# Oxygenation of Pyrazines and Pyrimidines

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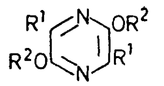
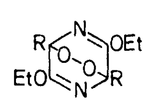
*Summary* A variety of substituted pyrazines and pyrimidines react with singlet oxygen to form *endo*-peroxides.

ALTHOUGH singlet oxygen is known to react with a variety of heterocyclic substrates, examples of additions to nitrogen containing systems are largely limited to 5-membered ring systems such as the pyrroles and indoles.[1] We report that singlet oxygen also adds to a range of substituted pyrazines and pyrimidines.

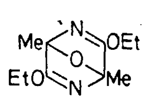
Irradiation with visible light, of an oxygenated solution of 3,6-dibenzyl-2,5-diethoxypyrazine[2] (**1**) in dichloromethane, with Methylene Blue as sensitiser, afforded a quantitative yield of the stable peroxide (**2**), as a colourless oil.† A slow oxidation of the pyrazine also occurred in the absence of the Methylene Blue, producing low yields of the peroxide and suggesting that the substrate can act as its own sensitiser. A photochemical process is required since no oxidation took place in the dark.



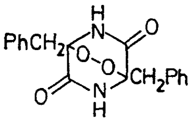
(**1**); $R^1 = PhCH_2$, $R^2 = Et$
(**3**); $R^1 = PhCH_2$, $R^2 = H$
(**5**); $R^1 = Me$, $R^2 = Et$



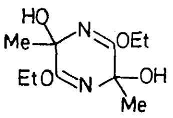
(**2**); $R = PhCH_2$
(**6**); $R = Me$



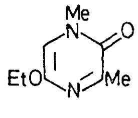
(**7**)



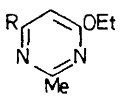
(**4**)



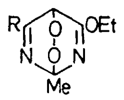
(**8**)



(**9**)



(**10**); $R = Me$
(**11**); $R = OEt$



(**12**); $R = Me$
(**13**); $R = OEt$

In a similar manner the dihydroxypyrazine (**3**) also produced the corresponding peroxide (**4**). In this case Fluorescein on a polymer support was an effective sensitiser.[3] The dimethylpyrazine (**5**) reacted likewise to give the relatively stable peroxide (**6**), which was unaffected, for example, by 0·1 N HCl at room temperature for several days. Reduction with triphenylphosphine resulted in abstraction of one oxygen atom to produce an oxide, formulated as the bicyclic product (**7**). Treatment of the peroxide (**6**) with sodium borohydride produced the diol (**8**).

These oxidations are reminiscent of the behaviour of the pyrazinone (**9**), which is known to react directly with oxygen.[4] The chemical properties of the peroxides bear comparison with those of the related disulphide-bridged dioxopiperazines, which occur in natural products of the gliotoxin and sporidesmin families.[5] Furthermore, since alkoxypyrazines are widespread flavouring constituents,[6] such oxidations may occur in nature.

These singlet oxygenations are not restricted to the pyrazines. Pyrimidine derivatives also undergo oxygenation. Thus the pyrimidines (**10**) and (**11**) can be photooxygenated to their corresponding unstable, but crystalline, peroxides (**12**) and (**13**).

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† All new compounds have been fully characterised by microanalytical and/or spectroscopic methods.

[1] *Cf.* K. Gollnick and G. O. Schenck, '1,4-Cycloaddition Reactions,' ed. J. Hamer, Academic Press, New York, 1967.
[2] K. W. Blake, A. E. A. Porter, and P. G. Sammes, *J.C.S. Perkin I*, 1972, 2494.
[3] A. P. Schaap, A. L. Thayer, E. C. Blossey, and D. C. Neckers, *J. Amer. Chem. Soc.*, 1975, **97**, 3741.
[4] P. J. Machin, A. E. A. Porter, and P. G. Sammes, *J.C.S. Perkin I*, 1973, 404.
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