

The Photosensitized Oxygenation of 2,4-Dimethylpyrrole and 2-Methylpyrrole.

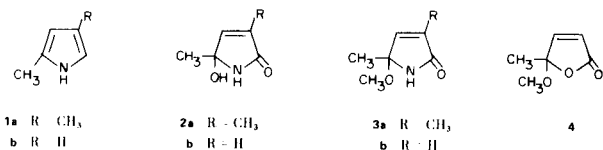
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Sir:

Despite the early observation that alkylpyrroles were susceptible to auto-oxidation (1) and later reports on the structure proofs of the products (2), their photo-oxidation reaction has been studied only recently (3). Other work on the photo-oxygenation of pyrrole compounds has been devoted largely to a study of pyrrole itself (4,5) and various phenyl substituted pyrroles (6). In this report we describe the dye-sensitized photo-oxidation of 2,4-dimethylpyrrole (**1a**) (7) and 2-methylpyrrole (**1b**) (8). The former reaction is a remarkably clean, high yield conversion to two new products.



The photo-oxygenation reaction was carried out in a water-cooled immersion apparatus containing a dilute (1.2-mmoles %) methanolic solution of either 2,4-dimethylpyrrole (**1a**) or 2-methylpyrrole (**1b**) and 2 mg. % of Rose Bengal (¹O₂ sensitizer). A slow stream (30 ml./min.) of oxygen was bubbled through the reaction vessel during an irradiation (9) period of 6 hours. Methanol was evaporated from the photolysate *in vacuo* at 25-30° to a volume of 15 ml. Precipitated platinum black (10) (35-45 mg.) was added to destroy hydroperoxide (gas evolution observed), and the mixture was stirred at room temperature for 21 hours. After removal of the platinum by filtration, methanol was completely removed *in vacuo* at 25-30°. Thus, after the photolysis of **1a**, column chromatography on silica gel (E. Merck, Darmstadt, 70-325 mesh ASTM) gave 67 wt. % of a relatively non-polar fraction (ethyl acetate) and 33 wt. % of a dark, highly polar fraction (methanol). Preparative thin layer chromatography (Silica gel F, M. Woelm, Eschwege, 1 mm, diethyl ether) of the ethyl acetate fraction yielded two main components, **2a** and **3a**; R_f 0.10 and 0.32; theoretical yield 48% and 16% respectively. Similarly, **1b** gave **2b**, R_f 0.07 in 15% yield and **3b**, R_f 0.23, in 20% yield along with trace amounts of other as yet unidentified products.

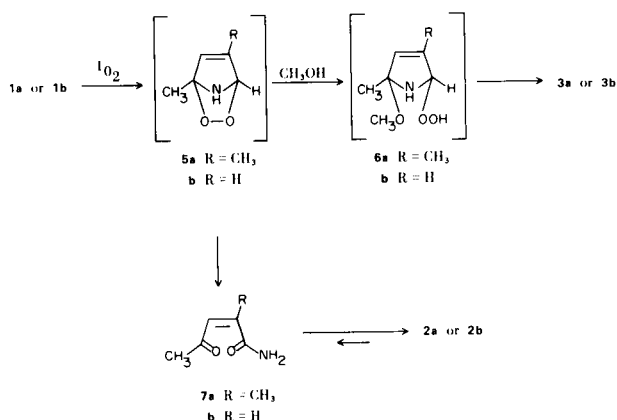
These reaction products from **1a** or **1b** are present even before the addition of platinum in the workup (as determined by gas chromatography).

The structure of **2a**, m.p. 134-135° [lit. (1,2) m.p. 145°, 149-151°], was established by its mass spectrum (11): *m/e* (relative intensity) 127.0633 [M⁺, C₆H₉NO₂] (4%), 112 [M-CH₃] (7%) and 109 [M-H₂O] (100%); nmr spectrum: δ (deuteriochloroform) 1.53 (3H, s, CH₃), 1.80 (3H, d, J 2 Hz, CH₃), 4.08 (1H, broad s, O-H), 6.52 (1H, m, =CH) and 7.22 (1H, s, N-H) ppm; and ir spectrum: ν max (chloroform) 3320 (broad O-H, N-H), 1705 (C=O) and 1660 (C=C) cm⁻¹. The methoxylactam structure **3a**, m.p. 106-107°, was proved by its mass spectrum: *m/e* (relative intensity) 141.0790 [M⁺, C₇H₁₁NO₂] (6%), 126 [M-CH₃] (6%), 110 [M-OCH₃] (36%) and 109 [M-CH₃OH] (100%); nmr spectrum: δ (carbon tetrachloride) 1.52 (3H, s, CH₃), 1.85 (3H, d, J 2 Hz, CH₃), 3.07 (3H, s, OCH₃), 6.30 (1H, m, =CH) and 7.89 (1H, s, N-H) ppm; and ir spectrum: ν max (carbon tetrachloride) 3230 (N-H), 1710 (C=O) and 1655 (C=C) cm⁻¹. Similarly the structure of **2b** was defined by its mass spectrum: *m/e* (relative intensity) 113.0481 [M⁺, C₅H₇NO₂] (7%), 98 [M-CH₃] (100%) and 95 [M-H₂O] (94%); nmr spectrum: δ (deuteriochloroform) 1.57 (3H, s, CH₃), 5.92 (1H, d, fine splitting, =CH), 6.94 (1H, d, fine splitting, =CH) and 7.70 (1H, s, N-H) ppm; and ir spectrum: ν max (chloroform): 3320 (broad O-H, N-H) and 1700 (C=O) cm⁻¹. Methoxylactam **3b** was characterized by its mass spectrum: *m/e* (relative intensity) 127.0638 [M⁺, C₆H₉NO₂] (5%), 112 [M-CH₃] (29%) and 96 [M-OCH₃] (100%); nmr spectrum: δ (carbon tetrachloride): 1.53 (3H, s, CH₃), 3.15 (3H, s, OCH₃), 6.05 (1H, d, fine splitting, =CH), 6.72 (1H, d, fine splitting) and 7.85 (1H, s, N-H) ppm; and ir spectrum: ν max (carbon tetrachloride): 3220 (N-H) and 1710 (C=O) cm⁻¹.

Citraconimide as a photo-product from **1a** or maleimide from **1b** is formed in barely detectable amounts (no more than 0.1% yield), detection by tlc or gas chromatography. This observation may be contrasted with the finding that another α-substituted pyrrole, 3,4-diethyl-2-methylpyrrole, gives a 3% yield of diethylmaleimide (4) but the α,α'-disubstituted pyrrole, 3,4-diethyl-2,5-dimethylpyrrole

gives a 20% yield of diethylmaleimide (12) and 3,4-diethylpyrrole gives a 34% yield of diethylmaleimide (3). However, the already established photo-lability of maleimide (*vs.* that of diethylmaleimide) under our reaction conditions (3) makes it unlikely to be formed in sufficient quantities to allow for isolation after the photo-oxygenation of **1a** or **1b** in the probable event it is formed during the course of reaction. Moreover, we believe that pyrroles with one α -alkyl group undergo other reactions more rapidly during photolysis.

SCHEME 1



The formation of **3a** or **3b** from either **1a** or **1b** might be rationalized (Scheme 1) by methanolysis of *endo*-peroxide (**5**) to form the hydroperoxide (**6**) which in turn decomposes to **3a** or **3b** in the reaction mixture. A completely analogous scheme has been postulated to account for the formation of the pseudoketone (**4**) from 2-methylfuran (13,14). The predominant formation of the hydroxylactam (**2a** or **2b**) was anticipated from earlier photo-oxidation work (4), although this principal product (**2a**) from photo-oxidation of 2,4-dimethylpyrrole (**1a**) is the same as that obtained by auto-oxidation (1,2), the yield in the former reaction is three times that obtained in the latter (16%) (1). The analogous hydroxylactam (**2b**) was not reported in the auto-oxidation of **1b** (1). For either **1a** or **1b** whether the mechanism involves an intramolecular hydrogen source in the decomposition of the assumed intermediate *endo*-peroxide (**5**) or whether H-abstraction occurs from the solvent is not clear. An intermediate such as **5** could collapse directly to **2a** or **2b** by transfer of the C₅-H to the oxygen at C-2 with O-O bond cleavage. An

alternative mechanism might involve collapse of **5** to the α,β -unsaturated keto-amide (**7**) followed by ring closure to yield **2**. The mechanistic details of these reactions and studies on the photo-oxidation of other alkylated pyrroles are currently under investigation in our laboratories.

Acknowledgment.

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- (7) Prepared by heating diethyl 3,5-dimethylpyrrole-2,4-dicarboxylate in potassium hydroxide-diethylene glycol at 200° and followed by distillation.
- (8) Kindly prepared by Miss Esther Thommen, by Wolff-Kishner reduction of pyrrole 2-carboxaldehyde. A. J. Castro, J. F. Deck, M. T. Hugo, E. J. Lowe, J. P. Marsh, Jr., and R. J. Pfeiffer, *J. Org. Chem.*, **28**, 857 (1963).
- (9) Westinghouse tungsten-halogen quartz lamp, 120 V, 500 W, No. 500 Q/LC, run at 50 V.
- (10) R. Feulgon, *Ber.*, **54**, 360 (1921).
- (11) All mass spectra were determined on a CEC MS 491-21 or AEI MS-9 mass spectrometer; all nmr spectra were run on a Varian T-60 instrument; ir spectra were recorded using a Perkin-Elmer 700 spectrometer.
- (12) G. B. Quistad, unpublished observation, this laboratory.
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