Tetrahedron Letters,Vol.27,No.46,pp 5637-5640,1986
Printed in Great Britain

0040-4039/86 $3.00 + .00
Pergamon Journals Ltd.

NEW AND STABLE ENDOPEROXIDE FROM THE PTERIDIN-2,4,7-TRIONE AND SINGLET OXYGEN

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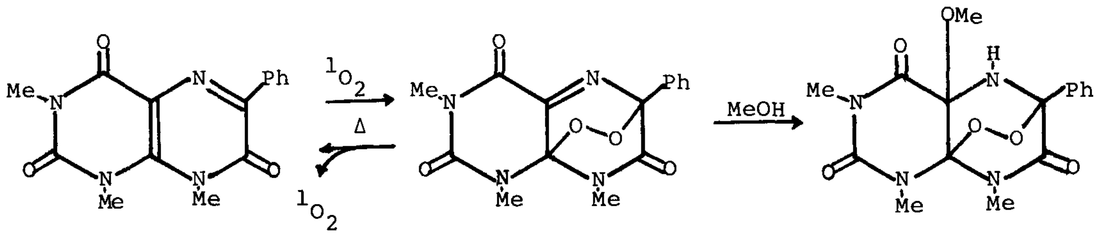
Summary: 1,3,8-Trimethyl-6-phenylpteridin-2,4,7-trione (1) reacted with singlet oxygen to give the pteridin-2,4,7-trione 6,8'-endoperoxide (2), which on warming generates singlet oxygen. Generation of singlet oxygen from thermolysis of the endoperoxide (2) was confirmed by trapping experiments using typical singlet oxygen acceptors.

Singlet oxygen is known to react with different types of organic compounds, giving rise to a variety of oxygenated products.[1] However, the reactions of singlet oxygen with heterocyclic substances containing nitrogen atom are largely limited to five-membered ring systems such as pyrroles, indoles, and imidazoles.[2] Markham and Sammes reported that six-membered heterocycles containing nitrogen atoms such as pyrazines and pyrimidines reacted with singlet oxygen to form endoperoxides.[3] We recently reported that dye-sensitized photooxygenation of pyrazin-2-ones gave stable pyrazin-2-one 3,6-endoperoxides.[4] Similar 1,4-dipolar cycloaddition of singlet oxygen to pyrimidinium-4-olates was reported by Gotthardt and Schenk.[5] Furthermore, dye-sensitized photooxygenation of uracil derivatives in liquid ammonia at -75 °C has been reported to give an unstable peroxy intermediate, which on warming fragments to give a complex mixture.[6] We report here that the pteridin-2,4,7-trione (1), which possesses both uracil and pyrazinone chromophores, can absorb singlet oxygen smoothly to produce the stable endoperoxide (2), which on warming reverts to 1 with the liberation of singlet oxygen.[7]

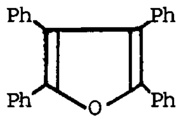
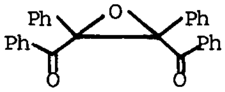
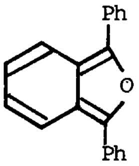
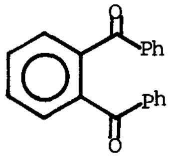
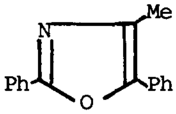
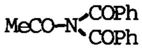
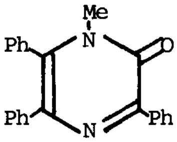
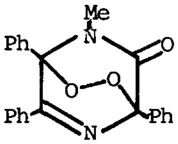
Irradiation of an oxygenated solution of 1,3,8-trimethyl-6-phenylpteridin-2,4,7-trione (1) in dichloromethane in the presence of rose bengal as a sensitizer with visible light at room temperature for 2 h gave the pteridin-2,4,7-trione 6,8'-endoperoxide (2),[8] m.p. 278-279 °C; IR(KBr) 1735, 1715, and 1680 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 3.18 (s, 3H), 3.28 (s, 3H), 3.37 (s, 3H), 7.56-7.73 (m, 3H), and 7.88-7.99 (m, 2H); ^{13}C-NMR($CDCl_3$) δ 28.5 (q), 29.2 (q), 31.9 (q), 91.6 (s), 93.3 (s), 128.6 (d), 128.9 (s), 130.9 (d), 159.1 (s), 154.6 (s), 161.4 (s), and 166.7 (s), in 79% isolated yield. On the contrary, when an oxygenated solution of 1 in methanol in the presence of rose bengal was irradiated under the same conditions, the dihydro-endoperoxide (3), which showed incorporation of one molecule of methanol, was obtained in 83% isolated yield. The dihydro-endoperoxide (3) was also produced in almost quantitative yield when the endoperoxide (2) was kept in methanol-dichloromethane at room temperature. An interesting thermal reaction was observed in the pteridin-2,4,7-trione 6,8'-endoperoxide (2). Heating of 2 to reflux in dichloromethane produced the parent pteridin-2,4,7-trione (1) in almost quantitative yield with the concomitant formation of singlet oxygen.



(1) (2) (3)

The formation of singlet oxygen was confirmed by the reaction with a variety of known singlet oxygen acceptors.[7a-c,9] For example, a solution of the endoperoxide (2, 2 mmole) and tetraphenylfuran (4, 1 mmole) in dichloromethane was refluxed for 4 h under argon to give cis-dibenzoylstilbene oxide (5)[9] and the pteridin-2,4,7-trione (1) in 84% and quantitative yields, respectively. When a singlet oxygen quencher, 1,4-diazabicyclo[2.2.2]octane (DABCO), was added to the reaction system, the yield of 5 (26%) was drastically reduced. In contrast, addition of a free radical inhibitor, 2,6-di-tert-butylphenol, did not effect the yield of 5 (74%). These results undoubtedly indicate that the reactive species generated from the endoperoxide (2) is singlet oxygen. Similarly, treatment of 2 with 1,3-diphenylisobenzofuran (6), 2,5-diphenyl-4-methyloxazole (8), and 1-methyl-3,5,6-triphenylpyrazin-2(1H)-one (10) gave o-dibenzoylbenzene (7),[7b] N-acetyldibenzamide (9),[10] and the pyrazin-2(1H)-one 3,6-endoperoxide (11).[11] The results were summarized in Table. In every case the reactions using the pteridin-2,4,7-trione 6,8'-endoperoxide (2) were exactly parallel, with comparable yields, to the results obtained by dye-sensitized photooxygenations. Thus present method provides a synthetically useful method for carrying out singlet oxygenation reactions,[9] since the pteridin-2,4,7-trione 6,8'-endoperoxide (2) is stable in a solid form and can be stored indefinitely at room temperature.

Table. Decomposition of the Pteridin-2,4,7-trione 6,8'-endoperoxide (2) with Acceptors

Acceptor	Mole ratio of (2) to acceptor	Product (yield, %)[a]		Photosensitized oxygenation[b] (yield, %)
 (4)	1 : 1	 (5)	(82)	(57)[c]
	2 : 1		(84)	
	5 : 1		(73)	
	10 : 1		(77)	
 (6)	1 : 1	 (7)	(88)	(84)[d]
	5 : 1		(85)	
	10 : 1		(81)	
 (8)	1 : 1	 $\mathrm{MeCO{-}N}\genfrac{}{}{0pt}{}{\mathrm{COPh}}{\mathrm{COPh}}$ (9)	(58)	(90)[e]
	10 : 1		(84)	
 (10)	1 : 1	 (11)	(82)	(96)[f]
	10 : 1		(86)	

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[a] The yield was based on used acceptor. [b] Photosensitized oxygenation was carried out in dichloromethane using methylene blue as a sensitizer under oxygen. [c] Reference 9. [d] J.R. Scheffer and M.D. Ouchi, Tetrahedron Lett., 1970, 223. [e] Reference 10. [f] Reference 11.

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8 All new compounds gave satisfactory spectral and microanalytical data. The dihydro-endoperoxide (3): m.p. 169-171 °C; IR(KBr) 3320, 3290, 1715, and 1675 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 3.15 (s, 3H), 3.18 (s, 3H), 3.24 (s, 3H), 3.25 (s, 3H), 4.56 (br s, 1H), and 7.38-7.58 (m, 5H); ^{13}C-NMR($CDCl_3$) δ 28.6 (q), 32.4 (q), 33.2 (q), 49.6 (q), 81.8 (s), 89.8 (s), 97.3 (s), 126.6 (d), 128.2 (d), 130.0 (d), 130.6 (s), 152.2 (s), 164.8 (s), and 167.4 (s).

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(Received in Japan 10 July 1986)