Pyrrole Photo-oxidation. The Direct Formation of Maleimides

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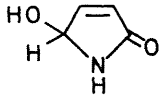
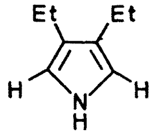
Summary Photo-oxidation of 3,4-diethylpyrrole in methanol gives mainly diethylmaleimide and 3,4-diethyl-5-methoxy-Δ^3-pyrrolin-2-one, photolysis of pyrrole under similar conditions gives mainly 5-methoxy-Δ^3-pyrrolin-2-one with a low yield of maleimide, but in aqueous solution only 5-hydroxy-Δ^3-pyrrolin-2-one and no maleimide is formed.

ALTHOUGH early studies on the photo-oxidation of pyrrole gave principally tarry products, de Mayo and Reid[1] isolated the white, crystalline 5-hydroxy-Δ^3-pyrrolin-2-one (**1**)[2] from photo-oxygenation of a dilute aqueous solution of pyrrole. Other work on pyrrole photo-oxidation has centred mainly on various phenyl substituted pyrroles.[3] No work on alkylated pyrrole photo-oxidation has appeared, but there has been a report on the oxygenation of 2,4-dimethylpyrrole in the absence of light.[4]

In our work on the singlet oxygen ($^1O_2$) sensitised photolysis of various alkylated pyrroles we investigated the reaction of 3,4-diethylpyrrole (**2**).[5] A dilute (0.1—0.2% w/v) methanolic solution of (**2**) containing 3 mg% of rose bengal ($^1O_2$ sensitiser) was photolysed† for 6 h while a slow stream of oxygen was bubbled through the reaction vessel. Methanol was evaporated from the photolysate *in vacuo* at room temperature, column chromatography on silica gel then gave ($CHCl_3$ fraction) diethylmaleimide (**3**) m.p. 68—70° (34%). The structure of (**3**) was confirmed by comparison with literature properties: m.p. 68°,[6] mass spectrum ‡ *m/e* (relative intensity) 153 (M^+) (52%), 138 (67), 110 (21), and 67 (49), n.m.r. spectrum δ (CCl_4) 1.17 (6H, t, *J* 7 Hz, 2 × Me), 2.44 and (4H, q, *J* 7 Hz, 2 × CH_2) p.p.m.; i.r. spectrum ν_{max} (CCl_4) 3250 (N–H) and 1710 cm^{-1} (C=O). A second product from the $CHCl_3$–EtOAc fractions was the expected 5-methoxypyrrolinone (**4**), an oil (33%) whose identity was established by its mass spectrum *m/e* (relative intensity) 169 (M^+) (65%), 154 (15), 140 (100) and 138 (82) and n.m.r. spectrum δ (CCl_4) 1.05 (3H, t, *J* 8 Hz, Me), 1.12 (3H, t, *J* 8 Hz), 2.30 4H, m, 2 × CH_2), 3.24 (3H, s, OMe), and 5.26 (1H, s, CH) p.p.m. The remaining tan, highly polar, and as yet unidentified photolysis products (28%) were eluted in methanol.


(**1**)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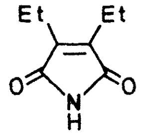
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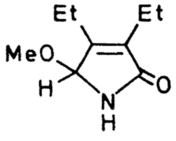
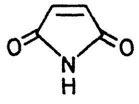
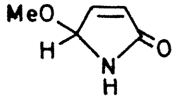

(**4**)


(**5**)


(**6**)

The formation of methoxy-compound (**4**) was expected from the work of de Mayo and Reid[1] on pyrrole, however, the surprising direct formation of an imide (**3**) has not yet been observed. We have therefore reinvestigated the earlier[1,2] photolyses of pyrrole in water and methanol with the expectation that maleimide (**5**) might be formed along with the known hydroxy-lactam (**1**) (H_2O solvent) but might remain undetected or that (**5**) should be formed along with methoxy-lactam (**6**) (in MeOH) in the event of an unusual solvent effect. The results are in the Table. In no instance could we detect any formation of maleimide (**5**) during the photo-oxidation of pyrrole in water, however, a small amount of (**5**) [m.p. 91—92.5° (lit.,[7] 93°), δ (CD_3OD) 6.67 p.p.m. (s, =C–H), i.r. spectrum identical with published spectrum[8]] was formed in MeOH along with the unreported methoxy-lactam (**6**). The structure of (**6**) was established from its mass spectrum *m/e* (relative intensity) 113 (M^+) (24%) and 82 (M-OCH_3) (100), and n.m.r. spectrum δ [$(CD_3)_2SO$] 3.19 (3H, s, OMe), 5.36 (1H, s, CH), 6.08 (1H, d, =C–H), and 7.02 (1H, d, =C–H, fine splitting) p.p.m.

TABLE

Partial product analysis after photo-oxidation of pyrrole

Solvent	Time of irradiation (in h)	Percent (w/v) pyrrole photolysed	Products isolated Maleimide (**5**)	 Methoxy-lactam (**6**) (%)	 Hydroxy-lactam (**1**) (%)
MeOH	0.75	0.1	1	13	0
MeOH	2.0	0.1	2	16	0
MeOH	4.0	0.1	3	14	0
H_2O	0.75	0.1	0	0	28
H_2O	4.0	0.1	0(0)^b	0	31(33%)^b

[a] Isolated by column chromatography and p.l.c. on silica gel. [b] The photolysis was repeated: in one work-up the water was lyophilised, in a second it was removed on a flash evaporator at 45—50 °C.

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† Colortran tungsten-halogen quartz lamp, 120 V, 1000 W, run at 50 V.

‡ All mass spectra were determined on a AEI MS-9 mass spectrometer, all n.m.r. spectra were run on a Varian T-60 instrument, i.r. spectra were recorded using a Perkin-Elmer 421 or 700 spectrometer.

In order to test the surmise that (**5**) may be formed and photo-destroyed at comparable rates, we irradiated a 0·03% (w/v) methanolic solution of (**5**) for 4 h under the usual conditions and recovered 26% of maleimide; the remainder was a tan mixture similar to the highly polar residue from all our pyrrole oxidations in methanol after removal of (**5**) and (**6**). We suggest therefore that maleimide is continuously formed and rapidly destroyed when the β-positions are unsubstituted (**5**), but that β-alkyl groups decrease the rate of photo-destruction of the imide (**3**) sufficiently to allow its build-up during the reaction.[9] No methoxy-lactam (**6**) was detected, and therefore compounds (**1**) and (**6**) are not formed from (**5**). They presumably arise from the suggested[1] pyrrole *endo*-peroxide intermediate.

The Table also shows that the percentage yield of (**1**) or (**6**) varies little during four hours of photo-oxidation but that the percentage of (**5**), when it is formed, increases with increased photolysis time. Moreover, a solvent dependence is also reflected in the yields of the equivalent substances (**1**) and (**6**). The mechanistic details of these reactions and the structures of the highly polar products are currently under investigation in our laboratory.

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[1] P. De Mayo and S. T. Reid, *Chem. and Ind.*, 1962, 1576.

[2] This substance had been isolated earlier, but its structure was undetermined. F. Bernheim and J. Morgan, *Nature*, 1939, **144**, 290.

[3] H. H. Wasserman and A. Liberles, *J. Amer. Chem. Soc.*, 1960, **82**, 2086; H. H. Wasserman and A. H. Miller, *Chem. Comm.*, 1969, 199; G. Rio, A. Ranjon, O. Pouchet, and M.-J. Scholl, *Bull. Soc. chim. France*, 1969, 1667; R. W. Franck and J. Auerbach, *J. Org. Chem.*, 1971, **36**, 31.

[4] E. Höft, A. R. Katritzky, and M. R. Nesbit, *Tetrahedron Letters*, 1968, 2028; 1967, 3041.

[5] H. W. Whitlock and R. Hanauer, *J. Org. Chem.*, 1968, **33**, 2169.

[6] H. Fischer and H. Orth, 'Die Chemie des Pyrrols,' vol. 1, Akademische Verlagsgesellschaft, M.B.H., Leipzig, 1934, p. 398.

[7] Ref. 10, page 396.

[8] Sadtler Standard Spectra, Sadtler Research Laboratories, Inc., Philadelphia, 1958, Spectrum no. 13219.

[9] The reactivity of maleimide toward reaction with sulphydryl groups is markedly decreased by two (or even one) β-substituents. M. Whitehouse, G. B. Quistad, and D. A. Lightner, unpublished work.