_3$, COPh



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MATERIALS AND METHODS

The proton magnetic resonance spectra were determined with a Varian EM360L (60 MHz) in carbon tetrachloride using methylene chloride or chloroform as internal standard, or with a Varian XL400 (400 MHz) in chloroform-d with tetramethylsilane as internal standard. The carbon-13 magnetic resonance spectra were recorded on a Varian XL200 (200 MHz) in chloroform-d. Chemical shifts were reported in δ value (ppm) with respect to tetramethylsilane. The IR spectra were recorded with a Perkin-Elmer 9839 IR spectrophotometer on a potassium bromide disc. Only strong and pertinent peaks are reported in cm^{-1}. Low-resolution mass spectra were determined with a Finnigan 4021 mass spectrometer with an electron impact source at 25 or 70 eV. High-resolution mass spectra were recorded on an AEI MS-50 with an EI source operated at 70 eV. Only pertinent fragments were recorded in m/z units.

Synthesis of substrates. 1-Phenyl-2-methyl-4,5-dihydropyrrol-3-carboxylic acid ethyl ester (**2a**), 1-*p*-methyl-phenyl-2-methyl-4,5-dihydropyrrol-3-carboxylic acid ethyl ester (**2b**) and 1-*p*-chlorophenyl-2-methyl-4,5-dihydropyrrol-3-carboxylic acid ethyl ester (**2c**) were prepared and purified according to our published procedure (18).

Photooxygenation reaction. A mixture of substrate **2** (0.2 *M*) and sensitizer, *meso*-tetraphenylporphine (TPP, 5×10^{-5} *M*), in dichloromethane was irradiated externally with a 500 W tungsten–halogen lamp, operated at 180 V, with oxygen bubbling through the solution continuously. The disappearance of the starting material was monitored with proton NMR (60 MHz). After reaction (around 15 min), the solvent was evaporated and the residue was subjected to column chromatography (basic alumina). Elution with methylene chloride–petroleum ether (1:10) yielded product **3.**

1. From substrate **2a,** the proton NMR spectrum of the crude reaction mixture after irradiation indicated that there was only one product formed, which was isolated in *ca* 40% yield after chromatography and identified to be 1-phenyl-2-methyl-pyrrol-3-carboxylic acid ethyl ester (*3a*) ν_{max}: 3056, 1703, 1599, 1560 cm^{-1}; δ_H: 1.25 (3H, t, J = 6 Hz, $COOCH_2CH_3$) 2.45 (s, 3H, $C=CCH_3$), 4.25 (q, 2H, J = 6 Hz, $COOCH_2CH_3$), 6.60 (s, 2H pyrrolic proton), 7.10–7.35 (m, 5H, Ph) ppm. δ_H (400 MHz): 1.362 (3H, t, J = 6.91 Hz, $CO_2CH_2CH_3$), 2.448 (3H, s, $C=CCH_3$), 4.302 (2H, q, J = 6.94 Hz, $CO_2CH_2CH_3$), 6.671 (2H, s, pyrrolic protons), 7.244–7.520 (5H, m, phenyl protons); δ_c (200 MHz): 10.908 (q, C-12), 13.495 (q, C-13), 59.41 (t, C-11), 110.09 (d, C-4), 113.251 (s, C-3), 121.272 (d, C-5), 126.251, 127.954, 129.258 (3d, C-7, C-8, C-9), 136.004 (s, C-2), 139.148 (s, C-6), 165.595 (s, C-10); m/z: 229 (M^+, 84%), 200 (M^+–CH_2CH_3, 73%), 184 (M^+–OCH_2CH_3, 90%), 156 (M^+–$CO_2CH_2CH_3$, 70%), 77 (Ph^+, 100%); high-resolution MS: 229.11058 (M^+); molecular weight calculated for $C_{14}H_{15}O_2N$, 229.11026.

Without sensitizer, the reaction took about 100 min to go to completion.

2. From substrate **2b,** 1-*p*-methylphenyl-2-methyl-pyrrol-3-carboxylic acid ethyl ester (**3b**) was isolated in 30% yield after column chromatography: ν_{max}: 3040, 1700, 1620, 1550 cm^{-1}; δ_H: 1.34 (3H, t, J = 6.8 Hz, $CO_2CH_2CH_3$), 2.34 (6H, s, $C=CCH_3$, $PhCH_3$), 4.23 (2H, q, J = 6.8 Hz, $CO_2CH_2CH_3$), 6.56, 6.58 (2H, ABq, J = 3.2 Hz, pyrrolic proton), 7.13, 7.24 (4H, 2 × ABq, J = 8.0 Hz, Ph); m/z: 243 (M^+, 100%), 214 (M^+–CH_2CH_3, 65%), 198 (M^+–OCH_2CH_3, 84%), 170 (M^+–$COOCH_2CH_3$, 51%), 81 ($PhCH_3^+$, 25%);

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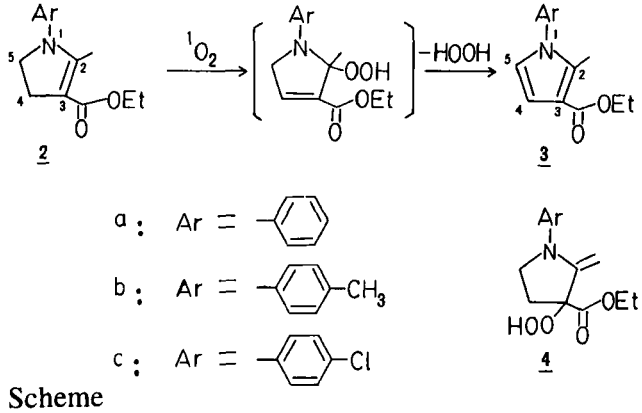
high-resolution MS: 243.12531 (M^+), 198.09188 (M^+–OCH_2CH_3); molecular weight calculated for $C_{15}H_{15}O_2N$, 243.12590, for $C_{13}H_{12}ON$, 198.09188.

3. From substrate **2c**, 1-*p*-chlorophenyl-2-methyl-pyrrol-3-carboxylic acid ethyl ester (**3c**) was isolated in 30% yield after column chromatography: ν_{max}: 3080, 1700, 1600, 1550 cm^{-1}; δ_H: 1.33 (3H, t, J = 6.8 Hz, $CO_2CH_2CH_3$), 2.40 (3H, s, $C{=}CCH_3$), 4.26 (2H, q, J = 6.8 Hz, $CO_2CH_2CH_3$), 6.60, 6.63 (2H, ABq, J = 2.8 Hz, pyrrolic protons), 7.18, 7.41 (4H, 2 × ABq, J = 8.8 Hz, phenyl protons). m/z: 263, 264 (M^+, CI isotope, 100%), 234 (M^+–CH_2CH_3, 77%), 218 (M^+–OCH_2CH_3, 82%), 190 (M^+–$CO_2CH_2CH_3$, 11%), 154 (M^+–$CO_2CH_2CH_3$–Cl, 77%), 111 (M^+–PhCl, 27%); high-resolution MS: 263.07067 (M^+), 154.06506 (M^+–$CO_2CH_2CH_3$–Cl); molecular weight calculated for $C_{14}H_{14}O_2NCl$, 263.07128; for $C_{11}H_9N$, 154.06567.

RESULTS AND DISCUSSION

The overall reaction is as follows:



Scheme

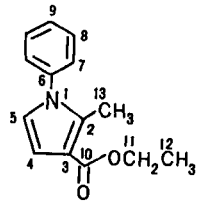
1-Aryl-2-methyl-pyrrol-3-carboxylic acid ethyl ester (**3**) is the dehydrogenated product of substrate **2** and is the only product that is very different from the oxygenated products usually obtained in singlet oxygenation reactions. In order to look at the conditions of the reaction closely, we have done a series of control experiments on substrate **2a.** It was observed that the reaction did not go without light or oxygen. In the presence of TPP, the reaction went to completion in 15 min. Further irradiation would destroy the reaction product. In the absence of TPP, the reaction still occurred but at a much slower rate. It took around 100 min for the reaction to reach completion. Further irradiation did not destroy the product. In the presence of DABCO (1,4-diaza-bicyclooctane), a singlet oxygen scavenger, the sensitized photooxygenation reaction was totally quenched.

Table 1. Reaction conditions and reaction time

Reaction conditions				
Oxygen	Light	TPP	DABCO	Reaction time
+	+	+	-	15 min
+	+	-	-	100 min
+	-	-	-	n.r.*
-	+	-	-	n.r.
-	+	+	-	n.r.
+	+	+	+	n.r.
+	+	-	+	n.r.

* no reaction

The proton NMR, IR, MS and carbon-13 NMR data clearly indicate the structure of the product **3a** to be **A**:



A

It is interesting to note that singlet oxygen attacks at position 2 in this five-membered cyclic enamine exclusively irrespective of the polarity of the solvent to give a product with a double bond conjugated to the ester moiety. We have carried out the reaction in carbon tetrachloride or methylene chloride, and the same product **3** was obtained. Attack at position 3 should give a product (**4**) with an exocyclic double bond. It would be difficult for compound **4** to lose a hydrogen peroxide molecule to give product **3.** This exclusive attack at position 2 is quite different from the results of our previous study on the six-membered cyclic enol ether (**1**) (12–17). In that case we observed that attack at both positions and the partition of the two products are solvent dependent. At the present time, we are not sure such a difference is caused by the amine moiety or the stereochemical consequence of the five-membered ring.

CONCLUSIONS

1. The primary reaction (see the Scheme) is a novel singlet oxygen reaction. Product **3** is the dehydrogenated product of substrate **2** (cyclic enamine) under singlet oxygenation conditions.

2. The novel reaction shows that reaction of singlet oxygen with cyclic enamines can give a dehydrogenated product in addition to the ene products and "dioxetane" products (8–10).

3. The substrates **2** (*N*-aryl cyclic enamines) themselves are sensitizers of singlet oxygen. This is a new observation.

4. *Meso*-tetraphenylporphine is much more efficient than substrate **2** itself in sensitizing the production of singlet oxygen.

5. Product **3** is not a sensitizer of singlet oxygen.

Further studies on the mechanism of this reaction are being carried out in our laboratory and the results will be presented elsewhere in a forthcoming publication.

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