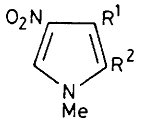
Unusual Conditions for *cine*-Substitution in the Pyrrole Ring: Isolation of a Pyrroline as an Intermediate

By Paolo Mencarelli and Franco Stegel*
(*Centro di Studio sui Meccanismi di Reazione del Consiglio Nazionale delle Ricerche, c/o Istituto di Chimica Organica, Università di Roma,* 00185 *Rome, Italy*)

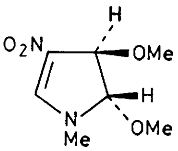
Summary 1-Methyl-3,4-dinitropyrrole (**1**) reacts with methoxide in methanol to yield a 2-pyrroline (**2**); the regiospecific acid-promoted decomposition of (**2**) yields 2-methoxy-1-methyl-4-nitropyrrole (**3**) formally the product of *cine*-substitution of (**1**).

As part of our work on the reactions of pyrrole derivatives with nucleophiles,[1,2] we report now the unusual formation of a pyrroline upon reaction of 1-methyl-3,4-dinitropyrrole[3] (**1**) with methoxide ion in methanol and the acid-promoted decomposition of the pyrroline itself. We wished to verify whether a 3,4-dinitropyrrole behaves similarly to such molecules as 3,4-dinitrothiophen[4] and 2,3-dinitronaphthalene,[5,6] where the nitro groups are present in vicinal, but hardly conjugated positions. These molecules are more likely to undergo *cine*-substitutions rather than direct replacements with nucleophiles.

A methanolic solution of (**1**) (0·02 M) was refluxed with 1 equiv. of sodium methoxide until disappearance of the substrate (t.l.c. analysis; 1·5—2 h). The residue following evaporation was a mixture of $NaNO_2$ and an organic product; the latter was extracted with warm hexane, purified from tars and traces of a yellow by-product by chromatography on silica gel with ethyl acetate, and identified as *trans*-4,5-dimethoxy-1-methyl-3-nitro-2-pyrroline (**2**) [m.p. 57—58·5 °C; M^+, *m/e* 188; n.m.r. ($CDCl_3$): δ 3·13 (s, 3H), 3·38 (s, 3H), 3·53 (s, 3H), 4·72 (br. d, 1H, *J* 1·2 Hz), 4·81 (d, 1H, *J* 1·2 Hz), and 7·87 (s, 1H); λ_{max} (MeOH):[7] 366 nm (log ε 4·5); yield 70%].



(1) $R^1 = NO_2, R^2 = H$
(3) $R^1 = H, R^2 = OMe$



(2)

Treatment of a methanolic solution of (**2**) (1·5 × 10^{-2} M) for *ca.* 4 h with 1 equiv. of CF_3CO_2H at room temperature, led to the product (**3**), which was isolated by evaporation, purified from small amounts of tars by chromatography on silica gel with benzene, crystallized from hexane (m.p. 89—90 °C), and readily identified as a methoxy-nitro-1-methylpyrrole from its mass (M^+ at *m/e* 156) and n.m.r. spectra [$(CD_3)_2SO$: δ 3·47 (s, 3H), 3·84 (s, 3H), 5·94 (d, 1H, *J* 2·4 Hz), and 7·64 (d, 1H, *J* 2·4 Hz); yield 90%]. Compound (**1**) could be converted directly into (**3**) without isolating (**2**) by adding CF_3CO_2H when the reaction with methoxide was complete.

The coupling constants reported for the ring positions of pyrrole derivatives[8] did not allow an unequivocal structure assignment for (**3**). The small coupling ($J \leqslant 0{\cdot}4$ Hz) between the N–Me signal and only one of the pyrrole ring signals, at δ 7·64, indicated that it was not a 3,4-substituted pyrrole. (These signals were in fact slightly broadened). Conclusive evidence that (**3**) was 1-methyl-2-methoxy-4-nitropyrrole, formally the product of a *cine*-substitution, was obtained by the nuclear Overhauser effect (n.O.e.) in $(CD_3)_2SO$: irradiation at the frequency of the N–Me signal increased the area of the weakly coupled downfield signal at δ 7·64 (+24%), leaving unchanged the resonance at δ 5·94; moreover, irradiation of the signal at δ 3·84 (OMe) increased the upfield aromatic signal at δ 5·94 (+34%), without affecting the other aromatic signal.

The formation of the pyrroline was accelerated by an excess of methoxide: this fact is in accordance with the hypothesis that the slow step may be the addition of the nucleophile. However, under these conditions, (**2**) was not converted into (**3**). Therefore (**3**) cannot be an intermediate in the formation of (**2**) from (**1**). The absence of *cine*-substitution in a basic medium, as opposed to the ready acid-promoted formation of (**3**), indicates that the base-catalysed addition–elimination mechanism envisaged for the formation of 2-arylthio-4-nitrothiophens from 3,4-dinitrothiophen[4] is unlikely to be operating in this reaction.

We thank Professor G. Illuminati for helpful discussions and Dr. Anna Maria Giuliani for her assistance with the n.O.e. measurements.

(*Received, 27th February* 1978; *Com.* 202.)

[1] F. De Santis and F. Stegel, *Tetrahedron Letters*, 1974, 1079.
[2] P. Mencarelli and F. Stegel, *J. Org. Chem.*, 1977, **42**, 3550.
[3] S. S. Novikov and V. M. Belikov, *Izvest. Akad. Nauk S.S.S.R., Ser. Khim.*, 1959, 1098.
[4] C. Dell'Erba, D. Spinelli, and G. Leandri, *Gazzetta*, 1969, **99**, 535.
[5] D. C. Morrison, *J. Org. Chem.*, 1962, **27**, 296.
[6] G. Guanti, S. Thea, and C. Dell'Erba, *Tetrahedron Letters*, 1976, 471.
[7] Maxima at *ca.* 360 nm (EtOH) have been reported for nitroenamines: L. Marchetti and V. Passalacqua, *Ann. Chim.* (*Rome*), 1967, **57**, 1266.
[8] R. A. Jones and G. P. Bean, 'The Chemistry of Pyrroles,' Academic Press, London, 1977, p. 472.