Peroxidic Intermediates in the Photosensitized Oxidation of 2-Methyl-4,5-diphenylimidazole

By M. LILIANA GRAZIANO, M. ROSARIA IESCE, and RACHELE SCARPATI*
(*Istituto di Chimica Organica e Biologica, Università di Napoli,* 80134 *Napoli, Italy*)

Summary Photosensitized oxygenation of 2-methyl-4,5-diphenylimidazole (**1**) at −15 °C gives 2-hydroperoxy-2-methyl-4,5-diphenyl-2*H*-imidazole (**2**) which isomerizes into 4-hydroperoxy-2-methyl-4,5-diphenyl-4*H*-imidazole (**4**), probably *via* the *endo*-peroxide (**7**); compound (**2**) and its deoxygenation product (**3**) are the first 2-hydroperoxy- and 2-hydroxy-2*H*-imidazole to be reported.

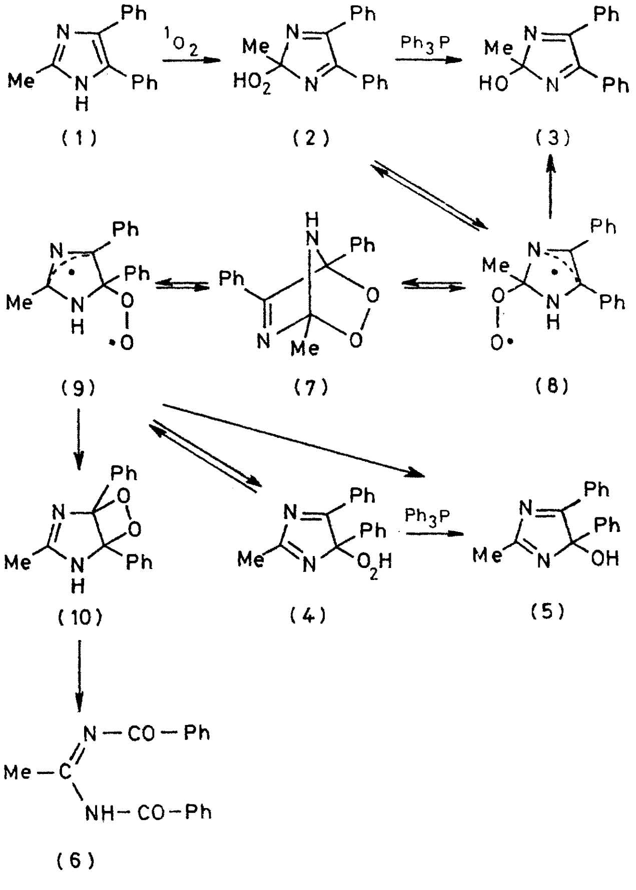
ALTHOUGH the loss of biological activity of some enzymes by dye-sensitized photo-oxidation has been correlated with the disappearance of histidine residues,[1] uncertainty remains as to the mode of the oxidative destruction of imidazole rings by singlet oxygen. It has been reported that sensitized photo-oxidation of 2,4,5-triphenylimidazole at 18 °C leads to *NN′*-dibenzoylbenzamidine *via* 4-hydroperoxy-2,4,5-triphenyl-4*H*-imidazole.[2,3] Some other imidazoles yielded compounds which it was suggested were formed *via* dioxetans[4–6] or, sometimes, *via endo*-peroxides.[4]

We report here results for the Methylene Blue sensitized photo-oxidation at −15 °C in anhydrous chloroform of 2-methyl-4,5-diphenylimidazole (**1**) which gave 2-hydroperoxy-2-methyl-4,5-diphenyl-2*H*-imidazole (**2**).† The hydroperoxide (**2**) was reduced by Ph_3P into 2-hydroxy-2-methyl-4,5-diphenyl-2*H*-imidazole (**3**).‡ Both (**2**) and (**3**) gave benzil and acetamide on acid hydrolysis.

The hydroperoxide (**2**) is stable only at temperatures below −15 °C. At room temperature, in the absence of solvent, under strictly anhydrous conditions, after 48 h it was partly transformed into 4-hydroperoxy-2-methyl-4,5-diphenyl-4*H*-imidazole (**4**) [δ($CDCl_3$) 2·35 (s, 3H, Me), 7·30—8·35 (m, Ph), 11·95 br (s, 1H, OOH)]. The i.r. spectrum [ν1635 (C=N) cm^{-1}, no NH absorption], and determination of the active oxygen content of this mixture which was shown by ^1H n.m.r. spectroscopy to contain only (**2**) and (**4**) in approximately equal quantities, confirmed the structure assignment. Furthermore, the above mixture was reduced by Ph_3P into (**3**) and 4-hydroxy-2-methyl-4,5-diphenyl-4*H*-imidazole (**5**) [δ($CDCl_3$) 2·50 (s, Me)]. Both (**4**) and (**5**) were sensitive to hydrolysis[7] and could not be isolated in pure form.§

When the hydroperoxide (**2**) was kept for 25 days, the ^1H n.m.r. spectrum showed, in addition to the signals of (**2**) and (**4**), three new Me singlets. Two of these are clearly attributable to (**3**) and (**5**), deriving from the deoxygenation of (**2**) and (**4**) respectively, as observed in similar cases.[8] The third singlet at δ 2·80 is due to *NN′*-dibenzoylacetamidine (**6**) which readily undergoes hydrolysis into acetylbenzamide and benzamide.[7]

Isomerization of (**2**) to (**4**) is very similar to the allylic hydroperoxide rearrangement previously observed.[9] In this case the high hydrolytic reactivity of the compounds (**4**), (**5**), and (**6**) makes a detailed study very difficult. However, a possible mechanism which takes into account all the available data is shown in the Scheme. The proposed formation of the *endo*-peroxide (**7**) is supported by the thermolysis of (**2**) at 60 °C which leads to benzonitrile and



SCHEME

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† Yield 95%, 5% of (**4**) was present; m.p. 94 °C (decomp.); ν($CHCl_3$) 2820 (OOH· · · N) (ref. 2 and K. Maeda and T. Hayashi, *Bull. Chem. Soc. Japan*, 1971, **44**, 533) and 1610 (C=N), 860 (–O–O–) cm^{-1}; ^1H n.m.r. δ ($CDCl_3$) 1·87 (s, 3H, Me), 7·30—7·60 (m, 10H, 2Ph), and 11·85 br (s, 1H, OOH); satisfactory active oxygen determination was obtained.

‡ Yield 95%; m.p. 160—162 °C; ν($CHCl_3$) 3600 (OH) and 1610 (C=N) cm^{-1}; ^1H n.m.r. δ ($CDCl_3$) 1·80 (s, 3H, Me), 6·10 (s, 1H, OH), and 7·35—7·65 (m, 10H, 2Ph); ^{13}C n.m.r. ($CDCl_3$) δ (p.p.m. from Me_4Si) 24·6 (q, Me), 119·1 (s, C-4 and C-5), 128·5 and 129·3 (2 × d, C-2, C-6, and C-3, C-5 of Ph groups), 131·1 (d, C-4 of Ph groups), 131·5 (s, C-1 of Ph groups), and 165·3 (s, C-2); satisfactory elemental analyses were obtained.

§ On hydrolysis a complex mixture was obtained.

acetylbenzamide (i.r. and g.l.c.). The equilibrium between *endo*-peroxides, like (**7**), and diradicals, like (**8**) or (**9**), was postulated in the oxidation with both singlet and triplet oxygen of alkoxyoxazoles.[10] A path involving the corresponding zwitterions, instead of the diradicals (**8**) and (**9**), is an alternative mode of reaction. Zwitterion formation should be induced by the basicity of the imidazoles.

Compounds (**2**) and (**3**) represent the first examples of 2-hydroperoxy- and 2-hydroxy-2*H*-imidazole.

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[1] E. W. Westhead in 'Methods in Enzymology,' Vol. XXV, eds. C. H. W. Hirs and S. N. Timasheff, Academic Press, London, 1972, p. 401.

[2] J. Sonnenberg and D. M. White, *J. Amer. Chem. Soc.*, 1964, **86**, 5685.

[3] E. H. White and M. J. C. Harding, *J. Amer. Chem. Soc.*, 1964 **86**, 5686; *Photochem. and Photobiol.*, 1965, **4**, 1129 obtained similar results in the absence of a photosensitizer.

[4] H. H. Wasserman, K. Stiller, and M. B. Floyd, *Tetrahedron Letters*, 1968, 3277.

[5] A. Ranjon and M. C. Dufraisse, *Compt. rend.*, 1968, **267**, 1822.

[6] H. H. Wasserman and I. Saito, *J. Amer. Chem. Soc.*, 1975, **97**, 905.

[7] R. H. DeWolfe in 'The Chemistry of Amidines and Imidates,' ed. S. Patai, Wiley-Interscience, London, 1975, p. 349.

[8] M. Nakagawa, H. Okajima, and T. Hino, *J. Amer. Chem. Soc.*, 1977, **99**, 4424.

[9] G. O. Schenck, O. A. Neumuller, and W. Eisfeld, *Annalen*, 1958, **618**, 202; W. F. Brill, *J. Amer. Chem. Soc.*, 1965, **87**, 3286.

[10] M. L. Graziano, A. Carotenuto, M. R. Iesce, and R. Scarpati, *J. Heterocyclic Chem.*, 1977, **14**, 1215.